Second Edition

Integrated Clinical Orthodontics

Edited by

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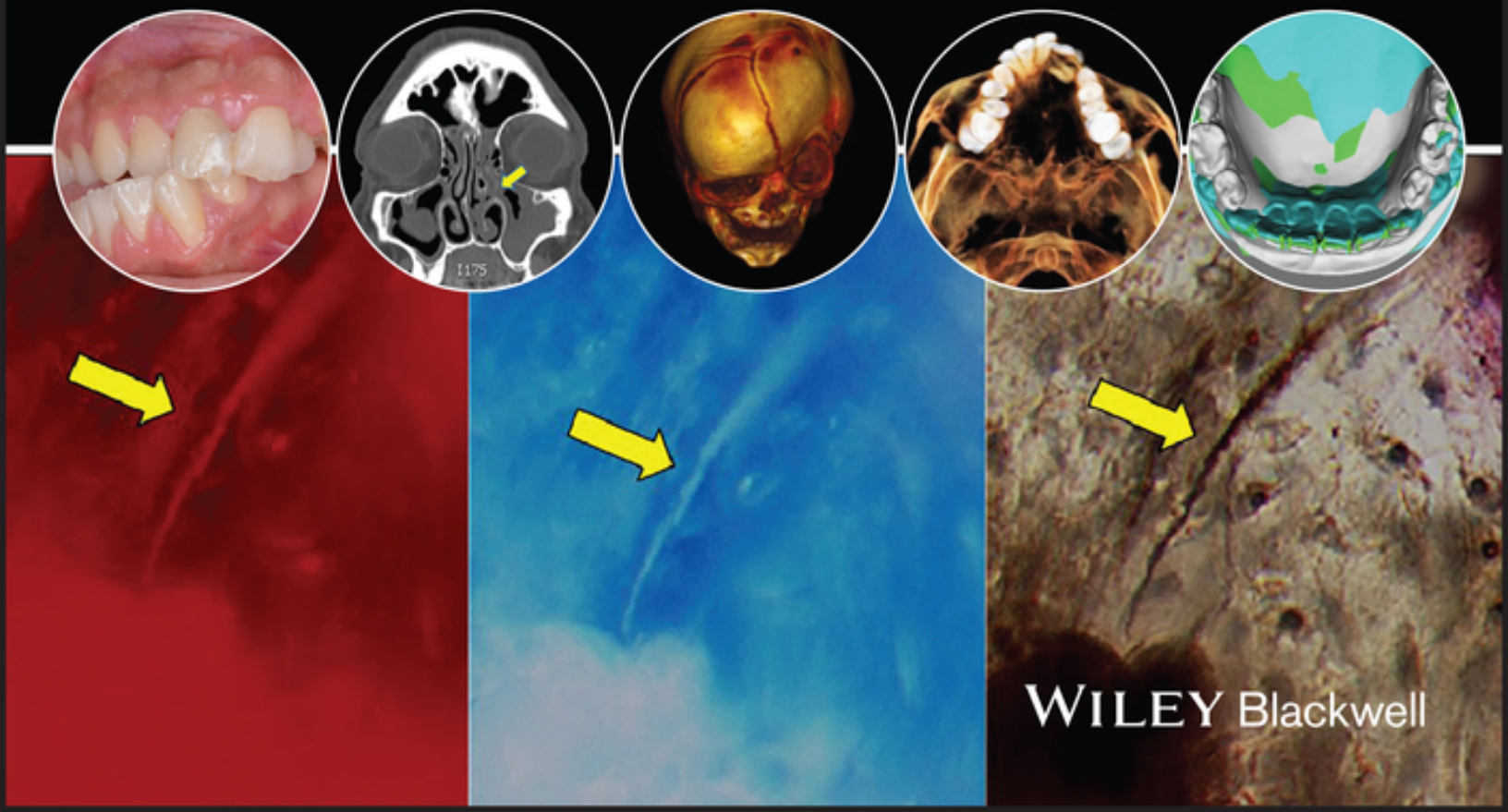

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Integrated Clinical Orthodontics

SECOND EDITION

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Dedication to Professor Ze'ev Davidovitch

Ze'ev Davidovitch was born in the British Mandate of Palestine on September 28, 1935. He grew up in Tel Aviv. Following high school, Ze'ev served in the Israeli Defense Forces from 1953 to 1956. As a lover of art, after his military service Ze'ev planned to enroll in the Bezalel Academy of Art and Design in Jerusalem; however, his father interceded and convinced him to apply his artistic skills to the practice of dentistry. Ze'ev studied at the Hebrew University in Jerusalem where he excelled, earning the Massler Award for his doctoral thesis. After graduating in 1961 with a DMD, Ze'ev was enticed to continue as a junior faculty member in the Department of Oral Diagnosis and Oral Medicine at Hadassah Medical Center.

These experiences nurtured Ze'ev's interest in the specialty of orthodontics, and he was accepted to study at the postgraduate program at Harvard-Forsyth in Boston, Massachusetts, from 1963 to 1966. At Harvard, Ze'ev was introduced to the vast field of research, which captured his interests and satisfied his active and inquisitive mind. There he was immersed in cutting-edge techniques and research and he developed a deep desire to ask the questions that, when answered, would impact orthodontics and beyond. During his residency at Harvard, Ze'ev performed histological studies and published his first scientific paper.

In 1966, Ze'ev returned to Hebrew University to the newly inaugurated Department of Orthodontics, marking the start of his full-time academic career; but by 1969, he realized that he would need to pursue his research dreams elsewhere. Encouragement from his teacher and mentor at Harvard, Professor Coenraad F. A. Moorrees, got him recruited to the faculty at the University of Nebraska. This was followed by an appointment to the University of Pennsylvania from 1970 to 1984, where he was the Director of Orthodontic Research for over 10 years. There he delved deeply and published widely on the biology of tooth movement and patented a medical device with his co-workers as a result of these research efforts.

From 1984 to 1993, Ze'ev served as the Chairman of the Department of Orthodontics at The Ohio State University in Columbus. In addition to developing and operating one of the premier orthodontics laboratories in the US, Ze'ev authored and published *The Ohio Bracer*, a quarterly departmental periodical detailing the activities at OSU, always including multiple satirical cartoons of his own design. In addition, he initiated and organized eight international conferences dedicated to the subjects of the biology of tooth movement, mechanisms of tooth eruption, root resorption, and implant replacement of teeth. These were all compiled as proceedings, containing hundreds of articles which Ze'ev co-edited.

In 1993, Ze'ev was beckoned back to Harvard and served as Chairman until 1998. There, he continued his research efforts and organizing of international conferences. He was also instrumental in building its alumni association, the Harvard Society for the Advancement of Orthodontics, which promoted The Coenraad Moorrees Lecture that has now evolved into a joint memorial symposium with the Forsyth Dental Infirmary.

From 1998 to 2000, Ze'ev joined the faculty at the University of Oklahoma, then until 2004 he was a clinical professor at Case Western Reserve in Cleveland, Ohio. From 2005 to 2010 he was a visiting professor at Nova University in Davie, Florida.

Throughout his research and academic career, Ze'ev's activities attracted many colleagues from multiple countries to his laboratories. His research on the biology of tooth movement also took him around the world as a keynote speaker at numerous prestigious scientific conferences. He always emphasized the need to engender the next generation of basic science researchers with the same spark that he received when he was a research fellow at Harvard-Forsyth. During his career, Ze'ev educated hundreds of orthodontic specialists, grounding their clinical skills in scientific knowledge.

Ze'ev earned multiple grants to support his research efforts from the National Institutes of Health (NIH), National Science Foundation, and private investors. He also served for many years in study groups at the NIH reviewing grant applications. In addition, he was a reviewer for leading orthodontics journals. Ze'ev published over 200

scientific papers in peer-reviewed journals, wrote chapters in multiple textbooks, and co-edited conference proceedings and three textbooks. He was a long-time member of the American Association of Orthodontists, the American Association for the Advancement of Science, and the International Association for Dental Research.

Along with his inquisitive mind, Ze'ev had a unique sense of humor that never abandoned him and that he used in every situation. He remained a talented artist throughout his life, finding self-expression in painting, drawing, and sculpting. He took pleasure in music of all genres, as well as cooking and studying history, but most of all he loved spending time with his family and friends.

For the past 20 plus years Ze'ev suffered from Parkinson's disease, which eventually limited his ability to speak intelligibly and disconnected him from the halls full of eager listeners he was accustomed to speaking to. Mounting physical limitations were not able to dampen his everlasting optimism or cause him any self-pity. With his patience, positivity, and sense of humor, Ze'ev continued to be involved in his profession. He remained intellectually engaged, starting and remaining as president of a medical device company called Rapid Orthodontics. By Ze'ev's side was Galia, his wife of 59 years. She supported him in his career and helped make his accomplishments possible. Galia's dedication during Ze'ev's lengthy battle with Parkinson's was the main reason that he was able to continue to contribute to his profession right up until his passing.

Ze'ev often was heard to espouse a pair of his guiding principles. First, that "the purpose of life is to make the world a better place" – his contributions as a husband, father, grandfather, educator, scientist, artist, and inventor, all pursued with devotion and good humor, have certainly been a service to humanity. Second, "that the time to rest is in the grave" – his tireless efforts marked a stalwart career that continues to ripple outward and around the world, but now it is his time to rest.

Ze'ev passed away peacefully on February 7, 2022, from Covid-19. He is survived by his wife, their four children, and seventeen grandchildren. Blessed be his memory.

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Preface to Second Edition

Orthodontics, from a technique-oriented profession, has evolved into a comprehensive specialty with a rapidly expanding scope, involving increased collaboration with experts from other disciplines. These interdisciplinary interactions provide the orthodontist with valuable information about individual patients, leading to modifications in diagnosis and treatment plans. Further, this approach has enabled orthodontists to carefully dissect, process and compare information across subject boundaries. Apart from the development of critical thinking, exposure to new ideas and frameworks evokes creativity leading to the development of innovative ideas.

Like many textbooks, the success of the first edition of 'Integrated Clinical Orthodontics' published in 2012, was accompanied by the realization that knowledge is subject to change. We understand that genuine wisdom stems from acknowledging that what we consider true today may appear absurd tomorrow. This second edition of 'Integrated Clinical Orthodontics' signifies a progression in this understanding. Our intention is for this book to serve as an extensive and current resource, offering comprehensive insights into orthodontic care within the context of related disciplines associated with our profession.

Just as in the first edition, we have chosen topics that clearly demonstrate the areas where orthodontists interact with experts from other fields, aiming to improve patient care. The new textbook provides a broad discussion of the basic and clinical sciences that are crucial to the understanding, diagnosis, and management of orthodontic patients. Nearly all existing chapters have been updated. To enhance its educational value, we have divided the book into five sections that reflect the areas where orthodontists, medical and dental specialists, biologists, geneticists, biomedical engineers, and other scientists intersect in modern orthodontics.

The inclusion of new chapters reflects the progress made in comprehensive orthodontics. This second edition features new chapters on endocrinological conditions, nutrition in orthodontics

practice, neuromuscular diseases, orthodontics for children with disabilities, artificial intelligence in orthodontic practice, and the seven pillars of professionalism, among others.

We extend our heartfelt thanks to the authors from a diversity of disciplines for their outstanding contributions to this book, sharing their knowledge and passion to make orthodontics an even better discipline, thereby making a difference for the patients. We would also like to express our sincere appreciation to those, who critically analyzed the first edition of the book and pointed out its shortcomings so that we could anticipate them in the second edition. We express our gratitude to our publisher, John Wiley and Sons, especially Susan Engelken, Loan Nguyen, Katherine King, Fraser Dart, Oliver Raj, Keerthana Baskaran, Pavithra Chandrasekharan, Anitha Jasmine Stanley, and our copyeditor Sally Osborn, whose expertise greatly assisted us in preparing this second edition.

The benefits of an integrated approach to orthodontic care have long been recognized. In 2016 the FDI World Dental Federation developed a new definition of oral health, emphasizing its multifaceted nature. According to the new definition, oral health encompasses various aspects such as speaking, smiling, smelling, tasting, touching, chewing, swallowing, and expressing emotions through facial expressions, with confidence, free from pain, discomfort, and diseases of the craniofacial complex (head, face, and oral cavity). Modern orthodontics aligns perfectly with this concept. Simultaneously, our understanding of the importance of evidence-based practice has grown significantly. We fully acknowledge that there is still a lack of evidence in many areas covered in this textbook. However, even in the absence of evidence, we must still provide treatment to our patients! We hope that this book inspires orthodontists and postgraduates to look beyond their own field, ultimately benefiting the patients they treat.

Vinod Krishnan
Anne Marie Kuijpers-Jagtman
Editors

Preface to First Edition

The subject of this book, Integrated Clinical Orthodontics, seemed initially to be a straightforward topic. After all, we know that we depend on each other, in all walks of life, not excluding orthodontics. Therefore, we thought that it would be helpful to try to compose a publication that would reflect clearly each area where orthodontists interact with experts in other medical specialties, in an effort to upgrade their services to their patients.

Each individual who needs, seeks, or receives orthodontic care, differs from every other individual, molecularly, functionally, and esthetically. This natural variability is reflected in the orthodontic clinic, defining the identity of the specialty whose experts could be beneficial to the orthodontist and the patient alike. Our goal has been to learn from people engaged in clinical research in different medical fields, about their experience and advice on interactions with orthodontists. These interactions stem from the simple fact that none of us knows everything, and whether we like it or not, we depend on the professional opinions of our colleagues in other specialties, whose knowledge can remedy the voids in our own.

In planning the contents of this book, we immediately realized that there are many fields of knowledge that can augment the diagnostic and therapeutic capabilities of the orthodontist. In fact, we were amazed at the large number of these specialties, clearly reflected in the number of chapters in this book, 25, each dedicated to a specialty whose members interact with orthodontists. This increasingly widening scope of orthodontics is enabled by the availability and relative ease of electronic communication, and the expanding new findings in medicine and dentistry. It becomes increasingly difficult to command all relevant information about emerging new and exciting fields, such as tissue engineering and stem cells, and becoming aware of ongoing progress in seemingly traditional fields, such as genetics, psychology, and material science. Interaction with others seems to offer the means to clarify and confirm the identity of clinical findings in the diagnostic phase, and elucidate the road

ahead, in terms of treatment plans and the choice of the most suitable mechanotherapy for the individual patient.

The concept emerging from this book is that orthodontics is not merely an exercise in wire bending, but rather a specialty leaning on many others. Interactions, whenever indicated, between the orthodontist and other medical specialists are a powerful tool on the way to excellence. In short, we would like to see each and every reader of this book to think like a healthcare professional and as a conscientious member of the dental profession who wishes to bring credit upon a high calling that has lifted itself from a questionable mechanical art to a most respected and esteemed health service to humankind.

We would like to extend our heartfelt thanks to all our contributing authors, who have generously shared their valuable knowledge and wisdom for the benefit of all those who are eager to learn about the advancements in ‘ science of orthodontics’. We were excited to read the manuscripts and are hopeful that the response of our esteemed readers will be the same too. Although the chapters are based on the contributors’ own work and experiences, all the information can be applied to similar settings across the world.

We would also like to express our sincere gratitude to all the staff at Wiley - Blackwell, Oxford, UK, especially Sophia Joyce, Nick Morgan, Catriona Cooper, Lucy Nash, and James Benefield, as well as Lotika Singha (copyeditor), and Anne Bassett (project manager) whose relentless efforts helped us to accomplish this laborious, but fulfilling, task.

Vinod Krishnan
Ze’ev Davidovitch
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Part I
Diagnosis, Psychology, and Genetics

1
The Increased Stature of Orthodontics

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Summary

Orthodontists treat patients with orofacial anomalies, including malocclusions, by applying mechanical forces to the crowns of teeth. These forces are transmitted to the tissues surrounding the roots of the teeth, enticing their cells to remodel these tissues, thereby enabling the teeth to move to new, preferred positions. Like any other tissues and organs in the human body, dental tissues and cells are controlled by the nervous, immune, vascular, and endocrine systems, as well as by factors such as psychological stress, nutrition, medications, and local and systemic diseases. Since the jaws are integral parts of the body, orthodontic diagnosis must include detailed information on any deviation from general health norms, and these data should be reflected in the treatment plan. Therefore, when specific pathologies are identified, an interaction with the appropriate healthcare provider who is treating the patient should occur, or a referral made to another specialist. The advice obtained from these experts can have a substantial impact on the orthodontic diagnosis and treatment plan. Continuing advances in medicine and dentistry increase the scope, importance, and value of these interactions. This introductory chapter discusses the need and rationale for interactions in specific situations, and this book includes details of conditions that require advice from specific specialists. The focus on this expanding scope is derived from the notion that biology plays a pivotal role in orthodontics, and that pertinent information regarding the health status of individual candidates for orthodontic treatment might have long-lasting effects on the course and outcomes of orthodontic treatment.

Facial esthetics, balance, and harmony, and/or their absence, have attracted attention from time immemorial, by artist and art viewer alike. Facial expressions can readily reflect various moods, emotions, and feelings, thereby conveying unspoken messages from person to person. The mouth is an essential component of this anatomical–physiological–emotional complex, by virtue of its ability to participate actively in these functions, involving its soft (cheeks, lips,

and tongue) and hard (jaws and teeth) tissues. Painters, sculptors, and photographers have noted these features, and frequently, when creating images of human faces, included the rest of the body, or at least the torso, in their artwork, demonstrating acceptance of the principle that the face and the rest of the body are one unit. The specialty of orthodontics is taught predominantly as a field of endeavor dedicated to the improvement of orofacial esthetics and function. Consideration of biological principles and constraints is shadowed by the desire of both the patient and his/her orthodontist to achieve noticeable improvement in the position and location of the malpositioned crown(s), ignoring the fact that the crowns are anchored in the jaws by their roots, which are surrounded by tissues that act and react like any other organ to any local or systemic factor that comes their way. This situation is like an iceberg, visible partially above the water surface, but invisible under it.

Malocclusions are situations where individual teeth or entire dental arches are positioned in undesirable locations, either esthetically or functionally. The goal of orthodontics is to correct or minimize deviations from accepted normal characteristics of dental occlusion, orofacial function, and esthetics. We tend to focus on these deviations from normalcy as the main target of our specialty, while keeping other health-related issues far in the background, sometimes behind the horizon, as if a malocclusion exists in a vacuum, detached from the rest of the body. Maintenance of this outlook may, however, jeopardize the quality of orthodontic diagnosis, treatment plan, outcome, and long-term maintenance of the corrected malocclusion. What is required for attainment of optimal results in orthodontics is broadening of its scope, to include other specialties, dental and medical, that may expose etiological factors, and biological processes that could determine the nature of the cellular/tissue response to mechanotherapy. In short, we should not treat a malocclusion, but rather *a person* with a malocclusion (McCoy, 1941; Kiyak, 2008).

Presently, orthodontics is still viewed by the general population as a field occupied mainly by concerns about facial esthetics, and limited to the application of “braces” or aligners to crooked teeth. This image has been cultivated and nurtured by many members of the orthodontic specialty, because it simplifies their lives by highlighting the known fact that teeth move when subjected to mechanical forces.

This outlook is deeply embedded in the curricula of the majority of the orthodontic educational/training programs around the world. Orthodontic residents are made to believe, at least subconsciously, that correcting a malocclusion in a human being is just as easy as moving metallic teeth through the warm, soft wax of a typodont (Davidovitch and Krishnan, 2009). Furthermore, this attitude has encouraged general dentists to engage in the practice of orthodontics without obtaining proper education that would qualify them for this task. An example of a poor outcome of such treatment is seen in Figures 1.1 and 1.2. However, orthodontics, which had been viewed until recently as being mainly a technique-oriented profession, has evolved into a comprehensive specialty, with a rapidly expanding scope, increasingly interacting with experts, among others, in biology, medicine, dentistry, engineering, and computer science. These interactions can provide the orthodontist with important information pertaining to individual patients that may lead to modifications in the diagnosis and treatment plans.

Voluminous expansion of the scientific and clinical bases of orthodontics is occurring in various directions, biological and technical. The role of biology in the diagnosis, treatment planning, and treatment of individual patients is becoming increasingly clear (Cartwright, 1941; Davidovitch and Krishnan, 2009). An orthodontist may be an expert in mechanics, but he/she is not a nutritionist, psychologist, pediatrician, endocrinologist, primary care physician, oral and maxillofacial surgeon, endodontist, prosthodontist, or any other medical and/or dental specialist. Therefore, it seems only prudent to request advice from other specialists whenever a condition is recognized in a person seeking orthodontic treatment, or in a patient who is already being treated.

The reality is that people who possess malocclusions may also have pathological conditions that could have significant impacts on the course and outcome of orthodontic treatment. This probability creates a need to consult and interact with other specialists familiar with an individual patient, or with the health problem afflicting this individual. Moreover, some people may have communicable diseases that may endanger the well-being of others who are in their environment. The existence of rapid communication systems enables an orthodontist to easily seek advice from other specialists, leading

to the crafting of diagnoses and treatment plans tailored specifically for each individual patient. These systems are also very useful in fostering strong doctor–patient trust, increasing cooperation and improving outcomes.

Likewise, recent advances in material science, metallurgy, and biomedical engineering have introduced an increasing array of alloys, capable of generating a wide spectrum of mechanical forces. A continuous interaction between the orthodontist and these engineers has already produced major changes in the design of orthodontic brackets, and the composition of the metallic and nonmetallic wires that generate the proper orthodontic forces, while controlling factors such as friction and strain. This interaction is fertile ground for the development of new appliances capable of engendering optimal tooth movement, biologically and mechanically, for each patient. The era has come wherein orthodontists are able to print customized brackets and wires tailored for the individual patient and can track individual patient progress with dental monitoring devices. Orthodontics nowadays is largely incorporating reverse engineering in the treatment planning and execution process, wherein malocclusion is treated to its end point with the help of digital models and computerized software and staged sequentially to fabricate aligners.

The pioneers of modern orthodontics were pathfinders in a field full of challenges and obstacles. Those leaders utilized the best therapeutic tools available for eliminating malocclusions, paving the way for greater achievements by their successors. Edward H. Angle, the “father of modern orthodontics,” advocated at the end of the nineteenth century the inclusion of basic medical sciences, such as anatomy, physiology, and pathology, in the curriculum designed for educating dentists as specialists in orthodontics. He apparently clearly saw the functional connection between the head and the rest of the body. Three decades on, one of his students, Albert Ketcham (1929), in attempting to elucidate the reasons for dental root resorption (a major undesirable side effect of tooth movement), concluded that the etiology is associated with the patient’s metabolism. In the following years, resorption of roots was attributed to factors such as nutritional deficiencies, hormonal fluctuations, genetic predisposition, and psychological stress. All

these factors point to the fact that tissue remodeling that facilitates tooth movement is dependent, at least in part, on the unique pathophysiological profile of the individual patient. Detailed information on this biological profile may be obtained from several different healthcare providers familiar with individual patients.

Figure 1.1 Poorly executed orthodontic treatment by a general practitioner. Ignoring the absence of mandibular central incisors, the practitioner extracted all the second premolars but was then unable to close the spaces entirely, ending with excessive overjet and a very deep bite.

However, despite recognition of the importance of life sciences in orthodontic education and practice, considerable emphasis is still

being placed on the mechanical aspect of this specialty. Consequently, conditions such as excessive root resorption are labeled idiopathic, unpredictable, and an “act of God.” These explanations fly in the face of the long-recognized principle of the intimate union between biology and mechanics in orthodontic therapy. This proximity was first suggested by Farrar (1888: 658), who speculated that tooth movement is facilitated by either resorption or bending of the alveolar bone, or by both processes. Farrar’s comment was surprisingly correct, although it was based on empirical evidence. Experimental evidence supporting Farrar’s hypothesis was provided by Sandstedt (1904) and by Baumrind (1969). While Sandstedt used histological sections to demonstrate that paradental cells are responsible for the force-induced tissue remodeling, Baumrind confirmed in experiments on rats that orthodontic forces do indeed bend the alveolar bone.

Figure 1.2 Another patient with poorly executed orthodontic treatment by a general practitioner. Poor planning is evidenced by extraction of all premolars (first and second) from all quadrants and finishing with lack of space closure, deep bite, rotated maxillary and mandibular molars, and posterior crossbite on the right side of the dental arch.

The broadening scope of orthodontics

In 2016 the FDI World Dental Federation developed a new definition of oral health that clearly states: “Oral health is multi-faceted and

includes the ability to speak, smile, smell, taste, touch, chew, swallow and convey a range of emotions through facial expressions with confidence and without pain, discomfort and disease of the craniofacial complex (head, face, and oral cavity)" (Glick et al., 2017). Orthodontics fits perfectly within this concept. Based on this definition, the Royal Dutch Dental Association defined orthodontic care as follows: "Orthodontic care is an integral part of oral health care and is concerned with optimizing the position of the teeth and the growth of the jaws and surrounding structures and makes an essential contribution to the health of an individual by promoting their psychosocial well-being and by creating optimal conditions for other facets of oral health and oral health care" (KNMT, 2020).

Nowadays orthodontics needs this kind of more holistic approach. Ideally, orthodontics should be practiced in a facility that houses all other medical specialists, such as a hospital or a large group practice. In such an environment, reaching various experts and obtaining their advice about health-related problems of individual orthodontic patients may be accomplished with relative ease. Specialists such as primary care/family physicians, orthopedists, surgeons, psychologists, and nutritionists may be within walking distance from the orthodontic clinic. However, the widespread network of electronic communications today has enabled an orthodontist to refer a patient for consultation and receive the specialist's opinion in a timely fashion, without dependence on geographical proximity or venue location.

Contemporary orthodontics is a fusion of biology and mechanics, starting with the process of diagnosis, which is based on estimating and documenting the extent of malocclusion, as well as asking: "Who is the patient, biologically?" This question must be answered before any plans for tooth movement can be contemplated. The presence of any systemic or local pathological condition may cause significant alterations in the orthodontic therapeutic plans for any and every individual patient, regardless of age or gender. A comprehensive orthodontic diagnosis should start with a detailed presentation of the patient's biological profile, including all conditions that may have an impact on mechanotherapy. This segment of the diagnosis is followed by a detailed description of the malocclusion. The biological segment is the part where interaction with specialists in various

medical fields is expressed and is later reflected in the crafting of an individual treatment plan. A brief example of such a diagnosis is as follows: “AZ is a 34-year-old female nurse, mother of two children, with multiple sclerosis that started 5 years ago, with a history of familial neuropathies. She has a Class II Division 1 malocclusion, with a steep mandibular plane, an 8° ANB angle, and a 12 mm overjet.” This diagnosis is a presentation of the main systemic and orofacial findings, which together pave the way for a proper treatment plan. For the sake of providing the best treatment plan for AZ, it would be beneficial to seek the advice of the other specialists who take care of her, such as her personal physician, neurologist, and nutritionist. Their opinions may turn out to be valuable in guiding the orthodontist toward a treatment plan that would be optimal and practical for this individual patient.

A similar malocclusion in a different patient may read as follows: “RM is a 14-year-old boy, entering the pubertal growth spurt, who has type 1 diabetes, allergies, and asthma, with a Class II Division 1 malocclusion, a steep mandibular plane, and an 8 mm overjet.” This concise but detailed diagnosis implies that the patient is growing and has health-related issues that may overshadow the orthodontic problem and its treatment outcome. Systemic issues of this nature, involving the immune, endocrine, and vascular systems, may alter the response of cells surrounding the teeth to applied mechanical stress, modify the velocity of tooth movement, and contribute to the creation of undesirable side effects to orthodontic treatment, such as irreversible loss of alveolar bone and shortening of dental roots. Moreover, if medical and/or socioeconomic problems are ignored, and are allowed to persist, maintenance of the corrected malocclusion may be jeopardized. Therefore, in the case of RM, it may be advisable for the orthodontist to communicate with the patient’s pediatrician, endocrinologist, and nutritionist prior to solidifying the diagnosis and treatment plan.

The orthodontic patient as a human being

Orthodontists do not only see young individuals, who are ready to face the world with a lot of enthusiasm and confidence, but also adult patients with various needs and expectations. In some instances

patients may be having psychosocial issues, and may seek orthodontic therapy in an attempt to alleviate their personality deficits, improve their social status, or find solutions to problems in their professional and personal life. It is extremely important to realize that every patient considered for treatment is an individual with a metabolic profile and physiological traits unique to him/her (Bartley et al., 1997), even though all humans share similar genetic, anatomical, physiological, and biochemical bases. The interindividual differences may arise from physical, social, ethnic, psychological, and metabolic variations, among other factors. It is important to realize that orthodontic treatment is provided to vital tissues that respond in a similar fashion in all patients. However, the extent, duration, and outcome of this response are frequently dependent on biological factors only remotely related to the malocclusion at hand.

The pattern and timing of craniofacial growth and development events are intimately associated with somatic growth-related functions, controlled and regulated by myriad chemical and physical factors, of internal and external origin, interacting with target cells in many or all organs and systems. This complex reality faces every orthodontist, as well as any other healthcare provider. It is rather unrealistic to expect that any one individual, in any medical specialty, would be able to comprehend, manage, and memorize all this voluminous knowledge. Hence there is a need for the orthodontist to keep abreast of new developments in the entire field of medicine, and to interact with members of other specialties whenever a situation arises that requires input from other experts.

One fundamental interaction in this formula is between orthodontists, who move teeth with mechanical forces, and the experts who create the means to generate these forces: biomedical and metallurgical engineers. The requirement for perpetual interaction between experts in these entities is because orthodontic tooth movement requires close interaction between the biological and the mechanical environments (Krishnan and Davidovitch, 2006a; Meikle, 2006) and, even in a healthy patient, the response to orthodontic forces can vary from time to time, because the duration of treatment is often measured in years. In addition, the presence of an underlying ailment that affects the physiological condition may

alter the nature of the acute and chronic inflammation that is a core event in tooth movement, and modify craniofacial growth and development (Alvear et al., 1986). Cellular signaling molecules generated either in the vicinity of the periodontal ligament or in distant sites have the potential to disrupt tooth movement by altering the levels of biomolecules in the local biological environment of the periodontal ligament (Krishnan and Davidovitch, 2006b).

The patient's biological status: does it influence orthodontic treatment?

Due to the uniqueness of every individual patient's biology, it is imperative for the orthodontist to create and maintain open communication channels with practitioners in every medical field. Patients may be referred for consultation to their personal physician, or to experts in specific areas, such as endocrinology, neurology, immunology, genetics, metabolism, pulmonology, nutrition, psychology, and infectious diseases. Each organ or tissue system in a pathological state may have profound effects on paradental cells and tissues, by transferring signal molecules through the vascular system to any tooth being moved, and all the cells surrounding it.

Inflammation and cellular mechanotransduction are central coordinators of orthodontic tooth movement, which ushers leukocytes and plasma out of the mechanically stressed capillaries, which become hyperpermeable in reaction to the release of vasoactive neurotransmitters from the strained nerve terminals. In this fashion, leukocytes that had become primed in remote diseased organs can enter strained dental and paradental tissues, and interact with cells carrying receptors for signaling molecules synthesized by the migratory immune cells. Experiments with human periodontal ligament (PDL) fibroblasts in vitro revealed that these cells respond readily to cytokines, growth factors, colony-stimulating factors, and chemo-attractant signals, all of which are produced and released by the newly arrived leukocytes (Saito et al., 1990a, b). Recent research has revealed the difference in morphology as well as reaction of PDL cells from young and adult patients subjected to the application of orthodontic force (Figure 1.3). Adult PDL cells exhibited senescent changes through increased beta-galactosidase activity that, along

with an increase in the inflammatory response and bone resorption activities, was evident by increased prostaglandin E2 (PGE2), interleukin (IL)-1B, and acid phosphatase mRNA expression levels (George et al., 2020; Mohanakumar et al., 2021). This intimate correlation between tooth movement and pathological conditions that happen elsewhere in the body is the main reason for interacting with physicians, nutritionists, psychologists, or other experts in healthcare provision.

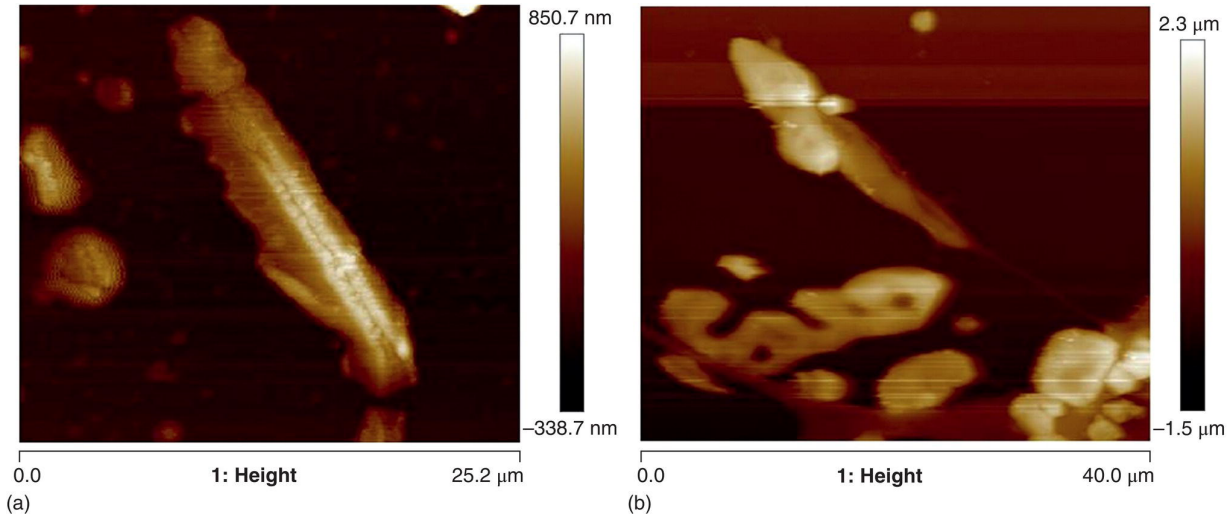


Figure 1.3 Representative atomic force microscopy images after nanoindentation showing an increase in surface irregularities and protrusions in the cell surface of periodontal ligament fibroblasts. (a) Young fibroblast and (b) adult fibroblast cells.

Many individuals seeking orthodontic care have systemic ailments, such as asthma, and are usually already under treatment for these conditions at the time of their orthodontic diagnosis appointment(s). This treatment often entails the use of various prescription and/or over-the-counter medications. Some of these medications may have insignificant effects on the process of tissue remodeling evoked by the orthodontic forces, but others, such as steroidal and nonsteroidal anti-inflammatory drugs, anti-cancer medications, immune suppressors, statins, and anti-osteoporotic medications, may reach the cells in and around moving teeth by exiting, in the plasma, through capillaries that have become hyperpermeable by the applied stress (Krishnan and Davidovitch, 2006b). It is therefore important to record all the medications taken regularly by a patient before the

onset of orthodontic treatment, as well as during the course of therapy. Once a complete list of medications taken regularly by a patient is obtained, it is essential to search for information about their desirable and undesirable effects. This information can be readily found on the internet and in current pharmacopeias. An example of a profound effect of a nonsteroidal anti-inflammatory drug on cells involved in orthodontic tissue remodeling is demonstrated in Figure 1.4, showing the mesially located, stretched PDL and alveolar bone surface lining cells of a maxillary cat canine that had been moved distally for 24 h, with a force of 80 g. The tissue sections were stained immunohistochemically for PGE2, a ubiquitous inflammatory mediator. A section taken from a control cat untreated by the nonsteroidal anti-inflammatory drug indomethacin shows cells intensely stained for PGE2, while a section obtained from an indomethacin-treated cat demonstrates a marked reduction of staining intensity, suggesting that this drug may have a profound effect on tooth movement.

Nutrition may play an important role in determining the pattern and course of tooth movement (Hickory and Nanda, 1981; Palmer, 2007). A modern diet consists of proper amounts of proteins, carbohydrates, lipids, vitamins, and trace elements. However, within the same community, marked differences between individuals may be found in the relative proportion of each dietary component, and even greater differences are known to exist between members of diverse communities, despite their geographical proximity. Some items in the diet may be essential for eliciting a vigorous cellular response to mechanical forces. For example, vitamin C is an essential co-factor in the synthesis of collagen by fibroblasts, and vitamin D_3 is a key regulator of the mobilization of calcium into and out of the intestine, kidney, and skeleton. Proteins provide the amino acids needed for building and remodeling tissues surrounding moving teeth; carbohydrates supply the energy required for all cellular activities; and lipids are a critical part of every cell's plasma membrane.

Some dietary components may be detrimental to the patient's health and well-being and have a negative effect on dental and paradental tissues. In the case of alcohol, its chronic excessive consumption may

cause dental root resorption in orthodontic patients by causing liver cirrhosis, disrupting the hydroxylation of vitamin D_3 in the liver, thereby evoking increased production of parathyroid hormone (PTH), necessary for the maintenance of calcium homeostasis (Ghafari, 1997). This hormone is implicated in the resorption of mineralized tissues, including dental roots. For these reasons it may be helpful to obtain detailed information about the dietary habits of every patient prior to the onset of orthodontic treatment. An evaluation of individual daily diets by a qualified nutritionist may supply the orthodontist with important clues regarding expectations of individual tissue responses to orthodontic mechanotherapy.

Regulation of mammalian body functions is dominated to a large extent by three systems: the nervous, immune, and endocrine systems. Persons seeking orthodontic care sometimes have ailments that affect one or more of these systems. Treating such patients orthodontically with little consideration for their systemic abnormalities may result in some unpleasant surprises for patients, as well as for their orthodontists. For example, a patient with an existing condition such as multiple sclerosis may develop trigeminal neuralgia early in the course of orthodontic treatment, because of the acute pain generated every time the orthodontic appliance is activated. The pain may even be amplified because of the direct contact between the denuded, unmyelinated trigeminal nerve fibers. In cases such as this, and in patients with other neurological diseases, either central or peripheral, administration of orthodontic forces may exacerbate the neurological condition and/or be affected by it. Moreover, medications taken by these patients may also alter the pattern of tissue response to orthodontic forces (Krishnan and Davidovitch, 2006b). Therefore, it may be prudent to seek the advice of the neurologists treating such patients.

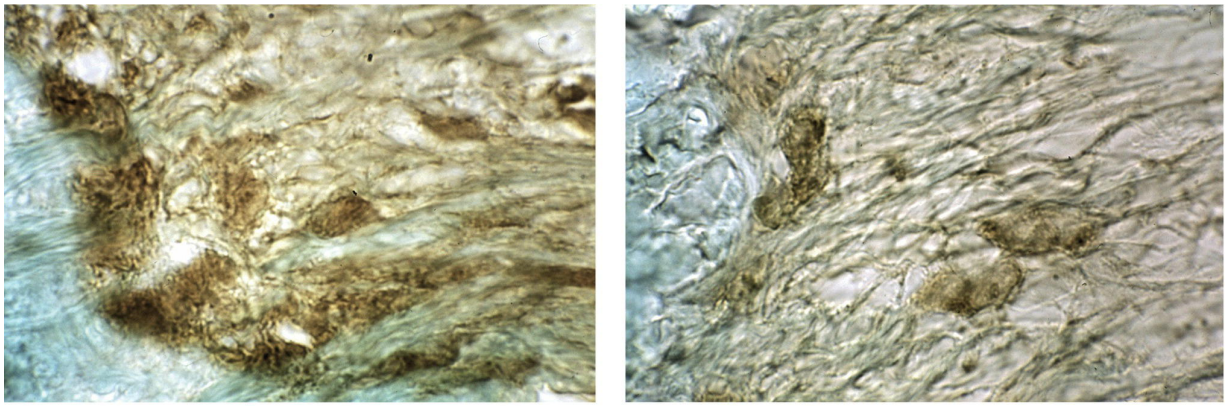


Figure 1.4 Immunohistochemical staining for prostaglandin E2 (PGE2) in sagittal sections, 5 μm thick, of maxillary canines of 1-year-old cats, after 24 hours of distal movement by an 80 g translatory force. (a) Periodontal ligament (PDL) tension site of control cat, showing distinct staining in alveolar bone osteoblasts. (b) PDL tension site of a cat injected subcutaneously with indomethacin, 5 mg/kg, at the time of appliance activation. The staining intensity for PGE2 in osteoblasts and PDL cells is light.

The immune system is a network of biological structures and processes within an organism that protects against disease by identifying and killing pathogens and tumor cells. It detects a wide variety of agents, from viruses to parasitic worms, and needs to distinguish them from the organism's own healthy cells and tissues in order to function properly. Detection is complicated as pathogens can evolve rapidly, producing adaptations that avoid the immune system and allow the pathogens to successfully infect their hosts (Abergerth and Gudmundsson, 2006). The immune system provides the leukocytes required for the induction and maintenance of inflammation, which is the mechanism whereby tissue remodeling facilitates tooth movement. Disorders of the immune system, such as immunodeficiency that occurs when the immune system is less active than normal, result in recurring and life-threatening infections. Immunodeficiency can be either the result of a genetic disease, such as severe combined immunodeficiency, or secondary to pharmaceutical therapy or an infection, such as acquired immune deficiency syndrome (AIDS), which is caused by the retrovirus human immunodeficiency virus (HIV). In contrast, autoimmune diseases result from a hyperactive immune system attacking normal

tissues, as if they were foreign organisms. Common autoimmune diseases include Hashimoto thyroiditis, rheumatoid arthritis, diabetes mellitus type 1, and lupus erythematosus. Figure 1.5 shows intraoral views in a 39-year-old man with a history of diabetes mellitus type 1, Hashimoto thyroiditis, and depression. He had an obvious malocclusion, and his systemic diseases were being treated by a variety of medications. In view of the multiplicity of diseases and the numerous medications taken by this patient, the patient's physician's recommendation was to refrain from orthodontic treatment. The decision not to consider orthodontics was reached based on input from the patient's physician, dentist, and a prosthodontist.

Figure 1.5 A malocclusion in a 39-year-old man with several systemic diseases. (a) Frontal view of the dentition, demonstrating a midline shift and bilateral posterior crossbite. (b, c) Left and right views of the dentition, showing spaces resulting from prior tooth extractions. Tipping of teeth into the extraction sites is visible in both dental arches. (d) The maxillary periapical radiograph reveals severe shortening of the premolar and molar roots.

The endocrine system is a system of glands, each of which secretes a specific type of hormone to regulate the body and act as an information signal system, much like the nervous system. A hormone is a chemical transmitter released from specialized cells into the bloodstream, which transports it to specialized organ-receptor cells that respond to it. Hormones regulate many functions of an organism, including mood, growth and development, tissue function, and metabolism. Together with the nervous system, the endocrine system regulates and integrates the body's metabolic activities. The endocrine system meets the nervous system at the hypothalamus. The hypothalamus, the main integrative center for the endocrine and

autonomic nervous systems, controls the function of endocrine organs by neural and hormonal pathways.

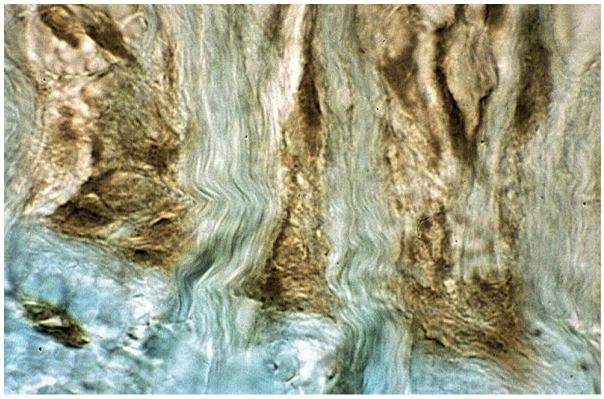
Application of orthodontic forces increases the blood flow into the tooth and the paradental tissues (Kvinnsland et al., 1989; Ikawa et al., 2001) and their capillaries become hyperpermeable, fostering plasma extravasation. This local alteration in the vascular system can cause an increase in the tissue concentration of hormones, of which some, like parathyroid hormone, calcitonin, and thyroxin, are known to regulate bone metabolism (Copp and Cheney, 1962; Mundy et al., 1976; Parfitt, 2003; Martin, 2004; Poole and Reeve, 2005). Figure 1.6 presents photomicrographs of the alveolar bone and PDL, as seen in sections stained immunohistochemically for 3′,5′-adenosine monophosphate (cyclic AMP or cAMP). The sections were obtained from three young adult cats. Figure 1.6a is from an untreated (control) cat and shows mild cellular staining intensity for cAMP near a maxillary canine. Figure 1.6b is from a cat whose maxillary canine was subjected to 24 hours of distal movement. This figure is from the zone of tension in the PDL, demonstrating intense staining for cAMP, resulting from the orthodontic force. Figure 1.6c was derived from a cat that had been treated in the same manner as the one shown in Figure 1.4b, and in addition received a subcutaneous injection of PTH, 30 IU/kg, 2 h before euthanasia. In Figure 1.6c the cells are stained extremely dark, reflecting a high concentration of cellular cAMP. Since this cyclic nucleotide represents cellular activation by extracellular signals, it is reasonable to conclude that the biological response to orthodontic forces may be sensitive to hormonal concentrations in the blood. These concentrations are modified significantly by pathological conditions that develop in specific endocrine glands, suggesting that an opinion of an endocrinologist about the patient's hormonal profile could be very helpful in crafting a proper orthodontic diagnosis and treatment plan.

Orthodontists treat human beings, who sometimes are unable or unwilling to acknowledge and comply with their share of responsibility and effort dictated by the treatment regimen. Frequently, such behavioral patterns stem from psychological stresses, rooted in genetic, developmental, and/or environmental etiological factors. Hence, psychology is apparently a crucial element

in determining and forecasting the degree of success or failure of orthodontic treatment. Psychology is a field that focuses on studying the mind. Psychologists attempt to understand the role of mental functions in individual and social behavior, while also exploring underlying physiological and neurological processes. Psychologists study such topics as perception, cognition, attention, emotion, motivation, brain functioning (neuropsychology), personality, behavior, and interpersonal relationships. Deviation from the norm in any of these areas may harbor the seed of failure of orthodontic treatment. A review of records of about 1100 patients who had completed orthodontic treatment revealed that those who had been diagnosed before the onset of treatment as having had psychological problems, such as mood swings and anxiety, displayed a high risk of developing excessive root resorption during the course of treatment (Davidovitch et al., 2000). This undesirable outcome could have been the result of alterations in the hypothalamic–pituitary–adrenal axis, caused by the psychological problems. Another unexpected side effect of orthodontic treatment in a psychologically stressed patient is alopecia totalis (Davidovitch and Krishnan, 2008) (Figure 1.7). Apparently, the mind is an important determinant of the degree of success of orthodontic treatment. Therefore, it seems advantageous to interact with a psychologist whenever a psychological issue is diagnosed, both before and during treatment.

Interactions between dentists who practice one or more specialties are almost axiomatic. Patients with malocclusions are frequently being referred to an orthodontist for an initial examination and assessment of the degree of need for orthodontic care. The referring person may be a general dentist who controls the dental health of the patient and his/her family, a periodontist, a pedodontist, or another dental specialist. After examining the patient, the orthodontist informs the referring dentist about his/her findings and recommendation, and whenever necessary they coordinate the timing of various treatment phases. However, sometimes elimination of a complex malocclusion, which involves the teeth, their surrounding tissues, as well as the facial muscles and skeleton, requires the construction of a comprehensive treatment plan by a number of specialists. Such is the case in caring for patients with orofacial clefts and other craniofacial anomalies, where teams of

experts convene to discuss each patient's individual needs in a detailed and carefully coordinated sequence. These teams include experts in pediatrics, plastic surgery, psychology, social work, nutrition, dentistry, and orthodontics. A similar team approach is adopted for the treatment of adults who require reconstructive treatment. The team in this case may include a general dentist and specialists in periodontics, endodontics, maxillofacial surgery, prosthodontics, and orthodontics.



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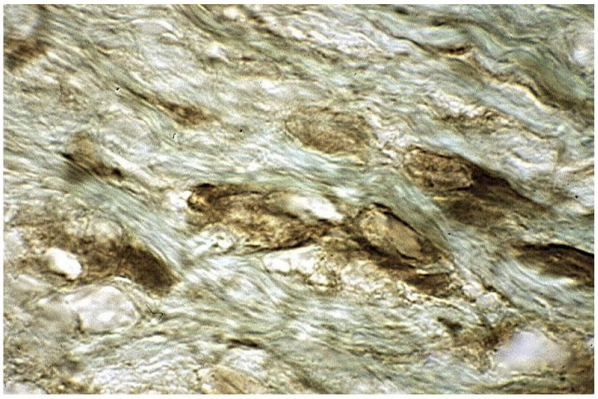

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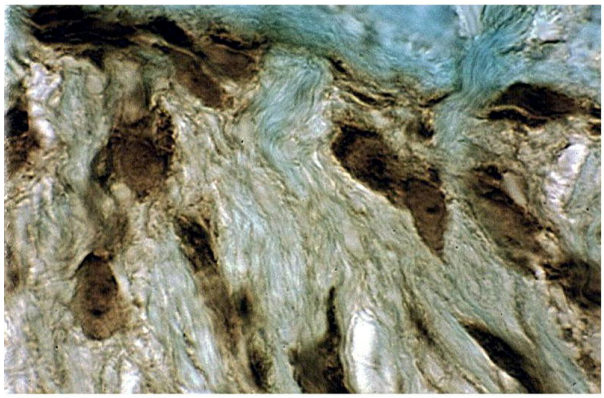

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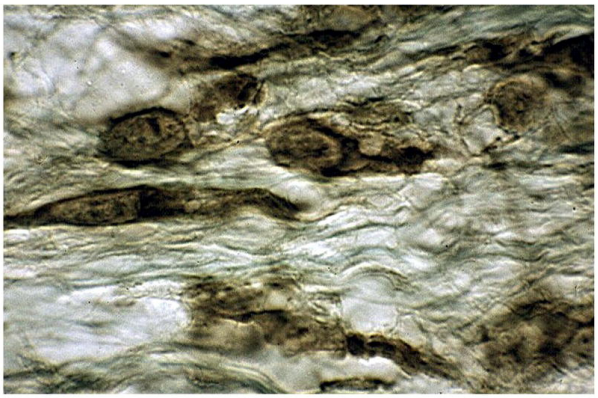

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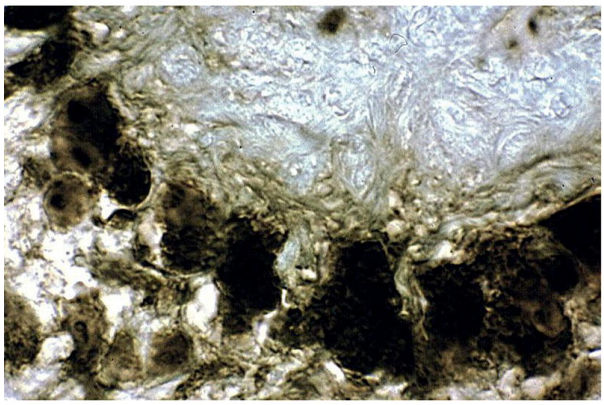

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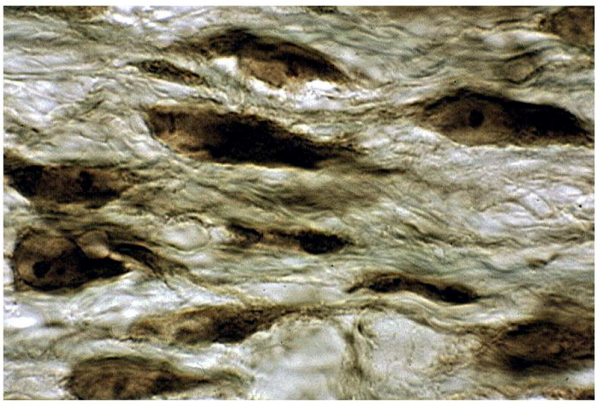
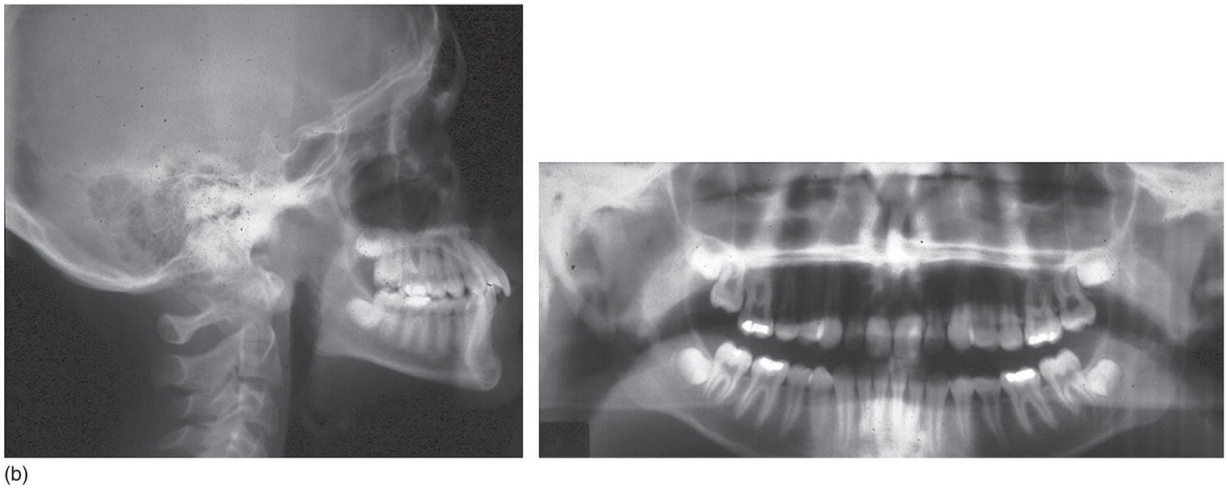


(f)

Figure 1.6 Immunohistochemical staining for cyclic adenosine monophosphate (cAMP) in sagittal sections, 5 μm thick, of maxillary canines of 1-year-old cats after 24 hours of distal movement by an 80 g translatory force. (a) Osteoblasts and (b) periodontal ligament (PDL) fibroblasts from a control cat (no orthodontic force). (c) Osteoblasts and (d) fibroblasts in the PDL tension site (the cat received orthodontic force, but no parathyroid hormone [PTH]). (e) Osteoblasts and (f) fibroblasts in the PDL tension site. This cat received orthodontic force and a subcutaneous injection of PTH, 30 IU/kg, at the time of the appliance activation. The intensity of staining for cAMP is light in the untreated control animal, pronounced in the animal that was treated by force alone, and very intense in the animal treated by force and PTH.

The orthodontist's professional wish-list includes a comfortable, painless experience for all patients, efficient treatment of short duration, avoidance of iatrogenic damage, and a guarantee that the teeth have been moved to their best position, from where there is no relapse. The duration of tooth movement may be shortened significantly by decortication of the alveolar bone, leading to release of stem cells from the bone marrow, and the engineering of new tissues (Wilcko et al., 2009).

(a)



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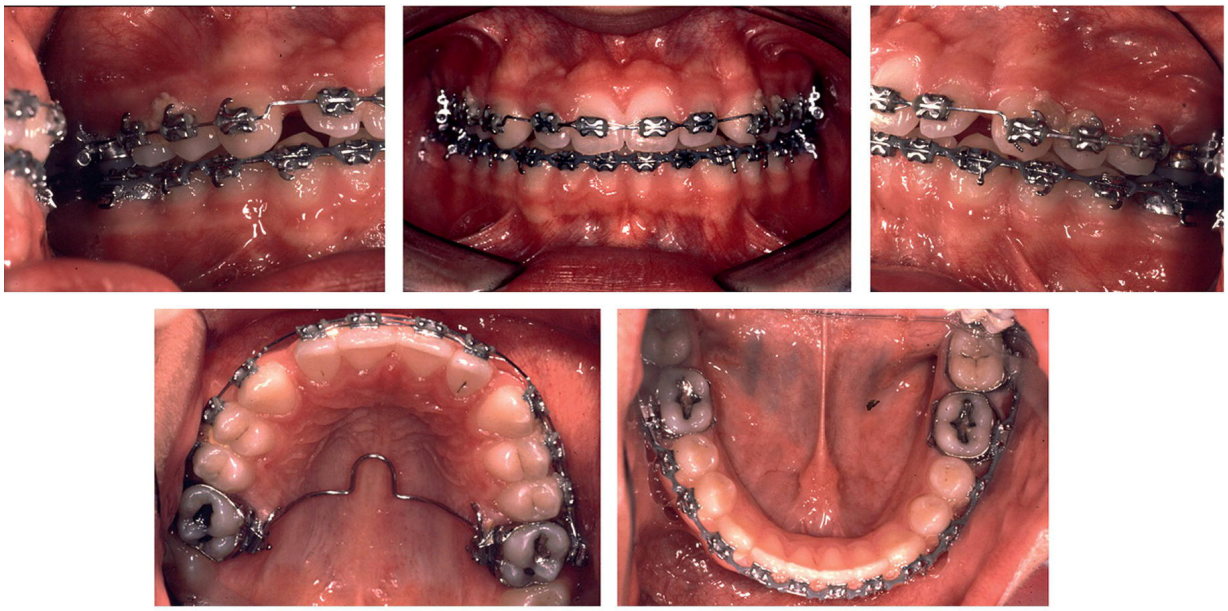

(c)

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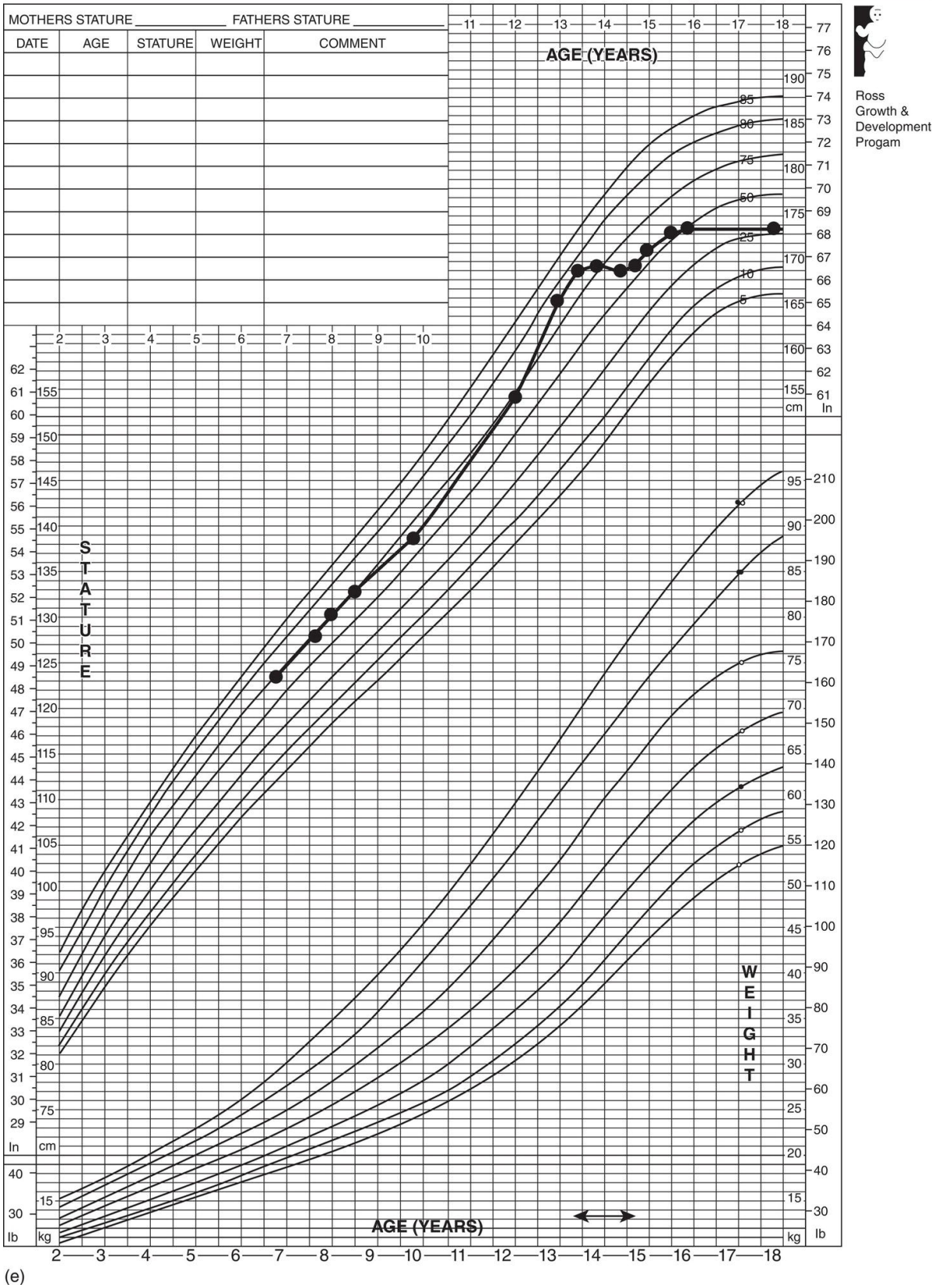
BOYS: 2 TO 18 YEARS
PHYSICAL GROWTH
NCHS PERCENTILES*

NAME _____ RECORD #_____



Ross
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Development
Progam

(e)

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Figure 1.7 (a) Pretreatment extra- and intraoral photographs of MV, at age 12 years and 10 months. Note good symmetry; smiling picture revealing maxillary midline is shifted 3.5 mm, a convex profile. Teeth in occlusion show a deep anterior overbite (80–90%) and spaces between the maxillary incisors. The maxillary midline is shifted 3.5 mm to the right. On the right side, the buccal occlusion is neutral and spaces are seen between the maxillary incisors and mesial to the canine. Left side shows Class II Division 1 molar relationship as well as spaces between the maxillary incisors and mesial to the canine. Occlusal view of maxillary dental arch shows a parabolic shape, spaces between the anterior teeth from canine to canine, and distolabial rotations of both central incisors. Mandibular dental arch shows a U-shape, without any spacing or crowding of teeth. (b) Pretreatment lateral cephalogram demonstrating normal anteroposterior and vertical relationships between the jaws, a favorable inclination of the anterior cranial base and the palatal and mandibular planes, and a deep overbite in the incisor region. The panoramic radiograph reveals all teeth to be present and normal dental development. (c) MV's dentition 1 year after the onset of orthodontic treatment. Frontal view and both left and right lateral views demonstrate accumulation of dental plaque and food debris in the canine and premolar regions between the brackets and the gingival margin. Occlusal view shows spaces between the maxillary canines and lateral incisors. (d) Photograph of MV 9 months after the beginning of orthodontic treatment, 1 month after he lost all his scalp hair (alopecia totalis).

Source: Davidovitch and Krishnan (2008), courtesy of Quintessence Publishing Co. Inc., Chicago.

(e) Physical growth (stature) curve of MV, revealing the somatic growth-inhibitory effects of the corticosteroid treatment that was implemented in an attempt to restart new hair growth. The hormonal treatment failed to stimulate hair growth. (f) Photographs of MV 11 months after the completion of his orthodontic treatment and 1.5 years of treatment with vitamin D_3. Apparently, this treatment mode was successful in restoring hair growth. (g) Extraoral photograph of MV taken in August 1999. His hair remained intact.

Source: Davidovitch and Krishnan (2008), courtesy of Quintessence Publishing Co. Inc., Chicago.

Conclusions

Treatment of a malocclusion requires high technical skills and a thorough comprehension of biological sciences, because teeth transfer the applied orthodontic force to their surrounding tissues, where strained cells remodel the PDL and alveolar bone, allowing the teeth to move to new positions. The biological component reflects the nature of the anticipated clinical response and highlights the plethora of differences between patients. These physiological and pathological differences may have profound effects on the outcomes of treatment. Detailed descriptions of these conditions may be found in the library or on the internet, but in addition it is advisable to communicate effectively with each patient, and with all experts who have examined and treated the patient previously. These specialists can share invaluable information about their own observations of the patient's biological and therapeutic profile. Such details should be included in the diagnosis, and reflected in the treatment plan, which may differ from a plan that addresses only the morphological features of a malocclusion.

The continuous evolution in material and biological sciences will strengthen further the interactions between orthodontists and other healthcare specialists, leading the way toward sustainable corrections of malocclusions and craniofacial anomalies. These unfolding advances will continue to reduce the distance to the elusive target of optimal orthodontics. The common thread that unifies specialists in various disciplines is the desire to share, contribute to, and participate in efforts to improve everyone's body and spirit, a universal goal that knows no boundaries.

References

Agerberth, B., and Gudmundsson, G.H. (2006). Host antimicrobial defence peptides in human disease. *Current Topics in Microbiology and Immunology* 306: 67–90.

Alvear, J., Artaza, C., Vial, M. et al. (1986). Physical growth and bone age of survivors of protein-energy malnutrition. *Archives of Disease in Childhood* 61: 257–262.

Bartley, A.J., Jones, D.W., and Weinberger, D.R. (1997). Genetic variability of human brain size and cortical gyral patterns. *Brain* 120(Pt 2): 257–269.

Baumrind, S. (1969). A reconsideration of the property of the pressure tension hypothesis. *American Journal of Orthodontics* 55: 12–22.

Cartwright, F.S. (1941). Extending the scope of orthodontics. *American Journal of Orthodontics and Oral Surgery* 27: 394–398.

Copp, D.H., and Cheney, B. (1962). Calcitonin – a hormone from the parathyroid which lowers the calcium level of the blood. *Nature* 193: 381–382.

Davidovitch, Z., and Krishnan, V. (2008). Adverse effects of orthodontics. A report of two cases. *World Journal of Orthodontics* 9: 268.

Davidovitch, Z., and Krishnan, V. (2009). Role of basic biological sciences in clinical orthodontics: A case series. *American Journal of Orthodontics and Dentofacial Orthopedics* 135: 222–231.

Davidovitch, Z., Lee, Y.J., Counts, A.L. et al. (2000). The immune system possibly modulates orthodontic root resorption. In: Z. Davidovitch and J. Mah (eds.), *Biological Mechanisms of Tooth Movement and Craniofacial Adaptation*. Boston, MA: Harvard Society for the Advancement of Orthodontics, pp. 207–217.

Farrar, J.N. (1888). *Irregularities of the Teeth and Their Correction*, vol 1. New York: DeVinne Press.

George, P., George, J. K., Krishnan, V. et al. (2020). Periodontal ligament cells in adolescents and adults: Genetic level responses to orthodontic forces. *American Journal of Orthodontics and Dentofacial Orthopedics* 158(6): 816–823.

Ghafari, J.G. (1997). Emerging paradigms in orthodontics – an essay. *American Journal of Orthodontics and Dentofacial Orthopedics* 111: 573–580.

Glick, M., Williams, D.M., Kleinman, D.V. et al. (2017). A new definition for oral health developed by the FDI World Dental Federation opens the door to a universal definition of oral health. *American Journal of Orthodontics and Dentofacial Orthopedics* 151(2): 229–231.

Hickory, W., and Nanda, R. (1981). Nutritional considerations in orthodontics. *Dental Clinics of North America* 25(1): 195–201.

Ikawa, M., Fujiwara, M., Horiuchi, H. et al. (2001). The effect of short-term tooth intrusion on human pulpal blood flow measured by laser Doppler flowmetry. *Archives of Oral Biology* 46: 781–787.

Ketcham, A.H. (1929). A progress report of an investigation of apical root resorption of vital permanent teeth. *International Journal of Orthodontics, Oral Surgery and Radiology* 15: 310–328.

Kiyak, H.A. (2008). Does orthodontic treatment affect patients' quality of life? *Journal of Dental Education* 72: 886–894.

KNMT – Dutch Dental Association (2020). Visienota Orthodontist 2025 [Vision Orthodontist 2025]. https://orthodontist.nl/wp-content/uploads/2020/11/VISIE-ORTHODONTIST-2025.pdf

Krishnan, V., and Davidovitch, Z. (2006a). Cellular, molecular, and tissue-level reactions to orthodontic force. *American Journal of Orthodontics and Dentofacial Orthopedics* 129: 469.e1–32.

Krishnan, V., and Davidovitch, Z. (2006b). The effect of drugs on orthodontic tooth movement. *Orthodontics and Craniofacial Research* 9: 163–171.

Kvinnsland, S., Heyeraas, K., and Ofjord, E.S. (1989). Effect of experimental tooth movement on periodontal and pulpal blood flow. *European Journal of Orthodontics* 11: 200–205.

Martin, T.J. (2004). Does bone resorption inhibition affect the anabolic response to parathyroid hormone? *Trends in Endocrinology and Metabolism* 15: 49–50.

McCoy, J.D. (1941). The general health benefits of orthodontic treatment. *American Journal of Orthodontics and Oral Surgery* 27: 369–378.

Meikle, M.C. (2006). The tissue, cellular, and molecular regulation of orthodontic tooth movement: 100 years after Carl Sandstedt. *European Journal of Orthodontics* 28: 221–240.

Mohanakumar, A., Vijay, G.L., Vijayaraghavan, N. et al. (2021). Morphological alterations, activity, mRNA fold changes, and aging changes before and after orthodontic force application in young and adult human-derived periodontal ligament cells. *European Journal of Orthodontics* 43(6): 690–696.

Mundy, G.R., Shapiro, J.L., Bandelin, J.G. et al. (1976). Direct stimulation of bone resorption by thyroid hormones. *Journal of Clinical Investigatoins* 58: 529–534.

Palmer, C.A. (2007). Effective communication in dental practice. In: C.A. Palmer (ed.), *Diet, Nutrition and Oral Health*, 2nd ed. Upper Saddle River, NJ: Pearson, pp. 409–452.

Parfitt, A.M. (2003). Parathyroid hormone and periosteal bone expansion. *Journal of Bone and Mineral Research* 17: 1741–1743.

Poole, K., and Reeve, J. (2005). Parathyroid hormone—a bone anabolic and catabolic agent. *Current Opinion in Pharmacology* 5: 612–617.

Saito, S., Ngan, P., Saito, M. et al. (1990a). Effects of cytokines on prostaglandin E and cAMP levels in human periodontal ligament fibroblasts in vitro. *Archives of Oral Biology* 35: 387–395.

Saito, S., Ngan, P., Saito, M. et al. (1990b). Interactive effects between cytokines on PGE production by human periodontal ligament fibroblasts in vitro. *Journal of Dental Research* 69: 1456–1462.

Sandstedt, C. (1904). Einige beiträge zur theorie der zahnregulierung. *Nord Tandlaeg Tidskr* 5: 236–256.

Wilcko, M.T., Wilcko, W.M., Pulver, J.J. et al. (2009). Accelerated osteogenic orthodontics technique: A 1-stage surgically facilitated rapid orthodontic technique with alveolar augmentation. *Journal of Oral and Maxillofacial Surgery* 67: 2149–2159.

2
Orthodontic Diagnosis and Treatment Planning: Collaborating with Medical and Other Dental Specialists

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Summary

Orthodontists – as specialists – are expected to be proficient in diagnosing anomalies of the face, teeth, and jaws and identifying any coexisting deviations in physiological functions and systemic pathologies. As a member of the healthcare provider system, an orthodontist should have sufficient knowledge to recognize and record the etiology of a presenting malocclusion, which may result from various systemic or local aberrations. This means that any anomalies of anatomy, physiology, and the various medical conditions that may directly or indirectly influence the orthodontic diagnosis, treatment plan, mechanotherapy, or the case's prognosis should be noted. In addition, the existing oral health conditions, and problems with the dentition, ranging from the quality and quantity of the dentition, the morbidity associated with childhood trauma, dental caries, and/or periodontal diseases, which might require close collaboration with a variety of dental specialists, should be recorded. This chapter deals with these issues and provides a framework for interaction and collaboration with medical and dental specialists based on a holistic approach to orthodontic diagnosis and treatment planning. The goal is to help the reader develop the aptitude to communicate with various healthcare specialists to undertake, reconsider, stop, or reschedule orthodontic treatment with due precautions.

Success in any healthcare profession depends largely on accurate diagnosis, formulation of appropriate treatment goals, and precise implementation. Currently, patients with orthodontic needs span a wide range of age groups, personalities, social strata, and ethnic backgrounds, with varying levels of expectations (Abu Alhaija et al., 2010). Additionally, the increasing number of adult patients means that the present-day orthodontist is faced with an array of systemic (van Venrooy and Proffit, 1985; Patel et al., 2009) as well as local conditions (Basdra et al., 2001; Altug-Atac and Erdem, 2007) that may affect both the general as well as the oral health status of the individual. It is now accepted that “it is no longer appropriate to

deny elective dental or medical care to patients with diagnoses that have historically been associated with poor outcomes" (Sonis, 2004: 277). The recent medical and dental advances have made it possible for many patients with significant medical and dental disorders to be successfully managed in the orthodontic office (Lux et al., 2005), provided that the orthodontist has a sound knowledge base and is keen to interact with other medical and dental professionals (Patel et al., 2009).

Before becoming a good orthodontist, an orthodontic graduate must be a competent diagnostician and a good physician. We, as orthodontists, often make a diagnosis after taking a short medical history, complemented by a physical examination concentrating only on facial appearance (in general) and occlusion (local) alone. This approach, which is more appropriately termed "regional diagnosis," reveals the existing malocclusion, but lacks an overall perspective and the bigger picture of the medical, psychological, and pathological processes occurring elsewhere in the body gets ignored. This approach makes proper recognition of existing systemic conditions and their effects on orthodontic treatment difficult, if not impossible, to comprehend. In our "play safe" approach, many orthodontists refuse treatment to patients who could be treated successfully with suitable precautions and professional interaction with other medical/dental specialists. Including a module on diagnosis and management of medical conditions in orthodontic training programs is recommended, with sufficient exposure in clinical settings in multispecialty hospitals. This will allow development of an attitude that encourages a more professional approach when interacting with our medical and surgical colleagues, while recognizing and realizing our responsibilities and limitations. Up-to-date knowledge of medical problems should be combined with following proper communication protocols while referring patients to other medical and dental colleagues.

The other side of the story

Since oral health can have a significant impact on general health, dental health is often a significant concern for the medical fraternity (George et al., 2010; Yasny, 2010). Mutual referral systems are useful

in these situations, with medical personnel – including specialists – referring patients with dental and oral health-related problems to dental specialists with greater zeal, provided that the specialists on both sides are confident about and comfortable interacting with each other. We should recognize that none of us can treat all the diseases of the human body. Thus, “two-way interaction” is essential for providing a better level of healthcare.

Teamwork is becoming increasingly significant and beneficial across a wide range of disciplines. The terms multidisciplinary, interdisciplinary, and transdisciplinary are often used interchangeably. They all relate to the varying degrees of involvement of multiple disciplines along the same continuum (Choi and Pak, 2006). The term multidisciplinary denotes working with several specialties but staying within their boundaries. For example, in multidisciplinary care patients are treated independently by various disciplines that share information, while the patient may be a mere recipient of care (Bernard-Bonnin et al., 1995; Choi and Pak, 2006). The interdisciplinary team denotes working between several disciplines to advance fundamental understanding or solve problems whose solutions are beyond the scope of a single discipline or area of research practice (Bernard-Bonnin et al., 1995; Choi and Pak, 2006). The interdisciplinary approach requires close communication between various disciplines and mutual respect and confidence. For instance, cleft lip and palate anomalies or craniofacial syndromes require interdisciplinary care by primarily involving craniofacial surgeons, orthodontists, clinical geneticists, otolaryngologists, speech-language pathologists, and clinical psychologists (Long and Kharbanda, 1999; Kharbanda, 2022). A transdisciplinary approach means working across or beyond several disciplines and transcending their boundaries (Choi and Pak, 2006).

Orthodontic diagnosis from a broad perspective

From a mere tooth-moving specialty, orthodontics has become a branch of dentistry with deep scientific and evidence-based perspectives for its biomechanical principles. Often, clinicians

remain preoccupied with the mechanotherapeutic features of various appliances and philosophies, ignoring that teeth are a part of larger, intricately linked biological systems of the body that influence the response of teeth to mechanical stimuli.

Every patient is unique, with metabolic traits that are individually specific to them (Sidell and Kaminskis, 1975; Morrison et al., 1992; Bartley et al., 1997), even though all humans have similar basic anatomical, physiological, and biochemical features. It must be appreciated that treatment is being delivered not to an artificial set of typodont teeth but rather to vital tissues – which respond differently to the same treatment protocol under the same physiological conditions in different individuals (Ren et al., 2003; McConkey, 2004; Williams, 2008), altered physiological conditions in the same individual (Brambilla et al., 1981), and various pathological conditions (Salerno et al., 1982; Verna et al., 2000).

The craniofacial complex can be considered an organization of many small organ systems and components, such as the dentoalveolar structures, the nervous system, the muscular system, the soft tissue matrix, and the air passages. These structures are so intricately interlinked that disturbances in the physiology, anatomy, or function of any one component structure are bound to cause an imbalance in the whole craniofacial complex. This understanding should be reflected in orthodontic diagnosis and treatment planning.

Concurrently, a thorough knowledge of subjects such as anthropology, genetics, growth and development, nutrition, psychology, endocrinology, and kinesiology can help us gather critical and essential data regarding the various aspects of general health and disease. Along with this knowledge, advanced biochemical, microbiological, and radiological investigative procedures can help optimally diagnose a malocclusion, thus reducing the chances of treatment failure. In brief, a comprehensive approach toward diagnosis and treatment planning helps categorize patients according to their general health status and biological limitations, and increases the probability of a successful treatment outcome.

The first interaction with the patient

The initial examination is the most overlooked step as far as orthodontic diagnosis is concerned. Planning for an orthodontic examination should begin even before the patient visits the orthodontic office, through careful screening via a telephone conversation with trained office personnel, or through emailing the patient's knowledge of their medical history to the orthodontic office before the scheduled appointment. This preliminary review will often highlight critical medical conditions such as endocrine, hematological, cardiac, renal, hepatic, pulmonary, and allergic disorders, as well as dental health-related conditions. Such information is vital for the orthodontist to prepare for the appointment and plan various investigative procedures and anticipated referrals, which can translate into increased efficiency and reduced time required for the screening and risk assessment of the patient. This strategy should ultimately lead to higher confidence levels and increased patient satisfaction, and lower chances of complications later during therapy.

Comprehensive diagnosis and treatment planning should start at the time of the first interaction with the prospective patient (Kharbanda, 2020). The short “look–see” examination is no longer considered adequate with the increasing number of patients with medical problems seeking orthodontic treatment. Therefore, at the first visit the orthodontist should enquire about the problems and what the patient and parents expect from orthodontic treatment (Figure 2.1) and concurrently perform an appraisal of the patient's psychological profile, as treating patients with unrealistic expectations or with extreme mood fluctuations may result in an unhappy ending (Al-Omiri and Alhaija, 2006). Following this initial scrutiny, a systematic examination procedure should be followed, starting with the craniofacial region. If the examination or the previous medical history indicates the presence of underlying pathology or abnormality, further investigations in the form of referrals and advanced diagnostic tests should be undertaken.

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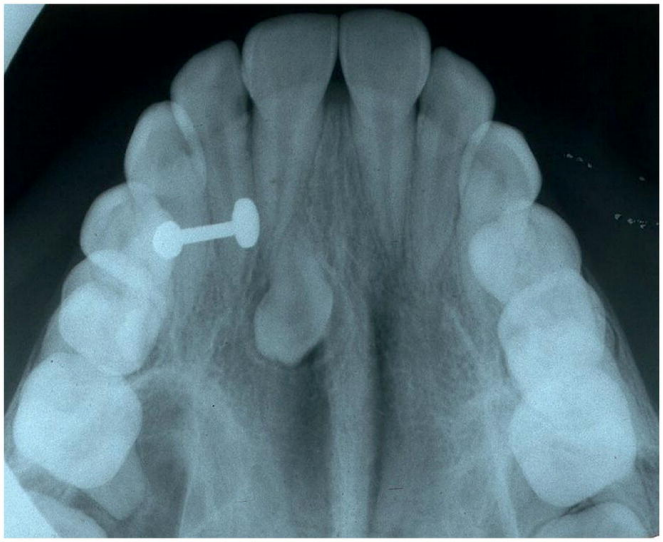
(b)

(c)



(d)

Figure 2.1 (a–d) A 12-year-old girl with severely compromised vision attended with her parents for protrusion of her upper anterior teeth and poor dental esthetics. She had a Class II malocclusion with bimaxillary protrusion and severe discoloration of the dentition due to fluorosis. The radiographic examination also revealed an inverted and unerupted mesiodens. The diagnosis and treatment plan in such a case must include evaluation of the patient's and parents' expectations in view of the reduced vision of the patient, who may not fully appreciate the benefits of improved esthetics following orthodontic treatment and correction of the discolored anterior teeth. It is also pertinent to elicit the intensity of concern in the patient and parents toward the discoloration and protrusion as well as the motivational factors with regard to treatment.

The importance of the medical history in orthodontic diagnosis and treatment planning

Many patients today would already be taking short- or long-term medications, which may influence paradental tissue remodeling (Krishnan et al., 2021) and, consequently, tooth movement. Drugs such as steroids, when taken for long periods as in chronic asthma or immunosuppression, may predispose teeth to iatrogenic root resorption following a mechanical stimulus (McNab et al., 1999). In certain instances, for example in the presence of sexually transmitted diseases such as human immunodeficiency virus (HIV) infection or syphilis, the patient may hesitate to give a complete and realistic history. Thus, it becomes the prerogative of the treating doctor to sufficiently evaluate the patient, both prospectively and retrospectively, to obtain a detailed health history during the first or subsequent visits. In this regard, the orthodontist and office personnel should judge the patient's mannerisms, attitude, and current health condition, and whether further investigations or precautions are warranted before or during treatment.

A detailed medical history is an extremely useful tool for evaluating the existing health status of an individual and identifying any medical disorders they may have. Diseases of chronic duration, those of severe intensity, those affecting bone metabolism, and those altering the inflammatory pathways have a particularly important

bearing on the orthodontic treatment plan (Sonis, 2004; Patel et al., 2009). Besides nutritional imbalances, developmental disorders, and skeletal malformations, chronic diseases, liver dysfunctions, renal impairments, cardiac and pulmonary anomalies, and erosive joint diseases can have impacts on physiological growth and, thus, orthodontic treatment (Table 2.1).

Table 2.1 Common causes of short stature.

Source: Adapted from: Lifshitz (2007); Crocetti and Barone (2004); Fujieda and Tanaka (2007); Matfin (2009).

Normal	
Constitutional growth delay	
Genetic/familial short stature	
Combined constitutional growth delay	
Pathological	
Nutritional	Micronutrient deficiency • Zinc deficiency • Iron deficiency Macronutrient deficiency: decreased intake • Hypocaloric diet • Kwashiorkor • Anorexia nervosa and other eating disorders • Nutritional dwarfing Macronutrient deficiency: reduced absorption • Inflammatory bowel disease • Celiac disease • Cystic fibrosis • Malabsorption

Endocrine	Hypothyroidism Isolated growth hormone deficiency Classic Neurosecretory Growth hormone insensitivity (insulin-like growth factor deficiency) Hypopituitarism Glucocorticoid excess Iatrogenic Cushing disease Precocious puberty
Chromosome defects	Turner syndrome Down syndrome Prader-Willi syndrome
Low birth weight short stature (intrauterine growth retardation)	Sporadic Characteristic • Russell-Silver syndrome • Cornelia de Lange syndrome • Seckel syndrome • Dubowitz syndrome • Bloom syndrome • Johanson-Blizzard syndrome
Defects in bone development	Achondroplasia/hypochondroplasia Chondrodystrophies Other skeletal disorders
Metabolic	Mucopolysaccharidoses Other storage disorders
Chronic diseases	Chronic renal disease Chronic liver disease Congenital heart disease (especially cyanotic conditions) Pulmonary (cystic fibrosis, asthma) Poorly controlled diabetes mellitus

	Chronic infections (including human immunodeficiency virus and tuberculosis) associated with birth defects or intellectual disability
Psychosocial deprivation	
Chronic drug intake	Glucocorticoids High-dose estrogens or androgens Methylphenidate Dextroamphetamine

Chromosomal aberrations and embryological defects, including deformities of the orofacial complex

The development of branchial arches relies on the contribution of endoderm, mesoderm, ectoderm, and neural crest cells that collectively interact to give rise to the skeletal, muscular, vascular, and nervous system elements of the craniofacial region (Frisdal and Trainor, 2014). In the fourth week of intrauterine life, the mandibular arch (also the hyoid and glossopharyngeal arches) forms discrete processes, which form the future maxilla and mandible. While the paired mandibular processes merge in the midline by the fourth week, the maxillary process continues to contribute to forming the secondary palate, the upper jaw, and lateral portions of the upper lip (Sperber et al., 2001). The period between the sixth and twelfth weeks of intrauterine life is critical for craniofacial development (Finkelstein, 2001), and anomalies during this period result in various craniofacial defects (these are covered in greater detail in Chapters 7–8). Most congenital disorders result from obscure etiology. However, in the light of newer research, many unknown causes have been identified, and now multifactorial etiology is considered the commonest cause of congenital defects, whereas isolated genetic defects have been described in 10–30% of cases (Kumar, 2008). Genetic inheritance can follow various patterns, from simple Mendelian inheritance to complex polygenic traits with variable penetrance and expression across generations. To

accurately diagnose the etiology of the condition and the inheritance pattern, the orthodontist has to identify the role of genetics and delineate it from the environmental influences. Familial comparisons, pedigree analysis, and sometimes a simple cephalometric analysis may be valuable tools in identifying and differentiating the role of genetic aberrations in the causation of these conditions.

Orthodontists often encounter conditions resulting from embryonic developmental defects, such as cleft lip and palate, hemifacial microsomia, maxillofacial dysplasias, vertical facial clefts, and micro/macrognathia. The orthodontist, as an active member of the craniofacial team, should be trained to recognize the features of congenital growth anomalies or genetically linked syndromes (Sennimalai and Singhal, 2022). A thorough extraoral and intraoral examination can reveal vital information about an underlying syndrome/congenital deformity (Tables 2.2–2.4 and Figure 2.2). Facial features such as sparse hair on the head, frontal bossing, depression of the nasal bridge, telecanthus, low-set ears, typical epicanthal folds, coloboma, external ear defects, and facial clefts are characteristic features seen in many craniofacial syndromes. It is important to note that many craniofacial deviations may be associated with systemic alterations, such as osteogenesis imperfecta with dentinogenesis imperfecta, or orofacial clefts, associated with velocardiofacial syndrome or Pierre Robin sequence. Early genetic testing can help plan the treatment strategy for these individuals, with the ultimate objective of improving their quality of life (Bartzela et al., 2017).

Table 2.2 Syndromes affecting the face and jaws associated with mandibular deficiency and Class II malocclusion.

Condition	Features	Etiology
Hemifacial microsomia (Goldenhar syndrome)	Unilateral dysplasia of the ear, hypoplasia of mandibular ramus, cardiac and renal abnormalities	Most cases sporadic; few familial instances; pedigrees compatible with autosomal dominant and recessive transmissions
Pierre Robin complex	Micrognathia; cleft palate and glossoptosis. This condition may occur as an isolated malformation complex or part of a broader pattern of abnormalities	Heterogeneous
Treacher Collins syndrome	Dysplastic low-set ears; down-slanting palpebral fissures; micrognathia	Genetic/autosomal dominant

Table 2.3 Syndromes affecting the face and jaws associated with midfacial deficiency and possible Class III malocclusion.

Condition	Features	Etiology
Apert syndrome	Craniosynostosis proptosis hypertelorism; down-slanting palpebral fissures; symmetric syndactyly of hands and feet	Genetic/autosomal dominant
Crouzon syndrome	Craniosynostosis; maxillary hypoplasia accompanied by relative mandibular prognathism; shallow orbits; proptosis	Genetic/autosomal dominant
Achondroplasia	Short-limbed dwarfism; enlarged head; depressed nasal bridge; lordosis; high palate	Genetic/autosomal dominant

Table 2.4 Syndromes associated with mandibular prognathism.

Condition	Features	Etiology
Basal cell nevus (Gorlin syndrome)	Macrocephaly; frontal and parietal bossing; prognathism; multiple jaw cysts; multiple basal cell carcinomas; bifid ribs	Genetic/autosomal dominant
Klinefelter syndrome	Mandibular prognathism; skeletal disproportion; gynecomastia; small testicles	Commonly XXY karyotype; XXXY and XXXXY also occur
Osteogenesis imperfecta	Fragile bones; blue sclera; deafness; mandibular prognathism	Autosomal dominant (common type)

In sum, an orthodontist should be able to identify severe conditions and make appropriate referrals to medical specialists or craniofacial and genetic centers while managing the less severe ones themselves, without inflicting further trauma on the psychological status of the already burdened patient.

Acute and chronic infections (systemic and local)

Various systemic diseases, and those locally affecting the craniofacial complex, have the propensity to contribute to the etiology of malocclusion, directly or indirectly, in both the prenatal and postnatal stages. Chronic systemic infections such as tuberculosis, hepatitis, nephritis, and HIV may indirectly contribute to malocclusion by disrupting systemic growth during childhood. Acute perinatal infections such as the TORCH complex (toxoplasmosis, other infections, rubella, cytomegalovirus, herpes simplex) can lead to congenital deformities in the offspring, including orofacial clefts. Diseases such as congenital syphilis, apart from systemic alterations, can lead to an array of orofacial malformations such as saddle nose, depressed nasal bridge, and hypoplasia of the molars and incisors.

Late postnatal or acute childhood infections can cause temporary cessation of tooth development, which may be evident as enamel hypoplasia (Figure 2.3). Antibiotics used to treat early-childhood infections may also contribute to the development of enamel defects (Faustino-Silva et al., 2020). In other instances, infections from distant foci, acute or chronic, may disseminate via blood and lodge in one of the jawbones, leading to osteomyelitis (Fabe, 1950; Carek et al., 2001) and consequent destruction of the bone architecture or growth disturbance. Involvement of the temporomandibular joint (TMJ), due to similar reasons or from a local spread of infections from adjacent structures, as in mastoiditis (Hadlock et al., 2001) or otitis media (Semlali et al., 2004; Prasad et al., 2007), can lead to arthrosis, adhesions, and regressive changes within the joint, which may affect growth and function of the mandible, resulting in malocclusion. The role of tonsillitis and rhinitis in the etiology of mouth breathing and the development of adenoid facies cannot be overemphasized. The resulting craniofacial disharmony and reduced upper airway are potent risk factors for developing obstructive sleep apnea (Neelapu et al., 2017).

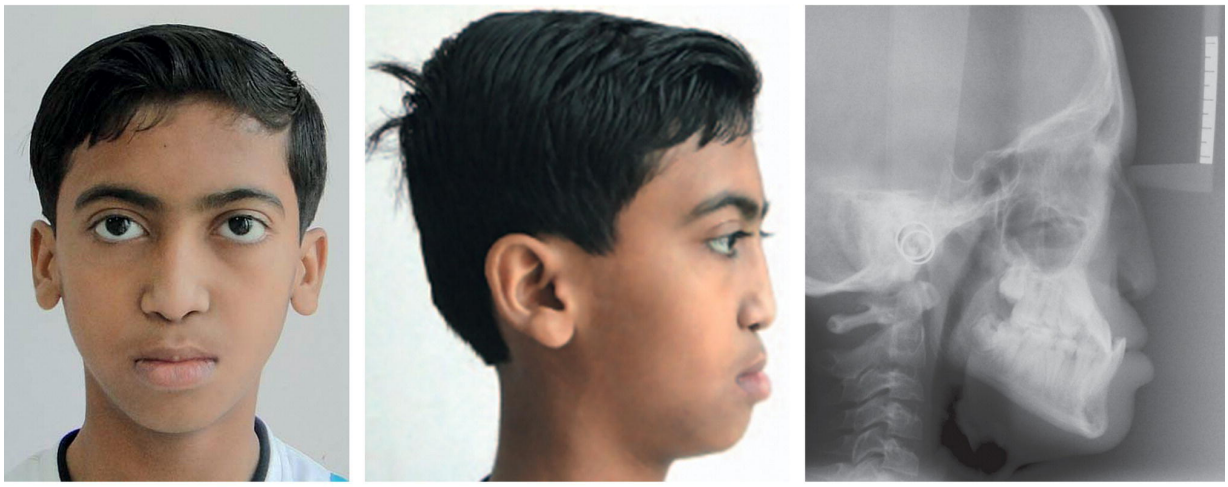


Figure 2.2 (a–c) Binder syndrome. This 11-year-old boy, who attended the orthodontic clinic for fixed appliance treatment, had a flat midface due to a retrognathic maxilla, broad flat nose, horizontal nostrils, short columella, and apparent lack of nasal bridge. The radiograph confirmed a short anterior cranial base, small cranial base angle, reduced sagittal depth of the nasopharynx, hypoplasia of the anterior nasal spine, downward inclination of the nasal bones, and extremely reduced sagittal maxillary length. The patient was diagnosed as having Binder syndrome after consulting with the oral medicine department, the differential diagnosis of which includes acrodysostosis and Stickler syndrome. Additional investigations may be required for differential diagnosis of the case from other similar conditions.

Figure 2.3 A 16-year-old female reported for treatment of anterior open bite. Intraoral examination revealed hypoplastic permanent maxillary and mandibular incisors, canines, and first molars, with characteristic defects only on the incisal/occlusal thirds. On detailed medical history, it was found that patient had recurrent episodes of upper respiratory tract infections during childhood and was treated with antibiotics. The hypoplastic teeth in this patient are possibly due the disturbances caused during the enamel matrix secretion phase of amelogenesis.

Deficiency states and malnutrition

The availability of essential nutrients profoundly influences craniofacial and dental development. Malnourished children tend to become disabled, incapable of resisting disease or withstanding its onset and progress. Animal studies have demonstrated that in rats fed on a low-calcium and vitamin D–deficient diet, the increase in body weight is impaired, and the craniofacial dimensions are reduced (Engström et al., 1982a, b). There is no general agreement on whether growth retardation during early infancy in humans is reversible in later years. Research findings on children surviving protein-calorie malnutrition (PCM) have shown that severe malnutrition early in life affects their postmalnutrition growth, with reduced height and head size (Krueger, 1969; Alvear et al., 1986). Other epidemiological studies have shown that catch-up growth after malnutrition compensates for previous growth retardation and results in normal stature for previously malnourished children (Garrow and Pike, 1967; Graham and Adrianzen, 1972). Dreizen et al. (1967) stated that chronic undernutrition in the presence of nutritional or metabolic disease slows the rate of skeletal maturation, delays the onset of menarche, and retards the epiphyseal fusion period.

These research findings may have diagnostic implications, wherein children with Class II malocclusion with nutritional deficiency could present with smaller physical and craniofacial dimensions in general. Those with unusual smaller dimensions may need to be discussed with a pediatrician and a nutritionist for their nutritional requirements, which might have a bearing on the quality of the

response to functional appliance treatment as well as on the tissue response during orthodontic tooth movement. Similarly, vitamin C (Litton, 1974) or D (Collins and Sinclair, 1988) deficiency may affect the remodeling response of the periodontal ligament and the alveolar bone to orthodontic forces. For a detailed description of how nutritional factors influence orthodontic diagnosis and treatment planning and how an orthodontist should obtain nutrition data from patients, see Chapter 6.

Endocrine and metabolic anomalies in the etiology of malocclusion

The endocrine system is an intricate network regulated by human physiological processes at various levels. This system is responsible for regulating the metabolic processes throughout the body, controlling the growth and differentiation of various parts of the skeleton. Hence, disruption of any part of this system may lead to widespread alterations of human physiology, resulting in metabolic, anatomical, or growth-related disturbances. Although a disturbance in virtually any part of the endocrine system would be expected to have orthodontic implications, disorders of the pituitary, thyroid, parathyroid, and pancreas are of particular interest to the orthodontist (Table 2.5). In many instances, an alert dental professional may be the first to suspect a systemic anomaly (Cohen and Wilcox, 1993; Vitral et al., 2006; Gosau et al., 2009), leading to the diagnosis of an underlying endocrine disorder.

Table 2.5 Common endocrinopathies encountered in orthodontic patients.

Source: Kamal et al. (2020) / Centre for Evaluation in Education and Science.

Condition	Significance	Comments
Diabetes mellitus	Periodontal disease	Monitor control of diabetes
Hyperthyroidism	↑ BMR, possible osteoporosis	Inquire about control of disease
Adrenal insufficiency	↓ Tolerance to stress, delayed healing	Inquire about steroid dosages
Osteoporosis	ONJ, delayed tooth movement	Inquire about medications
Osteopetrosis	↑ Bone mass, delayed dentition	Avoid orthognathic surgery
Vitamin D deficiency	Delayed eruption, dental abscesses	Inquire about nutritional disturbances
Fibrous dysplasia	Facial disfigurement, malocclusion	Consider delaying treatment

BMR, basal metabolic rate; ONJ, osteonecrosis of the jaw; ↑, increased; ↓, decreased.

Pituitary gland

The physical and mental development of a child is controlled to a great extent, apart from other genetic and nutritional factors, by the pituitary and the thyroid glands (Setian, 2007). Pituitary hormones control the functioning of various other endocrine glands, as well as the linear growth of the skeleton. Consequently, disturbances of the pituitary function (and that of the hypothalamus) are associated with the alteration of function of most other endocrine glands. Deficiency of growth hormone, one of the many hormones produced by the pituitary, is associated with reduced stature and reduced growth and development of the craniofacial complex and shortened cranial base length (Cantu et al., 1997; Van Erum et al., 1998). Patients also exhibited a reduced mandibular dimension, with a resulting

tendency to Angle's Class II occlusion, large overjet, and increased overbite (Torlińska-Walkowiak et al., 2021). Interestingly, it has been reported that dental age may not be retarded in growth hormone deficiency states (Van Erum et al., 1998). However, according to a systematic review, the dental age was delayed by about 1–2 years (Torlińska-Walkowiak et al., 2021). This discrepancy in results can be attributed to the use of different maturity indicators and nonstandardized definitions. With growth hormone administration, the daily rhythm of tooth formation or eruption remained unaltered (Davidopoulou and Chatzigianni, 2017). In conjunction with orthodontic treatment for growth modulation, hormone replacement therapy highlights the importance of interactive care (Davies and Rayner, 1995; Hwang and Cha, 2004; Zhang et al., 2020). On the other hand, growth hormone excess, which usually occurs secondary to a somatotrophic pituitary adenoma (Matfin, 2009), causes gigantism in childhood and acromegaly in adults. Any child or an adult who presents with unexplained gain in height or mandibular prominence should be suspected of gigantism (Yagi et al., 2004) and should be referred to an endocrinologist for further investigations and management. It is important to know that although gigantism/acromegaly typically occurs in isolation, it may be associated with other pathological endocrine conditions such as multiple endocrine neoplasia (MEN; Yagi et al., 2004; Accurso and Allem, 2010), McCune–Albright syndrome (MAS), neurofibromatosis, and the Carney complex (Eugster and Pescovitz, 1999). See Chapter 5 for a detailed description of these conditions.

Thyroid gland

The euthyroid state is essential for normal mental and skeletal development, maturation, and adult bone maintenance (Harvey et al., 2002; Murphy and Williams, 2004). Thyroid hormone has also been demonstrated to play a role in the maturation of teeth (Vucic et al., 2017). A hypothyroid state during pregnancy and early childhood results in various developmental disturbances and defects, including neurological deficits. Hypothyroidism (Figure 2.4) during pregnancy and early childhood causes intellectual disability, growth arrest, delayed bone maturation, and epiphyseal dysgenesis (Rivkees et al., 1988; Bassett et al., 2007). However, intellectual deficits may not be

marked in older children and adolescents, although the delay in skeletal maturation is evident. Orofacial alterations include enlargement of the tongue (Wittmann, 1977), delayed tooth eruption, the tendency for mouth breathing, Class II malocclusion due to a retruded mandible, short posterior facial height, and anterior open bite (Shirazi et al., 1999), all of which contribute to the development of malocclusion.

In contrast, juvenile thyrotoxicosis leads to accelerated growth and advanced bone age, but it also induces short stature due to premature fusion of the growth plates and craniosynostosis (Bassett et al., 2007). In adults, thyrotoxicosis accelerates bone loss, causing osteoporosis (Murphy and Williams, 2004), and even minor disturbances of thyroid status increase the risk of fractures (Bassett et al., 2007).

Due to early recognition of thyroid deficiency states, the classic manifestations of thyroid disease may not be evident in all individuals with thyroid disorders. Also, subclinical thyroid disease is being diagnosed more frequently in clinical practice in young and middle-aged people, as well as in the elderly, with a reported prevalence of 4–10% in the adult population (Canaris et al., 2000; Hollowell et al., 2002). Subclinical hyper- and hypothyroidism may have repercussions for the cardiovascular system, bone, and other organs and systems (Biondi and Cooper, 2008; Delitala et al., 2020). Hence, the clinician must be vigilant and informed to be able to suspect or diagnose underlying thyroid disease. For example, a lack of response to functional appliance treatment in a case of skeletal Class II malocclusion after a reasonable period and excellent patient cooperation may be because of an underlying growth hormone or a thyroid disorder. The literature supports the view that thyroid hormone replacement therapy results in rapid catch-up growth (Rivkees et al., 1988; Teng et al., 2004). It has been suggested that orthodontic treatment should be combined with hormone replacement therapy for optimum results (Verna et al., 2000).

(a)

(b)

(c)

Figure 2.4 (a, b) Intraoral views and (b) radiograph of an 18-year-old girl diagnosed with hypothyroidism show delayed eruption of multiple teeth.

Pancreas

Diabetes mellitus, a disorder of carbohydrate, protein, and fat metabolism due to an absolute or relative deficiency of insulin, is one of the commonest metabolic disorders. The disorder, especially when poorly controlled, leads to widespread changes such as nephropathy, neuropathy, retinopathy, and vascular disease, as well as cardiovascular and cerebrovascular complications, among other possibilities (Vernillo, 2001). Uncontrolled diabetes predisposes to severe and rapidly progressive periodontal disease, osteoporosis, and increased propensity to infections, all of which can be factors in the etiology of malocclusion. It can also alter the timing of tooth eruption, causing accelerated development until about 10–11 years of age and delayed development after that (Adler et al., 1973; Orbak et al., 2008). In addition, diabetes is also associated with an exaggerated inflammatory response during normal tooth eruption (Orbak et al., 2008), xerostomia, burning mouth syndrome, candidiasis, delayed and abnormal wound healing, diminished salivary flow, and salivary gland enlargement. A systematic review of animal studies has shown that diabetes mellitus may adversely affect bone remodeling and tooth movement during the application of orthodontic forces (Najeeb et al., 2017). A child or adult with symptoms of dry mouth/burning sensation, ketone smell from the mouth, unusual intensity of periodontal breakdown, and inflamed gingivae with pockets should raise the suspicion of underlying diabetes mellitus (Lamster et al., 2008).

Neuromuscular disorders in the etiology of orthodontic problems

The influence of neuromuscular harmony on dental development, occlusion, and functions such as mastication, deglutition, speech, and respiration is well established. Animal studies have confirmed alteration in the craniofacial skeletal structures secondary to loss of muscle tone (Babuccu et al., 2009; Tsai et al., 2010). Consequently,

any degenerative or inflammatory disorder affecting the neuromuscular system can significantly influence the growth and remodeling of the dentofacial structures. Disorders such as chronic seizures, hemiparesis, and cerebral and cranial nerve palsies can cause alterations in muscle tone, leading to an imbalance of forces and consequent adaptation of the skeletal structures (Fong et al., 2003), including the craniofacial skeleton, with subsequent development of a malocclusion (Cascino et al., 1993; Trujillo et al., 2002; Portelli et al., 2009). Among the muscular dystrophies, Duchenne muscular dystrophy (DMD), an X-linked neuromuscular disease, is most common and characterized by progressive muscle degeneration and weakness. It has been shown to influence facial morphology, dental arch dimensions, and oral functions like mastication and speech (Egli et al., 2018). Similar characteristics have been reported in patients with spinal muscular atrophy (Pucciarelli et al., 2020). The consequences of orthodontic therapy are discussed in Chapter 14.

Seizure disorders, which are one of the most common neurological disorders with an incidence of 1–3% (depending on age; Annegers, 1997), can result in orofacial trauma (Sheller, 2004) and asphyxiation because of appliance aspiration during an episode of seizures. Patients with chronic seizures may manifest body asymmetry (Fong et al., 2003), including forehead and facial structures (Tinuper et al., 1992), altered mental status, and poor oral hygiene, while patients on long-term drug therapy may show gingival hyperplasia (Sheller, 2004) and bone mineral loss (Sheth, 2004). Moreover, hypercementosis, root shortening, anomalous tooth development, delayed eruption, and cervical lymphadenopathy have also been documented in patients with seizure disorders (Johnstone et al., 1999). Since orthodontic appliances often consist of a variety of metal fixtures, they can alter or distort the signals produced by magnetic resonance imaging (MRI) and computed tomography (CT) machines (Sadowsky et al., 1988; Sheller, 2004). It has been shown that stainless steel brackets show maximum signal distortion during MRI, whereas ceramic and polycarbonate brackets, and fiber-reinforced composite retainers, did not cause distortion. Ceramic self-ligating brackets with metal slots, titanium retainers, multistranded stainless steel retainers, and combinations of fixed

retainers caused minimal distortion (Neela et al., 2021). Hence, in patients with suspected organic lesions causing seizures who may require MRI or CT scanning, the presence of an orthodontic appliance may impede the imaging process, which needs to be considered while planning the treatment (Alqahtani, 2019).

Overview of systemic disturbances in relation to orthodontic treatment planning

Although the discussion of each disease or organ system is beyond the scope of this chapter, this section will briefly highlight the diseases affecting major organ systems and their implications for orthodontic diagnosis and treatment planning.

Psychiatric disorders

Most patients attending an orthodontic clinic are children and young adults at various stages of maturation, with rapid and drastic changes occurring in their minds and bodies. As a result, these patients are prone to developing psychological/psychiatric disorders. It is reported that up to 14–20% of American children and adolescents may develop psychiatric disorders (Cassidy and Jellinek, 1998). In addition, adults going through difficult phases of life may also develop psychiatric problems. Therefore, the orthodontist must be sufficiently conversant with psychology and any abnormal behavior that might point toward a psychiatric disorder or substance misuse.

The psychiatric disorders encountered most by orthodontists are either major depressive disorder (MDD) or attention deficit hyperactivity disorder (ADHD; Neeley et al., 2006a). Any history, sign, or symptom that points toward a psychiatric disorder or a sudden or unusual change in a patient's behavior during treatment requires discussion with the parents and the family physician, who may consider a consultation with a clinical psychologist/psychiatrist. In addition, patients with ADHD may be under treatment with amphetamines such as methylphenidate, which predisposes them to xerostomia, dysphagia, sialadenitis, stomatitis, bruxism, and growth disturbances (Elia et al., 1999). These possibilities have important

orthodontic implications, as noncompliance with the maintenance of oral hygiene, instructions in the placement of elastics at home, difficult behavior during orthodontic procedures, and missed appointments can lead to treatment failure.

Body dysmorphic disorder (BDD) is another spectrum of psychiatric disorder in which a person has an abnormal preoccupation with one or more perceived physical flaws that are not observable or appear slight to others. Individuals with BDD are likely to seek orthodontic or combination orthodontic and orthognathic surgery (Rosten et al., 2018; James et al., 2019). Therefore, pretreatment evaluation of the patient must include questions about prior or current illness and medication. In addition, any treatment plan should include a discussion with the treating psychiatrist, as discussed in Chapter 3.

Substance misuse is also a significant problem among adolescents, with a reported prevalence of up to 40% among tenth graders in the USA (Neeley et al., 2006b). In addition, intravenous drug users may have diseases transmitted through blood, such as HIV infection (Leukefeld et al., 1990) and hepatitis B (Gillchrist, 1999). Therefore, a suspected case may need to be referred to a medical specialist after consultation with a psychologist.

Diseases of the respiratory system

Diseases of the respiratory system can be broadly divided into those affecting the upper and lower airways. Diseases of the upper airway can be an outcome of anatomical, physiological, or pathological restrictions of airway space in the nose, pharynx, and larynx. Chronic restriction of the nasal airway due to sinusitis, tonsillitis, adenoiditis, and allergic rhinitis leads to mouth breathing and further to the classic adenoid facies, as well as a change in the craniofacial flexure. Disorders of the lower airway, such as asthma, chronic bronchitis, and other chronic pulmonary diseases, increase the breathing effort, and affected cases may display orofacial changes like those seen with mouth breathing, apart from consequences related to impaired general health due to low oxygenation of the blood. Moreover, children with severe asthma may be using oral or inhaled steroids, which may cause a reduction in the salivary flow (Laurikainen and Kuusisto, 1998), predisposing them to oral candidiasis and increased

risk of root resorption (Davidovitch and Krishnan, 2009). However, a recent systematic review contradicted the increased predisposition to orthodontically induced root resorption (OIRR) in individuals with asthma or allergies. Other factors such as uniradicular teeth and longer treatment duration were attributed to increased risk of OIRR (Dos Santos et al., 2021). On the other hand, there is strong evidence of the association between asthma and periodontal destruction, especially gingivitis (Moraschini et al., 2018; Ferreira et al., 2019). A proper consultation with a pulmonologist is essential while treating these patients so that any complications that may develop during orthodontic treatment can be effectively managed.

Diseases of the cardiovascular system

Patients with congenital heart disease and valvular defects often have poor general health, retarded physical growth, and increased susceptibility to infections, such as infective endocarditis, and are at a high risk of bleeding (if on anticoagulants). In general, patients with mild valvular dysfunction can tolerate dental procedures well, but patients with mitral regurgitation are particularly susceptible to exacerbation of pulmonary oedema and acute shortness of breath (Warburton and Caccamese, 2006).

Infective endocarditis

Infective endocarditis is a serious condition with an incidence of 1.6–6.2 per 100 000 patients (Prendergast, 2006) and high annual mortality, approaching 40% (Cabell et al., 2002). Various dental and orthodontic procedures predispose the patient to systemic bacteremia, which may lead to episodes of infective endocarditis in the presence of predisposing cardiac defects. Therefore, any patient prone to infective endocarditis should be considered for treatment only after consultation with the treating physician. Although the need for routine antibiotic prophylaxis against infective endocarditis in dental procedures remains controversial (Gould et al., 2006), the use of prophylactic antibiotics in high-risk cases (Task Force on Infective Endocarditis, 2004) is still advisable for procedures likely to cause bacteremia. However, procedures that involve manipulation of gingival tissue or the periapical region of teeth or breach of the

oral mucosa may require antibiotic prophylaxis. Some high-risk procedures are placement of separators, orthodontic bands, suture removal, biopsies, and extractions (Vandersluis and Suri, 2020). If a patient develops symptoms of infective endocarditis during treatment, immediate referral to a cardiologist is advisable.

Coronary artery disease and hypertension

Patients with angina or uncontrolled hypertension will be poor orthodontic patients because they are prone to cardiovascular accidents and stroke. In addition, many of these patients take antiplatelet and anticoagulant drugs, making them prone to bleeding. It must be kept in mind that patients with a history of hypertension are prone to episodes of hypertensive emergencies leading to cardiovascular or cerebrovascular accidents (Marik and Varon, 2007) and that certain conditions, such as adrenal tumors, Grave's disease, chronic renal disorders, and vascular disorders, are known to trigger hypertensive crises (Lip and Beevers, 2005). Hence, a complete medical evaluation and consultation with the patient's cardiologist are imperative during diagnosis and treatment planning.

Diseases of the gastrointestinal tract

The liver is the principal metabolic storehouse of the body and carries out many important functions such as synthesis of plasma proteins and clotting factors, bile formation, drug elimination and detoxification of many substances, and formation of urea. Liver dysfunction leads to multiple, widespread alterations in the body. Patients with chronic liver disease may have malnutrition and growth failure, oedema due to loss of plasma proteins, portal hypertension, variceal bleeding, hypersplenism, coagulopathy, and susceptibility to infections, as well as renal, pulmonary, and neurological complications. In addition, patients with a liver transplant may be under immunosuppressive therapy, side effects of which include osteoporosis and susceptibility to infections (Patel et al., 2009). Consequently, given such patients' compromised health status, a gastroenterologist's opinion must be sought before considering them for orthodontic treatment.

Viral hepatitis

Viral hepatitis is perhaps the most common cause of hepatitis worldwide and is caused by six distinct viruses: HAV, HBV, HCV, HDV, HEV, and HGV (Gillchrist, 1999). In the developed world, the major contributors are the viral vectors, which spread via blood or person-to-person contact. In contrast, in developing countries, water-borne and orofecal transmission also plays a significant role. The disease burden of viral hepatitis is considerable. A worldwide concern is the person-to-person transmission of viral agents, especially blood-borne ones such as HBV, HCV, and HDV. Healthcare-related transmission is an important source of new HBV infections worldwide (Centers for Disease Control and Prevention, 1989; Shepard et al., 2006). An orthodontist should be aware of the risks associated with the transmission of viral agents in the symptomatic and the carrier stages. Moreover, patients with viral hepatitis may be under treatment with antiviral agents such as ribavirin, lamivudine, adefovir, and tenofovir, which have side effects such as renal tubular injury and hemolytic anemia. Similarly, therapeutic use of biological agents such as interferon 2α may be associated with flu-like symptoms, leukopenia, thrombocytopenia, psychiatric disturbances, hearing loss, and alopecia (Sonneveld and Janssen, 2010).

Gastric pathologies

Gastric pathologies such as acute and chronic gastritis and gastroesophageal reflux may present with halitosis, which may or may not be accentuated by poor oral hygiene. Moreover, gastric upset leads to various oral changes, such as excessively coated tongue and enamel erosions secondary to acid regurgitation. Enamel erosions are particularly common in conditions such as gastroesophageal reflux disease (Daley and Armstrong, 2007), hiatus hernia, chronic alcoholism, and bulimia (Little, 2002).

Intestinal pathologies

Intestinal pathologies such as inflammatory bowel disease (ulcerative colitis, Crohn's disease) cause malabsorption and deficiency of important vitamins and minerals, for example iron and

vitamin B_{12} (Field et al., 1995). In addition, patients with inflammatory bowel disease may present with oral mucosal ulceration (which may be confused with aphthous stomatitis; Ruiz-Roca et al., 2005), denudation of the mucosa, and papillary/polypoid growths. It is estimated that approximately 10% of patients with inflammatory bowel disease may develop TMJ arthritis (Ruiz-Roca et al., 2005).

Renal diseases

The incidence of chronic renal disease is increasing worldwide (Ansell et al., 2002). Renal disease often results in a wide array of endocrine and metabolic anomalies, altered serum ionic balance, edema, uremia, hypertension, hyperactivity of the renin–angiotensin system, reduced erythropoietin levels, anemia, malnutrition, bleeding disorders, reduced immunocompetence, and osteodystrophy (Jaffe et al., 1990; Nadimi et al., 1993; Proctor et al., 2005). The oral findings in azotemia include stomatitis, candidiasis, xerostomia, gingivitis, and the classic uremic fetor (Kho et al., 1999).

Dental alterations also include localized radiolucent jaw lesions with or without a “ground glass” appearance, the classic “brown tumors” of hyperparathyroidism (Okada et al., 2000), and enlargement of the skeletal bases (Nadimi et al., 1993). Pathological mobility of the teeth (Carmichael et al., 1995), loss of lamina dura, delayed tooth eruption (Jaffe et al., 1990), and an increased incidence of noncarious tooth loss (Proctor et al., 2005) are other manifestations. Additionally, enamel hypoplasia of the primary and permanent teeth (Kho et al., 1999; Al Nowaiser et al., 2003) and narrowing or calcification of the pulp chamber of teeth in adults with chronic renal disease have also been reported (Nasstrom et al., 1985; Galili et al., 1991; Nasstrom, 1996). Patients with end-stage renal disease or transplants are usually on corticosteroid or immunosuppressant therapy, making them prone to systemic infections, gingival hypertrophy, and steroid-related iatrogenic root resorption (Colvard et al., 1986; Kennedy and Linden, 2000). All these pathological conditions, especially osteodystrophy, have profound effects on the orthodontic treatment plan and should be considered while formulating a treatment plan

for the individual patient. Successful treatment in such compromised cases has been reported (Walker et al., 2007).

Allergic disorders

Allergic reactions to natural rubber latex (NRL), metals such as nickel and chromium, acrylics and composites, and disinfectants are not rare in orthodontic offices. Two types of immunological reactions, type I (acute reactions, anaphylaxis) and type IV (delayed hypersensitivity; contact dermatitis) reactions, are especially important to the orthodontist. NRL, used in manufacturing gloves and oral elastics, induces allergic reactions in less than 1% of the general population, 5–15% of healthcare workers, and 24–60% of patients with spina bifida (Poley and Slater, 2000). NRL allergy can manifest as type I and type IV reactions, while metal allergies, such as nickel allergy, are often associated with type IV cutaneous reactions. The classic clinical pattern of nickel allergy is characterized by eczematous dermatitis in sites of direct contact with the metal (Tramontana et al., 2020). An orthodontist should be cognizant of the manifestations of these allergies and interact with a dermatologist or allergy specialist while treating a patient with known allergic tendencies or on the appearance of allergic symptoms. The allergy can be confirmed with a patch or skin test, and possible precautions can be taken thereafter to prevent the occurrence of such reactions.

Hematological disorders and blood dyscrasias

Hemoglobin synthesis disorders such as thalassemia, sickle cell anemia, nutritional-deficiency anemias, red blood cell (RBC) structural defects (e.g. spherocytosis, elliptocytosis), and enzyme deficiencies (e.g. glucose 6-phosphatase deficiency) may lead to repeated episodes of RBC destruction. Patients with thalassemia (Figure 2.5) usually present with poor general growth due to chronic anemia and hyperparathyroidism, apart from iron overload and the consequences thereof. Other problems that must be considered in such patients include the propensity for bleeding episodes, frequent infections, spontaneous fractures, and hepatosplenomegaly.

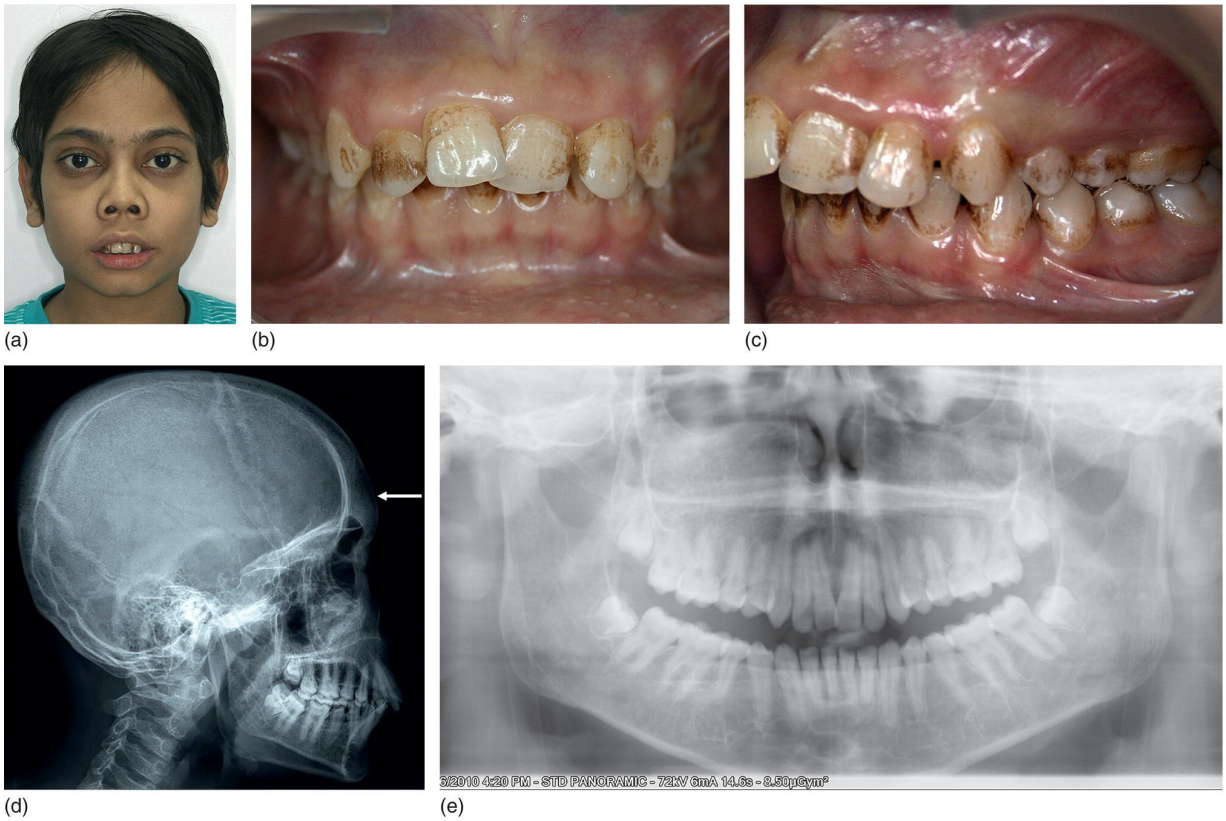


Figure 2.5 (a) Facial photograph of a patient with typical features of thalassemia intermedia: note the prominent midface region, frontal bossing, and convex facial profile due to maxillary excess, which is classically described as "chipmunk or rodent like." (b, c) Intraoral pictures show staining of teeth due to repeated bleeding episodes, Class II malocclusion, mild protrusion of anterior teeth, crowding, and deep bite. (d, e) Radiographs show typically widened diploic spaces of skull bones (arrow), trabecular rarefaction, loss of bone density, maxillary excess, and obliteration of the maxillary sinus due to erythroid medullary hyperplasia. The classic appearance is often described as "hair on end" or "chicken wire" appearance.

Sickle cell anemia

Patients with sickle cell anemia (Figure 2.6) usually have impaired growth, delayed maturation, excessive and recurrent hemolytic episodes secondary to sickling crisis, increased propensity to oral infections and jaw osteomyelitis, osteoporosis of bones, and altered splenic and liver function. They also show delayed teeth eruption and mostly exhibit a Class II skeletal base with vertical growth tendency

(Lopes et al., 2021). A sickling crisis can be precipitated by emotional and physical stress, sudden temperature changes, and hypoxia, among other causes. The associated pain in jawbones may be confused with pulpalgia. As a rule of thumb, extraction of teeth is contraindicated in such cases and, if it is planned at all, should be done after discussion with the patient's physician and the oral surgeon following evaluation of the coagulation function. Acetylsalicylic acid should be avoided as it interferes with platelet function, increases chances of gastric ulceration, and taxes the already stressed liver. Since such cases might have undergone multiple transfusions, precautions must be taken, considering the possibility of transmitting blood-borne infective agents.

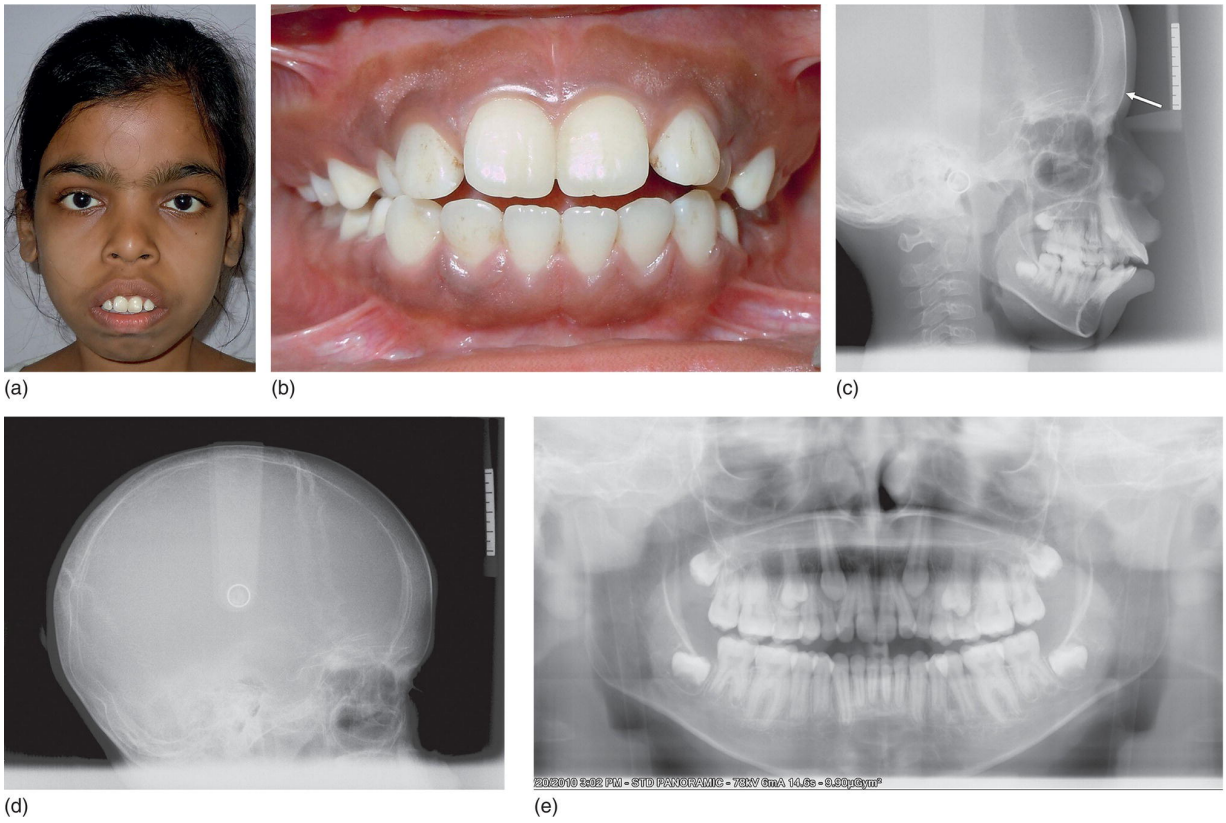


Figure 2.6 A 14-year-old girl with sickle cell anemia. (a) Note the frontal bossing, midface prominence, and icteric sclerae on the facial photograph. (b) The intraoral view shows an anterior open bite. (c) The lateral cephalogram reveals thinned out cortex (arrow) and developing bimaxillary protrusion. Also note the expanded maxillary bone due to medullary hyperplasia. (d) Widened diploic spaces are best recognized on a lateral skull radiograph. (e) The orthopantomogram also shows typical features secondary to marrow hyperplasia.

The compensatory extramedullary erythropoiesis commonly leads to widening bone marrow spaces and osteoporosis, causing craniofacial deformities such as frontal bossing, maxillary enlargement, and spacing of teeth. In addition, other dental anomalies such as dental hypoplasia and intrinsic staining of teeth are a direct consequence of the hemolytic episodes.

No high-quality studies recommend dental treatment, including orthodontic treatment in patients diagnosed with sickle cell anemia (Mulimani et al., 2019a) and thalassemia (Mulimani et al., 2019b). However, preventing complications is the best approach; therefore,

orthodontic treatment was only considered an elective procedure in these patients.

Leukemia

With advances in medical care children with childhood leukemia/lymphoma have improved life expectancy, and quite a few such patients in remission may seek orthodontic treatment. While planning their treatment, it must be realized that many of these individuals would have undergone total body irradiation (TBI) and a regimen of cytotoxic drugs. Consequently, secondary to excessive cellular destruction caused by the antineoplastic agents and due to leukemic infiltration of various organs by the blast cells, generalized growth retardation, bone osteoporosis, proneness to infections, bleeding episodes, salivary gland dysfunction, dental hypoplasia, reduction in root lengths, and delayed or non-eruption of teeth can be expected (Nasman et al., 1997; Michalak et al., 2019). In the light of such findings, growth modulation with functional appliances may have a guarded prognosis (Dahllof and Huggare, 2004). If fixed appliances are to be used, nickel-free brackets are recommended, since stainless steel brackets produce cytotoxicity by releasing free radicals (Alqahtani, 2019).

Conversely, a patient undergoing orthodontic treatment might be diagnosed as having a hematological malignancy (Isaac and Tholouli, 2008). In such cases, consultation with the oncologist would be required prior to any further orthodontic procedure because of the deranged physiological conditions.

Bleeding disorders

Bleeding disorders can lead to episodes of acute blood loss following minor trauma from orthodontic appliances. The pathophysiology underlying any bleeding disorder is usually related to disorders of the vessel wall, platelets, or the coagulation cascade. Among the inherited bleeding disorders, von Willebrand disease is the most common type, followed by hemophilia A and B, accounting for 95–97% of all inherited deficiencies of coagulation factors (Tuddenham and Cooper, 1994; Mannucci et al., 2004). Irrespective of the origin of the disorder, a clinical assessment of the severity of bleeding is

important (Favaloro, 2006; Quiroga et al., 2007) for clinical risk assessment, while advanced tests such as specific factors or component assays may be used for the identification of the underlying disorder. Interestingly, many patients with mucocutaneous bleeding may not show evidence of a diagnostically identifiable disease (Favaloro, 2007; Quiroga et al., 2007). Another important consideration in patients with known coagulation disorders is the probable history of blood product infusion and the consequent risk of viral infections such as hepatitis or HIV. This probability is not only valid for patients with a history of transfusions during the mid-1980s, when virus inactivation procedures for plasma were not in place (Brewer and Correa, 2006), but also for patients undergoing frequent transfusions, because blood transfusion from an infected patient in the window phase is usually difficult to screen for infections, which then often go unnoticed (Jayaraman et al., 2004).

Removable appliances may cause gingival irritation and should be avoided in patients with bleeding disorders. In the case of fixed appliances, nonextraction therapy, bonding over banding, self-ligating brackets, or ligation with elastomeric rings is preferred (Alqahtani, 2019).

Identifying local dental abnormalities before attempting orthodontic treatment

For the uninformed orthodontist, the intraoral examination would start and end with the classification of malocclusion and evaluate the patient for either extraction or nonextraction therapy. In such hasty and superficial assessments, recognizing localized aberrations of the dentition as contributing factors to the etiology of the malocclusion may go unnoticed. A routine examination of the soft and hard tissues is necessary to identify lesions so that differentiation between infectious diseases, noninfectious diseases, and other mucocutaneous lesions can be made. This knowledge would aid in deciding whether orthodontic treatment can be provided without further delay or if a referral to a specialist is necessary prior to orthodontic therapy. Hence, an oral examination, in an orderly

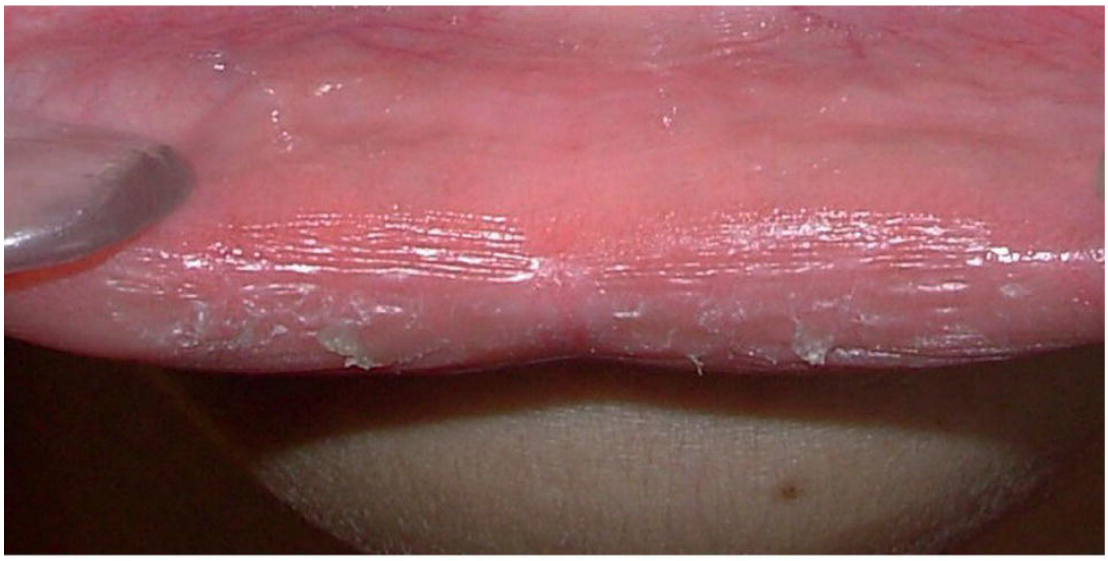
fashion, is imperative for a thorough evaluation of existing conditions and their optimal management.

The intraoral examination should be done in two phases. First, the soft and hard tissues, both in and around the oral cavity, should be evaluated with an overall view to ruling out the presence of any systemic or syndromic conditions, followed by an examination of each tissue individually in detail. The examination should start with a visual screening of the oral soft tissues, such as the vermilion area, lips, buccal mucosa, faucial pillars, tongue, and gingivae, for any physiological or pathological changes, such as discoloration, erythema, petechiae, abnormal keratinization areas, swellings, and sinus tracts. This exploration should be followed by a systematic evaluation of the hard tissues, namely the teeth, for the number, shape, and size, color, and quality of tooth material in each arch. Following the intraarch examination, an interarch examination should evaluate the occlusion, both dynamic and static, and the relation of the dentitions to each other. The intraoral examination should be supplemented by a radiographic examination of the jawbones and clinical and radiographic evaluation of the TMJ. Further advanced investigations should be conducted as and when deemed necessary.

Examination of soft tissues

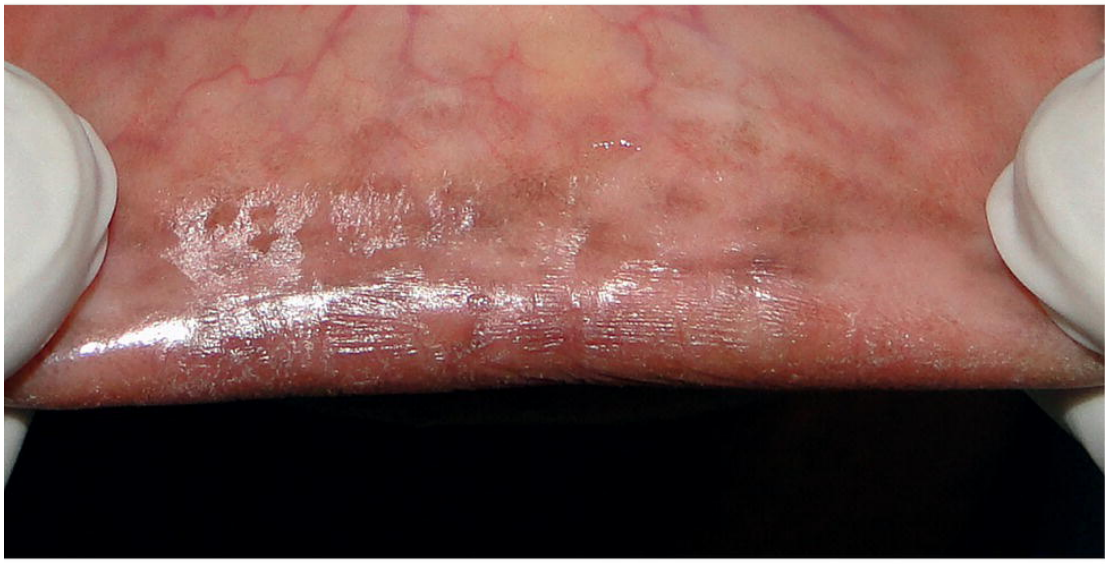
The presence of patching or crusting on lips or the perioral region may indicate dehydration; a mucosal, dermal, or mucocutaneous disease; or be a manifestation of an underlying systemic disorder (Figure 2.7). Nonerythematous pigmentation of the perioral region and the oral mucosa (Kauzman et al., 2004) may be seen in systemic disorders, such as hereditary intestinal polyposis, Gardner syndrome, Addison disease, heavy metal-induced discolorations, smoker's melanosis, and skin diseases. Erythematous pigmentation of the mucosa would usually indicate a hematological or bleeding disorder, a hemangioma, traumatic injury, or infections, among other possibilities. Erythematous spots on the buccal mucosa or palate may also be seen during the prodromal or initial phase of measles (Koplik spots) or chickenpox, while intraoral petechiae may

be seen in viral diseases such as infectious mononucleosis and dengue fever.



(a)

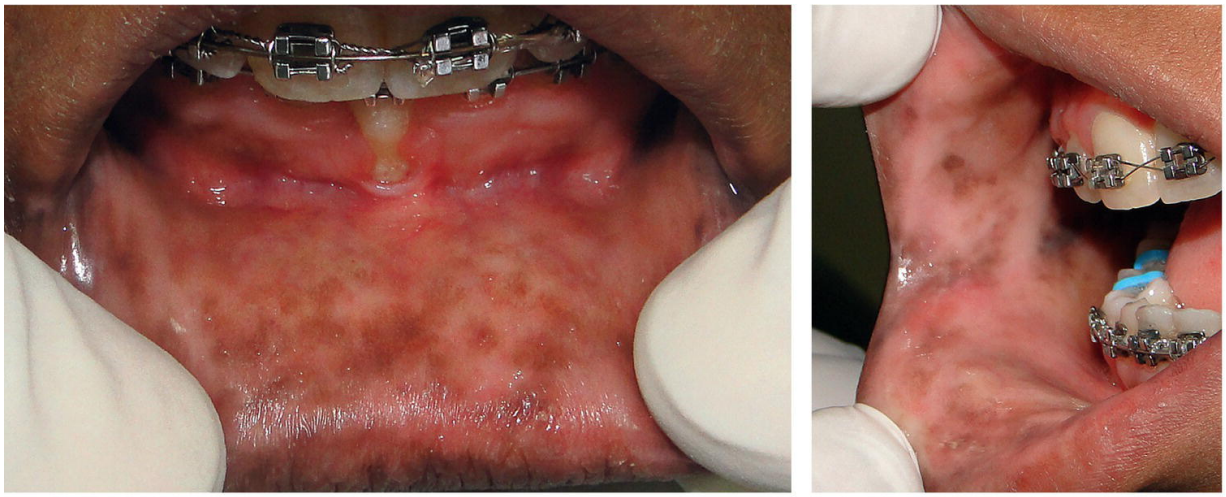
(b)



(c)

Figure 2.7 Crusting of the lips. (a) This crusting was the result of chronic lip separation at rest secondary to chronic mouth breathing. (b, c) Lip crusting due to oral mucosal disease, which makes referral to an oral pathologist necessary.

Localized white or red mucosal patches in the oral mucosa (Figure 2.8) might occur in a variety of conditions such as erythroplakia, leukoplakia, intraoral hemangiomas, traumatic injuries, bleeding disorders (Jolly, 1977; Castellanos and Díaz-Guzmán, 2008), various systemic conditions such as vitamin or mineral diseases, endocrine disorders, and skin diseases such as lichen planus, pemphigus, and white sponge nevus (Rajendran, 2009). Since quite a few of these lesions may have carcinogenic potential (Suter et al., 2008), additional history taking and evaluation in the form of a biopsy should be conducted, along with evaluation by an oral pathologist. In addition, care must be taken to dissociate such lesions from physiological variations such as Fordyce granules and lesions of minor significance, such as those due to chronic cuspal trauma, manifesting as white streaks on the buccal mucosa in the premolar–molar region.



(a) (b)

Figure 2.8 (a, b) Oral lesions in two patients that developed during orthodontic treatment. Such lesions must be investigated further for the causative factors, including allergy to orthodontic materials, before continuing with the orthodontic treatment.

Discoloration of the oral mucosa is seen in several systemic diseases, for example jaundice, heavy metal poisoning, and hypervitaminosis A (Daley and Armstrong, 2007), or as local lesions, such as amalgam tattoos and pigmented nevi. Rarely does the rapid increase in size or pigmentation of a hyperpigmented nevus indicate developing malignant melanoma (Hicks and Flaitz, 2000). Localized areas of desquamation or ulceration may occur in conditions such as burns (Figure 2.9), allergic reactions (Franz-Montan et al., 2008), and infections such as acute necrotizing ulcerative gingivitis, or secondary to systemic influences such as hormonal imbalances, skin diseases, and drug reactions. Persistent nonhealing ulcers may point toward tuberculosis (Dixit et al., 2008) or even a malignancy (Al-Rawi and Talabani, 2008; Villa et al., 2010), which requires further consideration and referral.

(a)

(b)

Figure 2.9 (a, b) A patient with facial scars from burns, showing malocclusion secondary to fibrosis of the facial tissues, loss of tissue elasticity, and loss of lip seal.

Any intraoral swelling should first be visually inspected, followed by palpation to record the color, surface texture, consistency, tenderness, local discharge, and any associated draining sinuses. Lesions with a soft texture or consistency may be primary soft tissue pathology or the extension of infection/pathology from underlying hard tissues. Inflammation of the mobile mucosa is usually not very painful when compared with lesions of attached mucosa, which usually exhibit less swelling but are very painful. Long-standing soft tissue swellings or lesions may eventually develop fibrosis or associated draining sinus tracts. Lesions with a palpably hard surface usually indicate a central pathology (bony lesion). Care must be exercised to exclude developmental variations such as benign bony exostoses (tori) from other infective, benign, and malignant lesions. Since tissue enlargement, either bony or soft tissue, may be idiopathic, infectious, allergic, tumorous, secondary to systemic alterations, or just a physiological variation, it must be carefully evaluated to diagnose the nature and extent of the lesions with the help of appropriate referrals and judicious use of supplemental diagnostic tests.

(a)

(b)

Figure 2.10 (a, b) Anterior open bite caused by an enlarged and altered position of the tongue. Further investigation in the form of biopsy confirmed the diagnosis of lymphangioma of the tongue, which needed surgical resection. Appropriate referrals were consequently made before orthodontic intervention.

Tongue examination must include an assessment of its size, shape, position, and mobility. Macroglossia may be seen in conditions such as acromegaly, amyloidosis, and lymphangiomas (Figure 2.10), and an altered protrusive tongue position may be particularly noticeable in Down syndrome and other craniosynostosis syndromes. The alterations seen in the tongue in patients with gastrointestinal disorders are described earlier in this chapter.

Evaluation of the periodontal status and oral hygiene

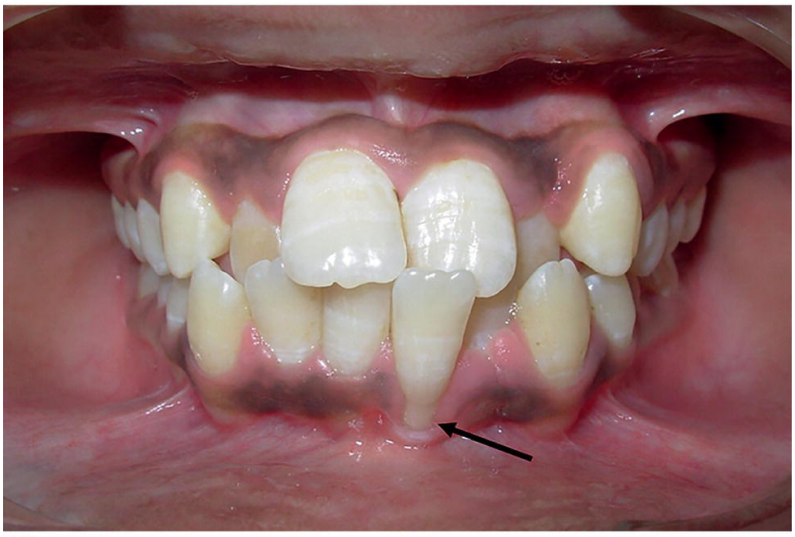
The oral hygiene status reflects many aspects of a patient's personality, physical health, and psychosocial condition. Patients with clinically evident depression or psychiatric disorders, low motivation, low awareness levels, physical deformities, or intellectual disability usually have poor oral hygiene. Certain patients, such as those with obsessive disorders and psychiatric tendencies, malingering or fictitious illness, may complain of nonspecific orodental pain or other oral health-related issues, even in its absence. Conversely, some patients are extremely conscious of their oral hygiene and might spend a lot of time and money to improve their oral health and dental condition in the hope that it may lead to changes in their personal or professional life. Extreme care should be exercised when dealing with such unstable personalities. Patients may also be poorly informed and unaware of the benefits of professional care. Even though such patients may present with suboptimal oral health, treating them would usually bring about a rapid and appreciable improvement in their oral health.

Following evaluation of the oral hygiene, a thorough periodontal examination of each tooth, along with charting all the pockets and lesions, should be mandatory. In cases with suspected periodontal bony lesions, the clinical examination should be supplemented with

a radiographic evaluation of the suspected areas. It must be remembered that, like other craniofacial structures, periodontal health is also governed by local and systemic factors. In a patient with severe generalized periodontitis, apart from local factors, one must look for underlying systemic influences such as diabetes mellitus, neutrophil chemotactic defects, vitamin deficiencies, and hormonal alterations. In contrast, patients with localized aggressive periodontitis usually have alterations in their microbiological flora around specific teeth, mostly the first molars and incisors. Areas of Stillman clefts (Figure 2.11), classically described as being related to traumatic occlusal loading, need consideration regarding the timing of the gingival graft before or after orthodontic treatment. All patients with pathological periodontal involvement require intensive periodontal therapy with the help of or by a competent periodontist before the onset of the planned orthodontic intervention.

Evaluation of the dentition

A planned sequence for examination of the dentition is preferred in the order described in the following. This examination starts with a note of the number of teeth present (both deciduous and permanent), the maturation status of the dentition, and the identification and number of missing teeth, followed by a note on the presence of dental abnormalities such as enamel defects, pathologies of individual teeth, color changes, attrition, irregularities in dental size or shape and pathological migration, and the presence of prosthetic devices.



(a)

(b)

(c)

Figure 2.11 Traumatic occlusion associated with an anterior crossbite. (a) Stillman's cleft in left lower central incisor (arrow). (b, c) Loss of tooth substance of anterior teeth and gingival recession of mandibular right central incisor.

Maturation of the dentition and its correlation with chronological age

This part of the examination is very important to gain insight into the existence of any developmental and growth-related problems (Figure 2.12). It is also essential to assess the status of unerupted teeth with respect to the formation of root/apex and to plan appropriate timing management strategies.

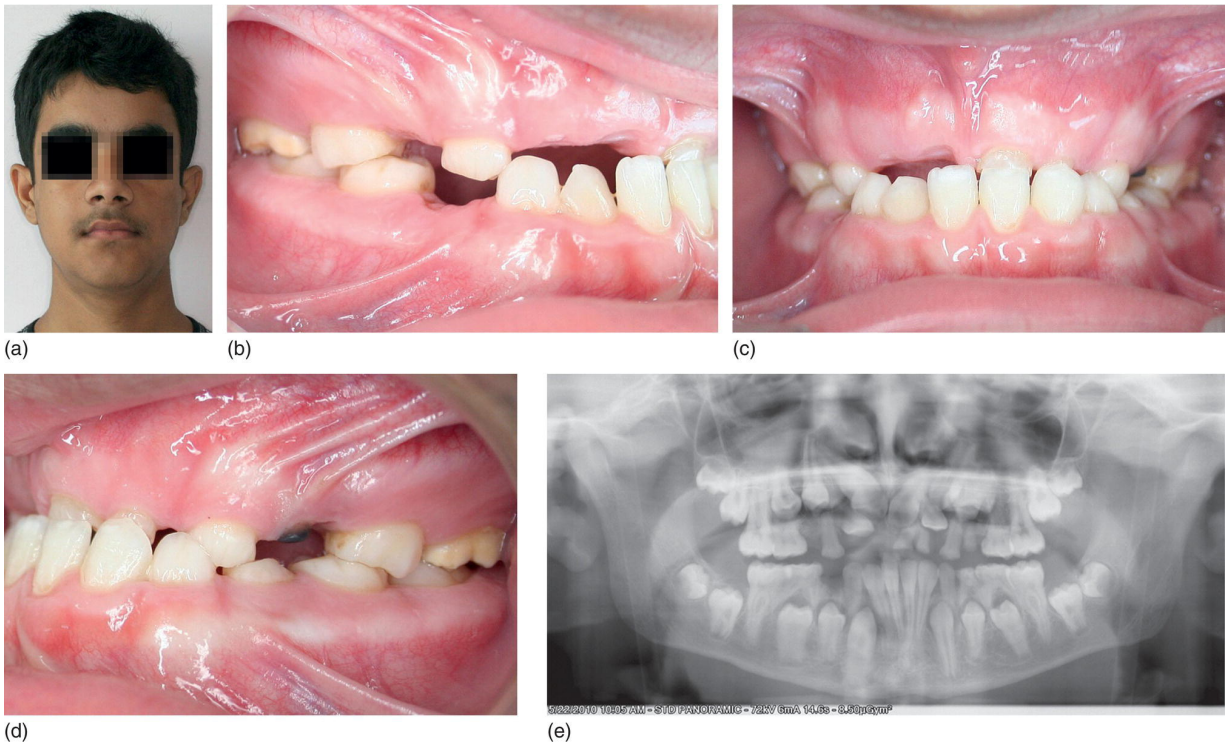


Figure 2.12 (a–e) A 13-year-old boy with delayed maturation of the dentition. Investigations revealed no apparent systemic problems. Note the excessive attrition of the deciduous teeth and the typical denture look during smiling due to hypodontia and loss of vertical dimension.

Changes in the number of teeth

Hypodontia and supernumerary teeth are common occurrences in permanent dentition, and both phenomena may occur as isolated events or as part of syndromes. The prevalence of hypodontia worldwide varies between 1.6% and 9.6% (excluding the third molar; Fekonja, 2005). As a rule, if a deciduous tooth is missing, its succedaneous counterpart would also be missing (Hall, 1983). In the permanent dentition, the most frequently missing teeth are the upper lateral incisor (Figure 2.13a,b) and lower second premolar (when the third molar is excluded; Figure 2.13c,d). As a rule, if only one or a few teeth are missing, the absent tooth will be the most distal tooth of any given type (Jorgenson, 1980). Interestingly, patients with generalized hypodontia may also manifest a tendency toward Class III malocclusion (Figure 2.14; Chung et al., 2000). Supernumerary teeth have a reported prevalence of 0.8% in primary dentitions and 2.1% in permanent dentitions (Brook, 1974). They may occur singly or as multiple teeth, unilaterally or bilaterally, may be erupted or impacted, and occur in one or both jaws (Figure 2.15a–c). Such teeth usually have a conical, tuberculate, supplemental, or odontoma morphology (Mitchell, 1996). They may be asymptomatic or may cause the failure of eruption of a permanent tooth, displacement of an adjacent tooth (Figure 2.15a), crowding, cyst formation, or, in rare cases, root resorption. The most common location is the anterior maxilla (Altug-Atac and Erdem, 2007), with mesiodens being the most common example (Basdra et al., 2001).

Dental caries and associated morbidity

A complete charting of the carious teeth should be done in an orderly fashion. The extent and location of the carious lesions can give an insight into the oral health status, the susceptibility of the individual to caries attacks, and their dietary habits. Patients with learning disabilities, salivary gland dysfunctions, and low motivational levels usually experience increased caries incidence. Loss of tooth structure leads to migration of teeth, which is associated with loss of arch length or supraeruption of an opposing tooth (Figure 2.16). Similarly, an extension of caries to the periapical region can lead to localized destruction of the alveolar bone, root resorption, and osteomyelitis in susceptible cases. In certain instances, the health

status of a tooth's crown or root may influence the decision to extract teeth for orthodontic treatment (Figure 2.17). Patients with increased caries susceptibility may require posterior bitewing examination at 6–12-month intervals until no new or active lesions are apparent if proximal surfaces cannot be examined visually or with a probe (American Academy of Pediatric Dentistry, 2021; European Commission, 2004). Additional consultation from a pediatric dentist/endodontist may be sought to manage these patients properly. Moreover, many patients with this tendency may be good candidates for applying caries-protective varnishes, which would require interaction with a pediatric/community dentist. Interestingly, fluoride varnish and sealants have not been shown to reduce the attachment bond strength (Kimura et al., 2004; Bishara et al., 2005; El Bokle and Munir, 2008; Keçik et al., 2008).

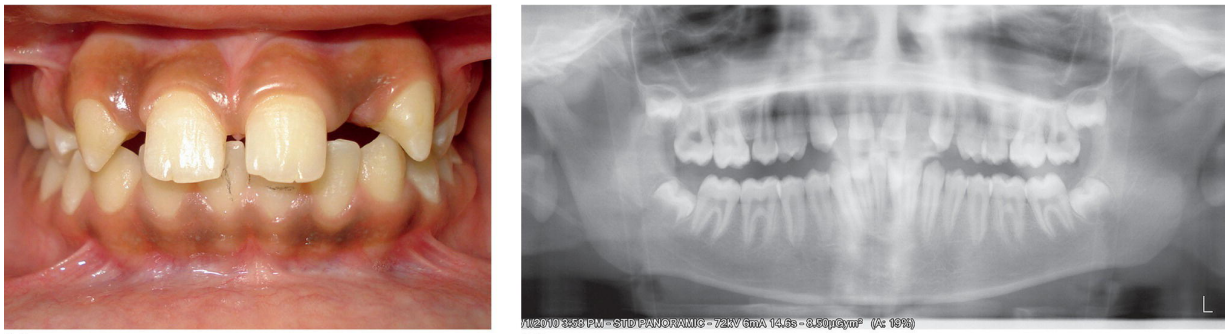
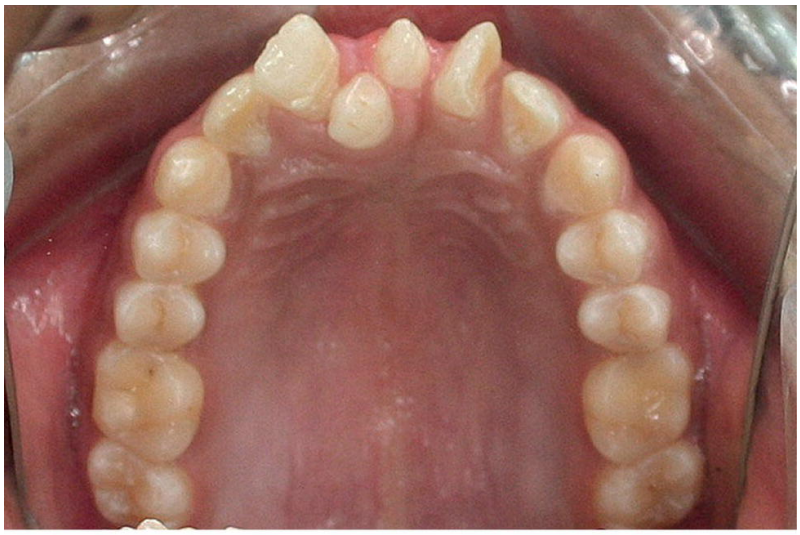


Figure 2.13 Hypodontia. (a, b) Bilateral congenitally missing maxillary lateral incisors. (c, d) Congenitally missing mandibular right second permanent premolar and an overretained deciduous second molar.

Figure 2.14 (a–e) Hypodontia of the maxillary and mandibular dentition with a typical Class III presentation. Also note the microdontic maxillary lateral incisors.

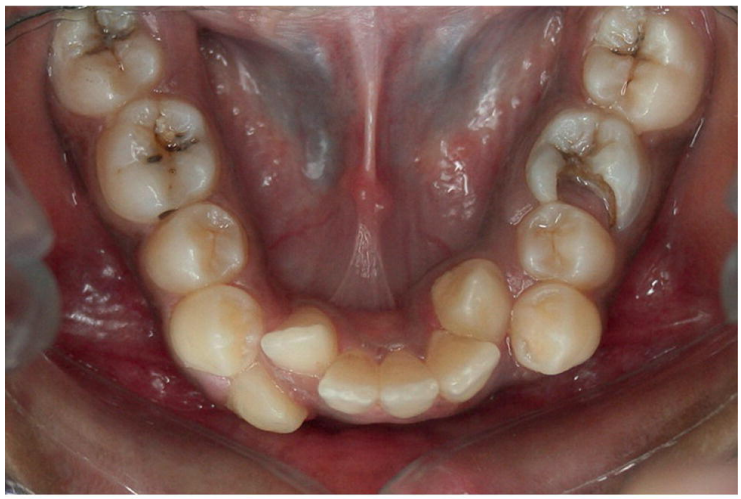


(a)

(b)

(c)

Figure 2.15 Supernumerary teeth. (a) Bilateral mesiodens causing malalignment of the maxillary central incisors and (b) trauma to the periodontium of the mandibular central incisors. (c) Supernumerary tooth in relation to a maxillary premolar.



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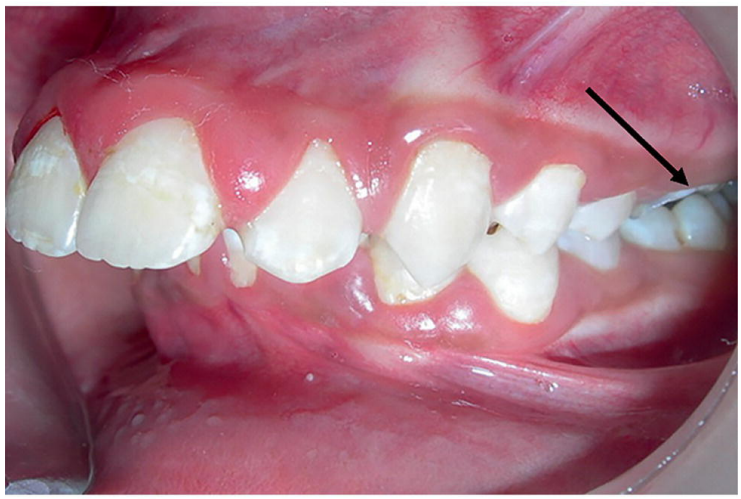

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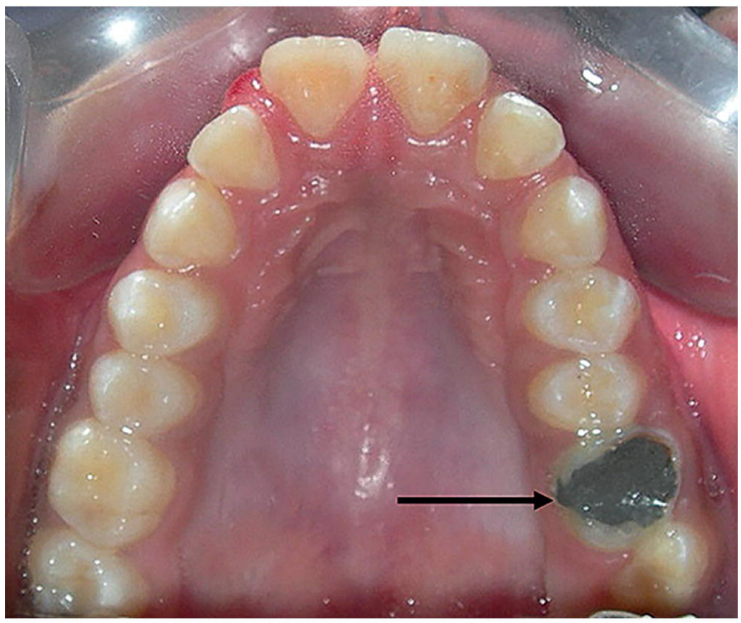


(c)

Figure 2.16 Loss of arch integrity due to caries. (a) A nonrestored mandibular left first molar has led to mesial migration of the molars. (b, c) The poorly restored occlusal surface of the maxillary left first molar (arrow) has allowed the lower molar to supraerupt.

(a) (b)

Figure 2.17 (a, b) A case with bimaxillary protrusion and an endodontically treated upper left central incisor. The radiograph reveals a poorly developed root of the concerned tooth, which makes the long-term prognosis of the tooth uncertain and its response to orthodontic forces unpredictable. The extraction plan in such patients may be modified to extract the tooth with a poor prognosis (i.e. the incisor) instead of a healthy premolar. Also note the crown dilaceration of the lower right central incisor.

Anomalies of size

Microdontia (Figure 2.18) is a relatively common condition affecting the permanent dentition and has a reported prevalence between 0.8% and 8.4% in various populations (Neville et al., 2005; Guttal et al., 2010). It most commonly affects the maxillary lateral incisors, apart from the third molars. In contrast, macrodontia is a relatively rare condition of permanent dentition. True generalized macrodontia is observed only in pituitary gigantism and pineal hyperplasia (Neville et al., 2005), while localized macrodontia is seen in conditions such as unilateral facial hyperplasia, hemifacial hypertrophy, and oculofacial-cardio-dental syndrome

(Turkkahraman and Sarıoglu, 2006). Both microdontic and macrodontic teeth contribute to Bolton discrepancy, thus creating treatment finishing and esthetic problems (Figure 2.19).

Anomalies of shape

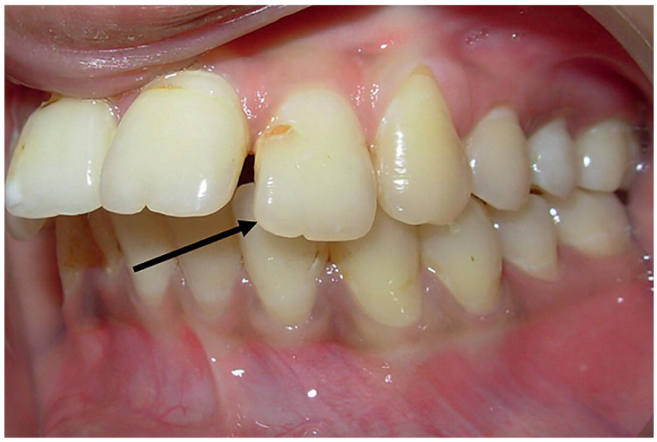
These include dens invaginatus, dens evaginatus, talon cusps, gemination, fusion, root dilacerations, taurodontism, and concrescence. Size and shape changes may be related to genetic influences or systemic conditions such as malnutrition or endocrinopathies, systemic fluorosis, infectious diseases such as congenital syphilis and rubella, local infections (Turner hypoplasia), trauma, or mechanical obstruction leading to dilacerations. Dens invaginatus has a population prevalence between 0.25% and 5.1% (Mupparapu and Singer, 2004) and is usually seen in the maxillary lateral incisor region. Talon cusp (Figure 2.20) has a prevalence of 1–8% (Dash et al., 2004), and again the maxillary lateral incisors are most affected, followed by the central incisors and canines. Talon cusps can lead to occlusal interferences, thus impeding the achievement of an ideal overjet and overbite and compromised esthetics, caries and periapical pathologies, and periodontal problems (Juan and Jiménez-Rubio, 1999). Similarly, fusion and gemination (Figure 2.21) can affect esthetics and may lead to dental crowding. The management concerns include esthetics and asymmetric tooth material, as well as reshaping after intentional endodontic therapy or prosthetic rehabilitation.

(a)

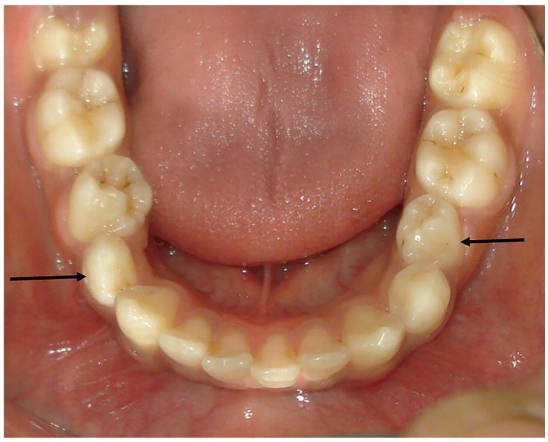
(b)

(c)

Figure 2.18 (a–c) A malformed maxillary right lateral incisor with associated canine impaction. The occurrence of malformed laterals is well known in cases of maxillary canine impaction. Also note the supraeruption and the distal inclination of the crown of the maxillary right central incisor due to the pressure on the root from the impacted canine.



(a)



(b)

Figure 2.19 Abnormal size and shape of teeth (arrows). During orthodontic finishing, problems can be anticipated with (a) esthetics and overjet-related issues and (b) intercuspation.

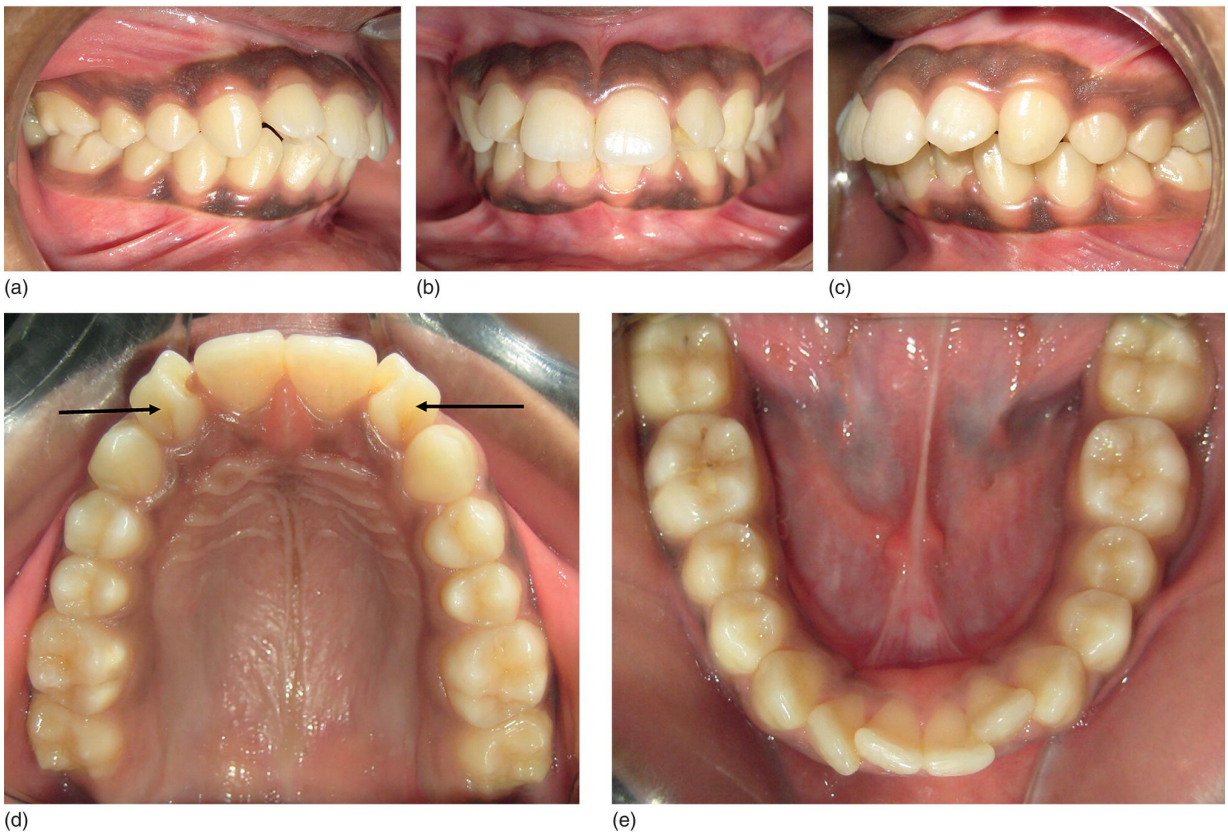


Figure 2.20 (a–e) Bilateral talon cusps on the maxillary lateral incisors (arrows) leading to protrusion of the affected teeth and lingual displacement of the lower incisors. An endodontist should be consulted before the reduction of talon cusps due to the risk of pulp exposure.

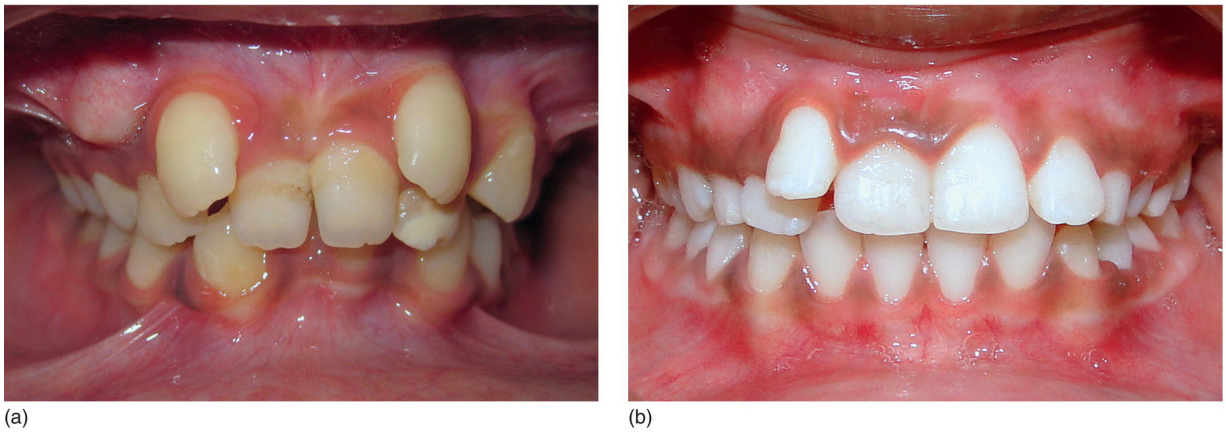


Figure 2.21 Two cases of dichotomy of maxillary lateral incisors. (a) Bilateral dichotomous maxillary laterals and (b) dichotomous right maxillary lateral incisor. The decision regarding the choice of tooth to be extracted should be based on tooth crown morphology, root morphology, bone support, and location of the tooth. Such cases should undergo a thorough radiographic evaluation for investigating the presence of any other supernumerary teeth, erupted or impacted.

Change in color

Systemic disorders such as porphyria, jaundice, heavy metal poisonings, systemic fluorosis (Figure 2.22), vitamin deficiencies, and drugs such as tetracycline (Figure 2.23) can lead to discoloration of teeth (Vogel, 1975; Sulieman, 2005). In addition, local conditions such as traumatic injuries, bacterial pigments, chemicals like chlorhexidine, internal resorption, and pulp calcification can lead to changes in the color of teeth. The orthodontic implications of these findings include the difficulty in bonding to these surfaces and the susceptibility of roots to the resorption process because of underlying defects.

Disorders of eruption

Infraocclusion may occur due to ankylosis, hypercementosis, mechanical obstruction, and habits such as tongue thrusting. Generalized failure of eruption is rare and is seen as part of hypophosphatasia and primary failure of eruption (PFE; Figure 2.24). PFE is a unique genetic condition characterized by a lack of inherent potential for the eruption of teeth. The first and second molar teeth are the most affected (Ahmad et al., 2006). Clinically, the condition presents characteristic features such as generalized lack of contact on posterior teeth, posterior open bite, excessive attrition of anterior teeth, canting and asymmetry of occlusal plane, multiple hypercementosis of teeth, and typical changes in the morphology of the mandible. The hallmark feature of PFE is the bilateral infraocclusion of the posterior teeth. If a patient is affected by PFE, all teeth distal to the most mesial affected tooth are also usually affected (Hanisch et al., 2018). Clinically, an infraerupted tooth would characteristically show a difference in the level of marginal ridges compared with the adjacent teeth, and the opposing

tooth would tend to supraerupt due to loss of occlusal contact. These factors lead to an imbalance of occlusal forces, anteroposterior space problems, and periodontal problems.

Regressive alterations of teeth

Teeth should be inspected for the presence of any attrition, abrasion, or erosions. Although some amount of attrition in the deciduous dentition and old age is expected, excessive attrition should be particularly investigated (see Figure 2.11). Generalized wear or loss of enamel in the deciduous and permanent dentition may be because of defective dental hard tissue development in conditions such as amelogenesis imperfecta (Figure 2.25; Crawford et al., 2007), dentinogenesis imperfecta (Barron et al., 2008), and dentine dysplasia (Barron et al., 2008), while generalized attrition in adults may be indicative of bruxism. Localized attrition may occur because of traumatic occlusion, excessive occlusal loading, and improper restorative or prosthetic appliances. Abrasion of teeth and cervical abrasion may occur with long-term use of abrasive toothpaste, tooth powder, or faulty brushing technique (Litonjua et al., 2003). Cervical abrasion may also occur due to abfraction (McCoy, 1982), which should alert the orthodontist to manage occlusal forces. Erosion of teeth may occur in chronic exposure of enamel to acidic substances. Excessive consumption of citrus fruits, gastric reflux disease, and diseases such as anorexia nervosa and bulimia nervosa may contribute to the etiology of the problem (Daley and Armstrong, 2007).

Figure 2.22 (a–d) Various grades of tooth discoloration due to systemic fluorosis.

Figure 2.23 Tetracycline discoloration.

Evaluation of the occlusion and the temporomandibular joint

A thorough assessment of the TMJ is essential, as many local and systemic processes influence the form and function of this unique ginglymoarthrodial joint. A malocclusion may be an outcome of TMJ pathology resulting from the hematogenous spread of infective organisms or extension of local infections from structures such as the ear (Semlali et al., 2004; Prasad et al., 2007) and the mastoid (Hadlock et al., 2001). In addition, diseases such as rheumatoid arthritis and disorders of bone and joints (for example, Ehlers-Danlos syndrome) can lead to altered function of the TMJ. Another heterogeneous group of inflammatory arthropathies with clinical symptoms similar to rheumatoid arthritis is juvenile idiopathic arthritis (JIA). It usually occurs in patients younger than 16 years, the common age group of patients undergoing orthodontic

treatment. It may cause growth disturbances and developmental anomalies (Alawsi et al., 2020).

Idiopathic condylar resorption (ICR) or cheerleader syndrome has been hypothesized to cause anterior open bite (Wolford et al., 2001). It is characterized by progressive, bilateral, symmetric volume loss of the mandibular condyles and rami, resulting in decreased posterior facial height, steepening of the mandibular plane, and anterior open bite (Ji et al., 2020; Figure 2.26). ICR may also occur during the orthodontic retention phase, leading to anterior open bite (Park et al., 2019). Therefore, the patient must be informed of the complications if further management is planned.

(a)

(b)

(c)

Figure 2.24 (a–c) A patient with primary failure of eruption.

It is essential to differentiate the pain originating primarily due to internal derangement of the joint, organic or inorganic, from that which occurs due to alterations of the other structures of the craniofacial region. In case an organic disturbance of the joint is suspected, additional radiographic aids may be used to delineate the pathology of the condyle from those of the articular disc and the glenoid fossa, as the problem in each of these structures may be affected by specific systemic and/or local influences.

Similarly, examining the occlusion, both static and dynamic, forms an important aspect of orthodontic diagnosis. Examination of the centric relation, centric occlusion, centric shift, and protrusive and laterotrusive shifts (Figure 2.27) helps assess the synchronicity of the movements of the TMJ. This examination is particularly useful in patients with an existing TMJ disorder, those with a mutilated dentition, and those requiring alteration of the occlusal scheme. The clinical consequences of disorders of the temporomandibular joint are discussed extensively in Chapter 21.

Radiographic examination of the craniofacial region

Several institutions, such as the European Commission, the British Orthodontic Society, and the American Academy of Oral and Maxillofacial Radiology, have published guidelines for orthodontic radiography. According to the British Orthodontic Society, “a radiograph should only be taken after a clinical examination when it is deemed to provide sufficient benefit to the exposed individual and will influence clinical management” (Isaacson et al., 2015). Although the radiation exposure is less, the prescription for a dental radiograph should be based on individual clinical assessment while following the ALARA (As Low As Reasonably Achievable) principle. The European Academy of Paediatric Dentistry (EAPD) recommends that the application of dental radiography needs to be optimized, aiming at limiting the patient’s exposure to ionizing radiation according to the ALADAIP (As Low As Diagnostically Achievable being Indication-oriented and Patient-specific) principle (Kühnisch

et al., 2020). A systematic review attempted to develop a clinical practice guideline on orthodontic radiography. Clinical recommendations for orthopantomograms, lateral cephalograms, hand-wrist radiographs, periapical radiographs, bitewings, antero-occlusal radiographs, and cone-beam computer tomographic imaging were formulated based on patient preferences, organizational matters, and expert opinions (Kapetanović et al., 2021).

Apart from routine cephalometric analysis, many developmental aberrations may become evident only on radiographs, for example cervical spine fusion (Figure 2.28), root dilacerations, hypercementosis, supernumerary and impacted teeth, jawbone pathologies such as cysts (Figure 2.29), tumors, secondaries of systemic tumors, hyperostotic or resorptive bone lesions, tooth-related pathologies such as a periapical abscess or cyst, idiopathic root resorption, and internal resorption. Skull radiographs may reveal bony lesions secondary to systemic ailments such as thalassemia, leukemias, and multiple myeloma (Shimano, 1995; Neyaz et al., 2008) and are also helpful in the evaluation of sinus pathologies, craniosynostoses, and pathologies of the TMJ. Variations in the morphology of sella turcica are prevalent in patients with craniofacial syndromes like bulbous dorsum sellae in cleidocranial dysplasia, a bulbous dorsum sellae and uneven contours of the clivus in cri du chat syndrome, a steep clivus in Axenfeld-Rieger syndrome, and an oblique anterior wall in Down syndrome (Kjær, 2015; Roomaney and Chetty, 2021). Advanced diagnostic techniques such as cone-beam computed tomography (CBCT) are useful in the assessment of bone pathologies, hard tissue architecture, and assessment of bone density, but the radiation dose should be taken into consideration when deciding on such a radiograph. According to the SEDENTEXCT guidelines from 2011, CBCT should not be prescribed unless history and clinical examination have been performed. It was recommended that where the imaging method of choice is multislice computed tomography (MSCT), as in the localized assessment of impacted teeth, cleft palate, and TMJ disorder, CBCT with the smallest size compatible may be preferred if the radiation dose is lower (European Commission, 2012). In patients with suspected hyperactivity or

hypoactivity of an organ (e.g. condylar hyperplasia), radionuclide imaging with the isotope ^{99m}Tc is useful (Henderson et al., 2009). MRI is a useful aid in assessing the anatomy, function, and pathologies of soft tissues such as the condylar disk, salivary glands, and sinuses.

Figure 2.25 An adult male patient showing the rough hypoplastic type of amelogenesis imperfecta with generalized yellowish-brown discoloration of teeth. The thickness of enamel was reduced, especially in the occlusal surface of posterior teeth, with dentin exposure and restoration in some teeth.

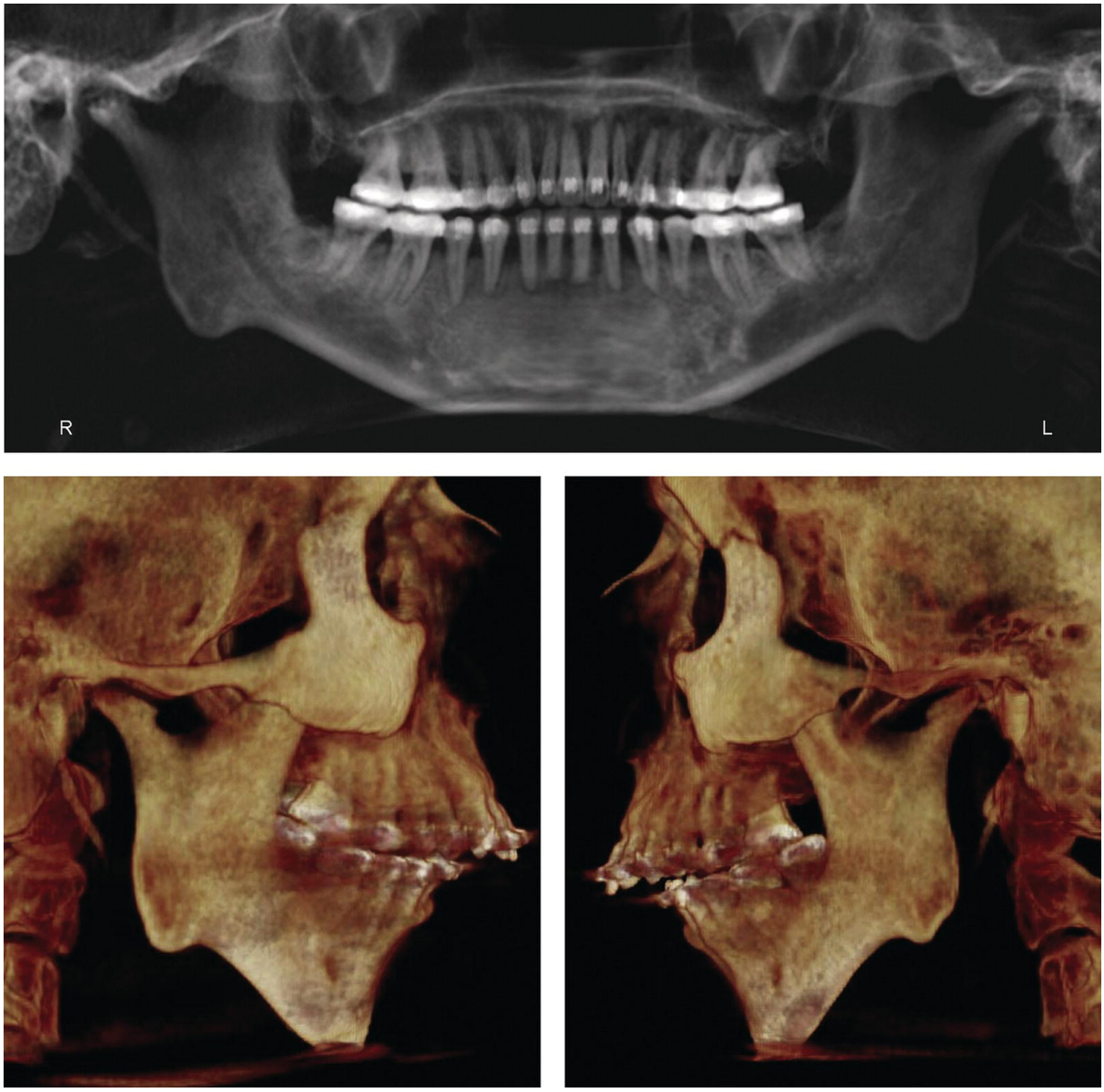


Figure 2.26 An adult male patient undergoing fixed orthodontic treatment showing symmetric idiopathic condylar resorption on bilateral condyles associated with anterior open bite, steep mandibular plane, and prominent antegonial notch.

Figure 2.27 Functional occlusion shifts. (a, b) An anterior shift in the deciduous dentition leading to a pseudo-Class III malocclusion and (c, d) a lateral shift in the early permanent dentition. Such pathological shifts may contribute to regressive alterations within the temporomandibular joint.

Figure 2.28 Cervical spine fusion (C2–C3; arrow) seen in a patient who reported for an orthodontic consultation. The patient was asymptomatic, and the fusion was detected on a routine orthodontic investigation. C2–C3 fusion is seen in 0.4–0.7% of the population; there is no sex predilection. The anomaly occurs in the third to eighth weeks of prenatal development due to a reduction in blood supply. Patients are generally asymptomatic, but with age or injury premature degenerative changes may be seen at adjoining motion segments due to greater biomechanical stress on them. Discal tears, rupture of the transverse ligament, fractures of the odontoid process, and spondylosis are common consequences. The orthodontist should make a referral to a specialist even in the absence of symptoms.

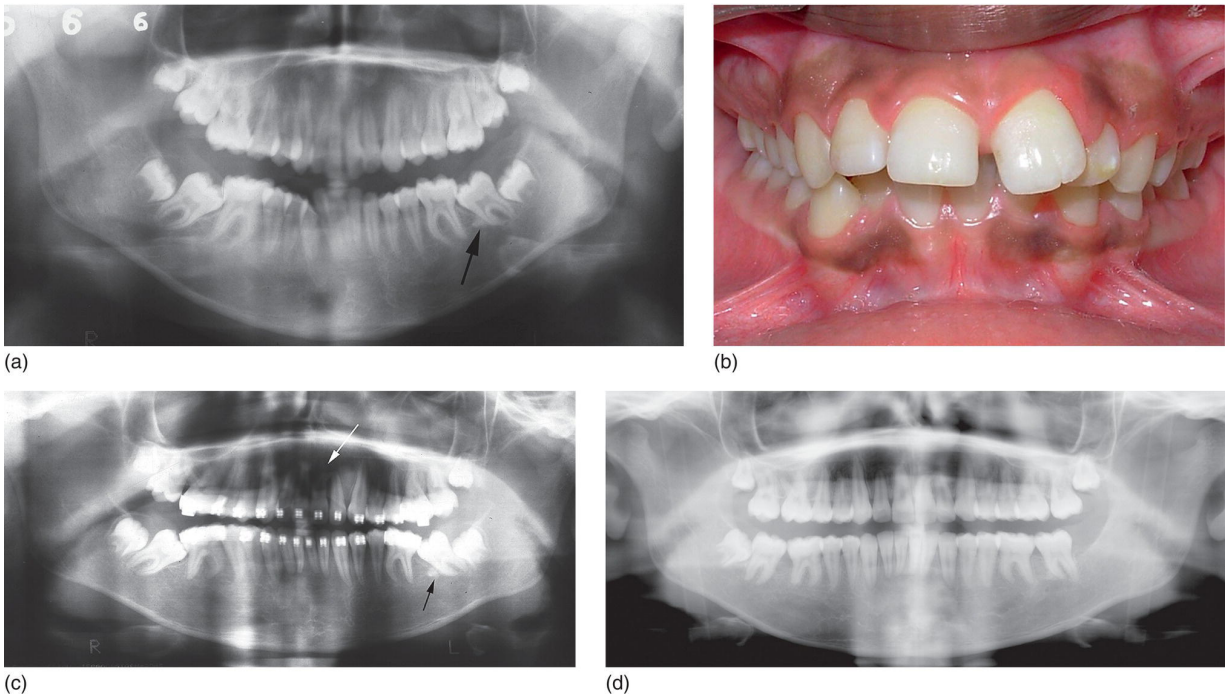


Figure 2.29 A patient with a developing cystic lesion in relation to the mesial root of the mandibular left second molar associated with a radiopaque mass (black arrow in a and c) and root dilaceration of the maxillary left central incisor. Both the conditions, unfortunately, were not noticed during the initial examination. Note the distal tilt in the inclination of the upper left central incisor (b), which should have aroused the suspicion of a potential dilaceration, as such conditions are common in the upper central incisors. Image (c) shows a cyst (white arrow), which was noted on routine radiographic examination eight months into treatment. The cyst had enlarged significantly in size. The case was discussed with an oral surgeon, and enucleation of the lesion led to successful resolution of the lesion (d). Endodontic therapy was not required for the second molar. Image (d) also depicts root resorption of the dilacerated central incisor, which occurred as bracket placement did not take into consideration its altered morphology.

Conclusion

Orthodontics is a healthcare specialty concerned with the development and clinical application of effective means of identifying, diagnosing, and correcting deviations from normal orofacial form and function. The process of orthodontic diagnosis and treatment planning is not merely a detailed description of the dental malocclusion, but also a representation of a broad search for causative factors, both local and systemic; the coexisting systemic conditions, if any, could alter the approach to treatment.

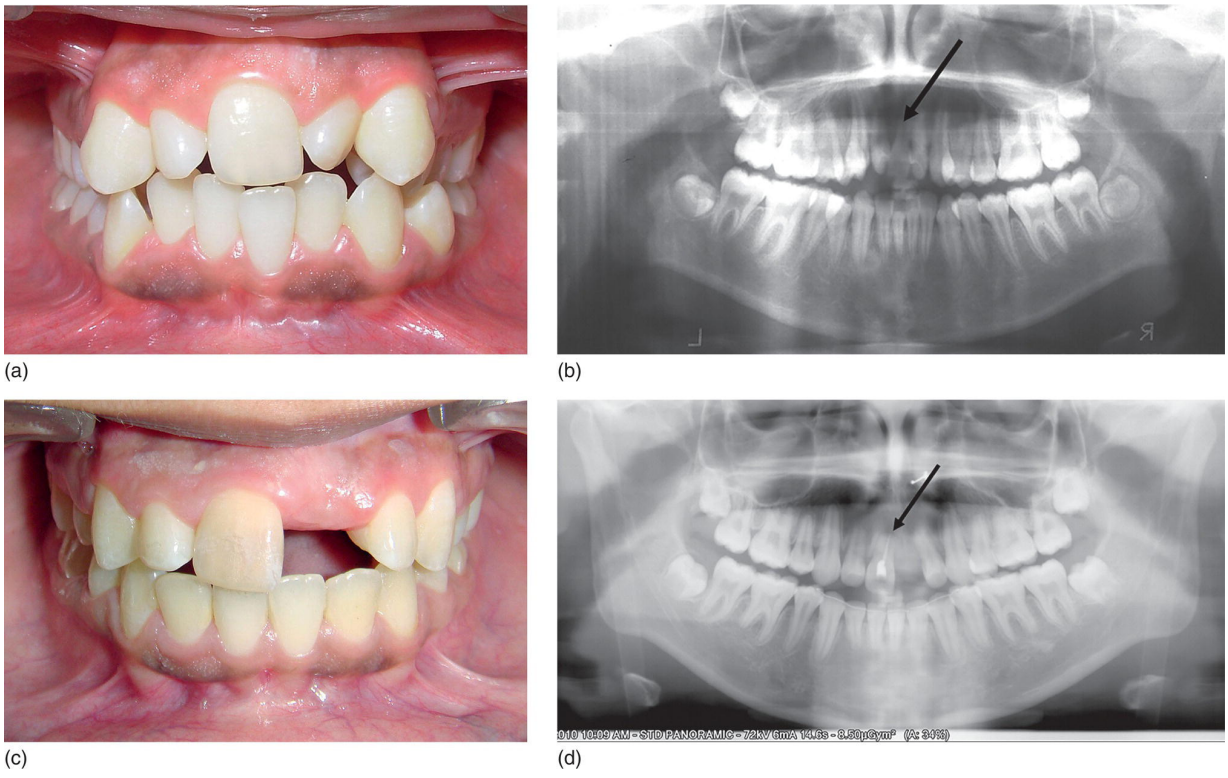


Figure 2.30 (a, b) Traumatic loss of upper left central incisor during childhood. The right central incisor showed calcification of the root canal (arrow). No endodontic intervention was sought for the upper right central incisor prior to orthodontic treatment. (c, d) During the later stages of treatment, when the tooth was undergoing torquing, it developed severe sensitivity and root resorption and had to be endodontically treated (arrow). These sequelae could perhaps have been prevented by considering endodontic treatment prior to orthodontic therapy.

An orthodontist should be aware that no single patient has orthodontic needs in isolation. Although a few patients can perhaps be managed by the orthodontist alone, most require interactions with the family physician or other medical or dental specialists to achieve optimum oral health (Figure 2.30). However, ongoing research in clinical and basic sciences continually produces new findings that augment the potential to improve the quality of orthodontic diagnosis and treatment planning. Therefore, it is imperative that practicing orthodontists stay abreast of emerging new knowledge in biological and material sciences and, above all, establish and maintain channels of collaboration and interaction

with all other specialists in dentistry and medicine, thereby always advancing their capabilities to the benefit of each of their patients. In addition, certain systemic conditions may preexist or appear during the treatment. Therefore, the orthodontist should be vigilant not to miss these and be alert to changing the course of treatment should that be required in consultation with a medical practitioner or a specialist.

References

Abu Alhaija, E.S., Aldaikki, A., Al-Omairi, M.K. et al. (2010). The relationship between personality traits, pain perception and attitude toward orthodontic treatment. *Angle Orthodontist* 80: 1141–1149.

Accurso, B., and Allem, C.M. (2010). Multiple endocrine neoplasia-2B presenting with orthodontic relapse. *Angle Orthodontist* 80: 585–590.

Adler, P., Wegner, H., and Bohatka, L. (1973). Influence of age and duration of diabetes on dental development in diabetic children. *Journal of Dental Research* 52: 535–537.

Ahmad, S., Bister, D., and Cobourne, M.T. (2006). The clinical features and aetiological basis of primary eruption failure. *European Journal of Orthodontics* 28(6): 535–540.

Alawsi, F., Sawbridge, D., and Fitzgerald, R. (2020). Orthodontics in patients with significant medical co-morbidities. *Journal of Orthodontics* 47(suppl 1): 4–24.

Al Nowaiser, A., Roberts, G.J., Trompeter, R.S. et al. (2003). Oral health in children with chronic renal failure. *Pediatric Nephrology* 18: 39–45.

Al-Omiri, M.K., and Alhaija, E.S.A. (2006). Factors affecting patient satisfaction after orthodontic treatment. *Angle Orthodontist* 76: 422–431.

Alqahtan, i H. (2019). Medically compromised patients in orthodontic practice: Review of evidence and recommendations.

International Orthodontics, 17(4): 776–788.

Al-Rawi, N.H., and Talabani, N.G. (2008). Squamous cell carcinoma of the oral cavity: A case series analysis of clinical presentation and histological grading of 1,425 cases from Iraq. *Clinical Oral Investigations* 2(1): 15–18.

Altug-Atac, A.T., and Erdem, D. (2007). Prevalence and distribution of dental anomalies in orthodontic patients. *American Journal of Orthodontics and Dentofacial Orthopedics* 131: 510–514.

Alvear, J., Artaza, C., Vial, M. et al. (1986). Physical growth and bone age of survivors of protein energy malnutrition. *Archives of Disease in Childhood* 61: 257–262.

American Academy of Pediatric Dentistry (2021). Caries-risk assessment and management for infants, children, and adolescents. In: *The Reference Manual of Pediatric Dentistry*. Chicago, IL: American Academy of Pediatric Dentistry, pp. 252–257.

Annegers, J.F. (1997). The epidemiology of epilepsy. In: E Wyllie (ed.), *The Treatment of Epilepsy: Principles and Practice*, 2nd ed. Baltimore, MD: Lippincott Williams & Wilkins, pp. 165–172.

Ansell, D., Feest, T., and Calvani, M. (2002). *UK Renal Registry Report 2002*. Bristol: Bristol University.

Babuccu, B., Babuccu, O., Yurdakan, G. et al. (2009). The effect of the Botulinum toxin-A on craniofacial development: An experimental study. *Annals of Plastic Surgery* 63(4): 449–456.

Barron, M.J., McDonnell, S.T., Mackie, I. et al. (2008). Hereditary dentine disorders: Dentinogenesis imperfecta and dentine dysplasia. *Orphanet Journal of Rare Diseases* 3: 31.

Bartley, A.J., Jones, D.W., and Weinberger, D.R. (1997). Genetic variability of human brain size and cortical gyral patterns. *Brain* 120 (Pt 2): 257–269.

Bartzela, T.N., Carels, C., and Maltha, J.C. (2017). Update on 13 syndromes affecting craniofacial and dental structures. *Frontiers*

in Physiology 8: 1038.

Basdra, E.K., Kiokpasoglou, M.N., and Komposch, G. (2001). Congenital tooth anomalies and malocclusions: A genetic link? *European Journal of Orthodontics* 23: 145–152.

Bassett, J.H.D., Nordstrom, K., Boyde, A. et al. (2007). Thyroid status during skeletal development determines adult bone structure and mineralization. *Molecular Endocrinology* 21(8): 1893–1904.

Bernard-Bonnin, A.C., Stachenko, S., Bonin, D. et al. (1995). Self-management teaching programs and morbidity of pediatric asthma: A meta-analysis. *Journal of Allergy and Clinical Immunology* 95(1 Pt 1), 34–41.

Biondi, B., and Cooper, D.S. (2008). The clinical significance of subclinical thyroid dysfunction. *Endocrine Reviews* 29: 76–131.

Bishara, S.E., Oonsombat, C., Soliman, M.M. et al. (2005). Effects of using a new protective sealant on the bond strength of orthodontic brackets. *Angle Orthodontist* 75(2): 243–246.

Brambilla, F., Cocchi, D., Nobile, P. et al. (1981). Anterior pituitary responsiveness to hypothalamic hormones in anorexia nervosa. *Neuropsychobiology* 7: 225–237.

Brewer, A., and Correa, M.E. (2006). *Guidelines for Dental Treatment of Patients with Inherited Bleeding Disorders*. Montreal: World Federation of Hemophilia.

Brook, A.H. (1974). Dental anomalies of number, form and size: Their prevalence in British schoolchildren. *Journal of the International Association of Dentistry for Children* 5: 37–53.

Cabell, C.H., Jollis, J.G., Peterson, G.E. et al. (2002). Changing patient characteristics and the effect on mortality in endocarditis. *Archives of Internal Medicine* 162: 90–94.

Canaris, G.J., Manowitz, N.R., Mayor, G. et al. (2000) The Colorado thyroid disease prevalence study. *Archives of Internal Medicine* 160: 526–534.

Cantu, G., Buschang, P.H., and Gonzalez, J.L. (1997). Differential growth and maturation in idiopathic growth-hormone-deficient children. *European Journal of Orthodontics* 19: 131–139.

Carek, P.J., Dickerson, L.M., and Sack, J.L. (2001). Diagnosis and management of osteomyelitis. *American Family Physician* 63(12): 2413–2420.

Carmichael, D.T., Williams, C.A., and Aller, M.S. (1995). Renal dysplasia with secondary hyperparathyroidism and loose teeth in a young dog. *Journal of Veterinary Dentistry* 12: 143–146.

Cascino, G.D., Luckstein, R.R., Sharbrough, F.W. et al. (1993). Facial asymmetry, hippocampal pathology, and remote symptomatic seizures: A temporal lobe epileptic syndrome. *Neurology* 43(4): 725–727.

Cassidy, L., and Jellinek, M. (1998). Approaches to recognition and management of childhood psychiatric disorders in pediatric primary care. *Pediatric Clinics of North America* 45: 1037–1052.

Castellanos, J.L., and Díaz-Guzmán, L. (2008). Lesions of the oral mucosa: An epidemiological study of 23785 Mexican patients. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* 105(1): 79–85.

Centers for Disease Control and Prevention (1989). Guidelines for prevention and transmission of HIV and HBV to health care and public safety workers. *Morbidity and Mortality Weekly Report (MMWR)* 38: 1–37.

Choi, B.C., and Pak, A.W. (2006). Multidisciplinarity, interdisciplinarity and transdisciplinarity in health research, services, education and policy: 1. Definitions, objectives, and evidence of effectiveness. *Clinical and Investigative Medicine* 29(6): 351–364.

Chung, L.K., Hobson, R.S., Nunn, J.H. et al. (2000). An analysis of the skeletal relationships in a group of young people with hypodontia. *Journal of Orthodontics* 27: 315–318.

Cohen, R.B., and Wilcox, C.W. (1993). A case of acromegaly identified after patient complaint of apertognathia. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* 75: 583–586.

Collins, M.K., and Sinclair, P.M. (1988) The local use of vitamin D to increase the rate of orthodontic tooth movement. *American Journal of Orthodontics and Dentofacial Orthopedics* 94(4): 278–284.

Colvard, M.D., Bishop, J., Weissman, D. et al. (1986). Cardiazem-induced gingival hyperplasia. *Periodontal Case Reports* 8: 67–68.

Crawford, P.J., Aldred, M., and Bloch-Zupan, A. (2007). Amelogenesis imperfecta. *Orphanet Journal of Rare Diseases* 2: 17.

Crocetti, M., and Barone, M.A. (2004) Growth disorders. In: M. Crocetti and M.A. Barone (eds.), *Oski's Essential Pediatrics*, 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins, p. 567.

Dahllof, G., and Huggare, J. (2004). Orthodontic considerations in the pediatric cancer patients: A review. *Seminars in Orthodontics* 10: 266–276.

Daley, T.D., and Armstrong, J.E. (2007). Oral manifestations of gastrointestinal diseases. *Canadian Journal of Gastroenterology* 21(4): 241–244.

Dash, J.K., Sahoo, P.K., and Das, S.N. (2004). Talon cusp associated with other dental anomalies: A case report. *International Journal of Paediatric Dentistry* 14: 295–300.

Davidopoulou, S., and Chatzigianni, A. (2017). Craniofacial morphology and dental maturity in children with reduced somatic growth of different aetiology and the effect of growth hormone treatment. *Progress in Orthodontics* 18(1): 10.

Davidovitch, Z., and Krishnan, V. (2009). Role of basic biological sciences in clinical orthodontics: A case series. *American Journal of Orthodontics and Dentofacial Orthopedics* 135(2): 222–231.

Davies, T.I., and Rayner, P.H. (1995). Functional appliance therapy in conjunction with growth hormone treatment: A case report. *British Journal of Orthodontics* 22: 361–365.

Delitala, A.P., Scuteri, A., and Doria, C. (2020). Thyroid hormone diseases and osteoporosis. *Journal of Clinical Medicine* 9(4): 1034.

Dixit, R., Sharma, S., and Nuwal, P. (2008). Tuberculosis of oral cavity. *Indian Journal of Tuberculosis* 55(1): 51–53.

Dos Santos, C., Bellini-Pereira, S.A., Medina, M. et al. (2021). Allergies/asthma and root resorption: A systematic review. *Progress in Orthodontics* 22(1): 8.

Dreizen, S., Spirakis, C.N., and Stone, R.E. (1967). A comparison of skeletal growth and maturation in undernourished and well-nourished girls before and after menarche. *Journal of Pediatrics* 70(2): 256–263.

Egli, F., Botteron, S., Morel, C. et al. (2018). Growing patients with Duchenne muscular dystrophy: Longitudinal changes in their dentofacial morphology and orofacial functional capacities. *European Journal of Orthodontics* 40(2): 140–148.

El Bokle, D., and Munir, H. (2008). An in vitro study of the effect of Pro Seal varnish on the shear bond strength of orthodontic brackets. *World Journal of Orthodontics* 9(2): 141–146.

Elia, J., Ambrosini, P., and Rapoport, J. (1999). Treatment of attention deficit hyperactivity disorder. *New England Journal of Medicine* 340: 780–788.

Engström, C., Linde, A., and Thilander, B. (1982a) Craniofacial morphology and growth in the rat. Cephalometric analysis of the effects of a low calcium and vitamin D-deficient diet. *Journal of Anatomy* 134(Pt 2): 299–314.

Engström, C., Magnusson, B.C., and Linde, A. (1982b). Changes in craniofacial suture metabolism in rats fed a low calcium and vitamin D-deficient diet. *Journal of Anatomy* 134: 443–458.

Eugster, E.A., and Pescovitz, O.H. (1999). Gigantism. *Journal of Clinical Endocrinology and Metabolism* 84: 4379–4384.

European Commission (2004). Radiation Protection 136. In: *European Guidelines on Radiation Protection in Dental Radiology: The Safe Use of Radiographs in Dental Practice*. Luxembourg: Office for Official Publications of the European Communities. https://op.europa.eu/en/publication-detail/-/publication/ea20b522-883e-11e5-b8b7-01aa75ed71a1

European Commission (2012). Radiation protection 172. In: *Evidence Based Guidelines on Cone Beam CT for Dental and Maxillofacial Radiology*. Luxembourg: Office for Official Publications of the European Communities. https://www.sedentexct.eu/files/radiation_protection_172.pdf

Fabe, S.S. (1950). Acute hematogenous osteomyelitis of the mandible; report of a case. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* 3(1): 22–26.

Faustino-Silva, D.D., Rocha, A.F., da Rocha, B.S. et al. (2020). Use of antibiotics in early childhood and dental enamel defects in 6- to 12-year-old children in primary health care. *Acta Odontologica Latinoamericana*, 33(1): 6–13.

Favaloro, E.J. (2006). Laboratory identification of von Willebrand disease: Technical and scientific perspectives. *Seminars in Thrombosis and Hemostasis* 32: 456–471.

Favoloro, E.J. (2007). Investigating people with mucocutaneous bleeding suggestive of primary hemostatic defects: A low likelihood of a definitive diagnosis? *Hematologica* 92: 292–296.

Fekonja, A. (2005). Hypodontia in orthodontically treated children. *European Journal of Orthodontics* 27: 457–460.

Ferreira, M., Ferreira, R.O., Castro, M. et al. (2019). Is there an association between asthma and periodontal disease among adults? Systematic review and meta-analysis. *Life Sciences* 223: 74–87.

Field, E.A., Speechley, J.A., Rugman, F.R. et al. (1995). Oral signs and symptoms in patients with undiagnosed B12 deficiency. *Journal of Oral Pathology and Medicine* 24: 68–70.

Finkelstein, M.W. (2001). Overview of general embryology and head and neck development. In: S.E. Bishara (ed.), *Textbook of Orthodontics*. Philadelphia, PA: W.B. Saunders, pp. 2–24.

Fong, G.C., Mak, Y.F., Swartz, B.E. et al. (2003). Body part asymmetry in partial seizure. *Seizure* 12(8): 606–612.

Franz-Montan, M., Ranali, J., Ramacciato, J.C. et al. (2008). Ulceration of gingival mucosa after topical application of EMLA: Report of four cases. *British Dental Journal* 204(3): 133–134.

Frisdal, A., and Trainor, P.A. (2014). Development and evolution of the pharyngeal apparatus. *Wiley Interdisciplinary Reviews: Developmental Biology* 3(6): 403–418.

Fujieda, K., and Tanaka, T. (2007). Diagnosis of children with short stature: Insights from KIGS. In: M.B. Ranke, D.A. Price, and E.O. Reiter (eds.), *Growth Hormone Therapy in Pediatrics: 20 Years of KIGS*. Basel: Karger, p. 16.

Galili, D., Berger, E., and Kaufman, E. (1991). Pulp narrowing in renal end stage and transplanted patients. *Journal of Endodontics* 17: 442–443.

Garrow, J.S., and Pike, M.C. (1967). The long-term prognosis of severe infantile malnutrition. *Lancet* 289(7480): 1–4.

George, A., Johnson, M., Blinkhorn, A. et al. (2010). Promoting oral health during pregnancy: Current evidence and implications for Australian midwives. *Journal of Clinical Nursing* 19(23–24): 3324–3333.

Gillchrist, J.A. (1999). Hepatitis viruses A, B, C, D, E and G: Implications for dental personnel. *Journal of the American Dental Association* 130: 509–520.

Gosau, M., Vogel, C., Moralis, A. et al. (2009). Mandibular prognathism caused by acromegaly – a surgical orthodontic case.

Head and Face Medicine 5: 16.

Gould, F.K., Elliott, T.S., Foweraker, J. et al. (2006). Guidelines for the prevention of endocarditis: Report of the Working Party of the British Society for Antimicrobial Chemotherapy. *Journal of Antimicrobial Chemotherapy* 57(6): 1035–1042.

Graham, G.G., and Adrianzen, B.T. (1972). Late catch up growth after severe infantile malnutrition. *Johns Hopkins Medical Journal* 131: 204–211.

Guttal, K.S., Naikmasurb, V.G., Bhargava, P. et al. (2010). Frequency of developmental dental anomalies in the Indian population. *European Journal of Dentistry* 4: 263–269.

Hadlock, T.A., Ferraro, N.F., and Rahbar, R. (2001). Acute mastoiditis with temporomandibular joint effusion. *Otolaryngology Head and Neck Surgery* 125(1): 111–112.

Hall, R.K. (1983). Congenitally missing teeth – a diagnostic feature in many syndromes of the head and neck. *Journal of the International Association of Dentistry for Children* 14: 69–75.

Hanisch, M., Hanisch, L., Kleinheinz, J. et al. (2018). Primary failure of eruption (PFE): A systematic review. *Head & Face Medicine* 14(1): 5.

Harvey, C.B., O'Shea, P.J., Scott, A.J. et al. (2002). Molecular mechanisms of thyroid hormone effects on bone growth and function. *Molecular Genetics and Metabolism* 75: 17–30.

Henderson, M., Wastie, M., Bromige, M. et al. (2009). Technetium-99m bone scintigraphy and mandibular condylar hyperplasia. *Clinical Radiology* 41(6): 411–414.

Hicks, M.J., and Flaitz, C.M. (2000). Oral mucosal melanoma: Epidemiology and pathobiology. *Oral Oncology* 36(2): 152–169.

Hollowell, J.G., Staehling, N.W., Flanders, W.D. et al. (2002). Serum TSH, T(4), and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination

Survey (NHANES III). *Journal of Clinical Endocrinology and Metabolism* 87(2): 489–499.

Hwang, C.J., and Cha, J.Y. (2004). Orthodontic treatment with growth hormone therapy in a girl of short stature. *American Journal of Orthodontics and Dentofacial Orthopedics* 126: 118–126.

Isaac, A.M., and Tholouli, E. (2008). Orthodontic treatment for a patient who developed acute myeloid leukemia. *American Journal of Orthodontics and Dentofacial Orthopedics* 134(5): 684–688.

Isaacson, K.G., Thom, A.R., Atack, N.E. et al. (2015). *Orthodontic Radiographs: Guidelines for the Use of Radiographs in Clinical Orthodontics*, 4th ed. London: British Orthodontic Society.

Jaffe, E.C., Roberts, J., Chantler, C. et al. (1990). Dental maturity in children with chronic renal failure assessed from dental panoramic tomographs. *Journal of the International Association of Dentistry for Children* 20: 54–58.

James, M., Clarke, P., and Darcey, R. (2019). Body dysmorphic disorder and facial aesthetic treatments in dental practice. *British Dental Journal* 227(10): 929–933.

Jayaraman, G.C., Bush, K.R., Lee, B. et al. (2004). Magnitude and determinants of first-time and repeat testing among individuals with newly diagnosed HIV infection between 2000 and 2001 in Alberta, Canada: Results from population-based laboratory surveillance. *Journal of Acquired Immune Deficiency Syndromes* 37(5): 1651–1656.

Ji, Y.D., Resnick, C.M., and Peacock, Z.S. (2020). Idiopathic condylar resorption: A systematic review of etiology and management. *Oral Surgery, Oral Medicine, Oral Pathology, and Oral Radiology* 130(6): 632–639.

Johnstone, S.C., Barnard, K.M., and Harrison, V.E. (1999). Recognizing and caring for the medically compromised child: 4.

Children with other chronic medical conditions. *Dental Update* 26(1): 21–26.

Jolly, M. (1977). White lesions of the mouth. *International Journal of Dermatology* 16(9): 713–725.

Jorgenson, R.J. (1980). Clinicians' view of hypodontia. *Journal of the American Dental Association* 101: 283–286.

Juan, J.S., and Jiménez-Rubio, A. (1999). Talon cusp affecting permanent maxillary lateral incisors in 2 family members. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* 88: 90–92.

Kamal, A.T., Mahmood, H.T., and Fida, M. (2020). The implications of endocrinology in orthodontics–literature review. *Balkan Journal of Dental Medicine* 24(1): 8–13.

Kapetanović, A., Oosterkamp, B.C.M., Lamberts, A.A. et al. (2021). Orthodontic radiology: Development of a clinical practice guideline. *La Radiologia Medica* 126(1): 72–82.

Kauzman, A., Pavone, M., Blanas, N. et al. (2004). Pigmented lesions of the oral cavity: Review, differential diagnosis, and case presentations. *Journal of Canadian Dental Association* 70(10): 682–683.

Keçik, D., Cehreli, S.B., Sar, C. et al. (2008). Effect of acidulated phosphate fluoride and casein phosphopeptide-amorphous calcium phosphate application on shear bond strength of orthodontic brackets. *Angle Orthodontist* 78(1): 129–133.

Kennedy, D.S., and Linden, G.J. (2000). Resolution of gingival overgrowth following change from ciclosporin to tacrolimus therapy in a renal transplant patient. *Journal of Irish Dental Association* 46: 3–4.

Kharbanda, O.P.(2020). Orthodontic treatment with contemporary fixed appliance Phase I: laying the foundation. In: O.P. Kharbanda (ed.), *Orthodontics Diagnosis and Management of Malocclusion and Dentofacial Deformities*, 3rd ed. New Delhi, India: Elsevier, pp. 549.

Kharbanda, O.P. (2022). Management *Matrix* of Cleft Lip and Palate. In: O.P. Kharbanda (ed.), Cleft Orthodontics: A Holistic and Interdisciplinary Approach, 1st ed, New Delhi, India: Thieme India, pp. 68.

Kho, H., Lee, S., Chung, S.C. et al. (1999). Oral manifestations and salivary flow rate, pH, and buffer capacity in patients with end-stage renal disease undergoing haemodialysis. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* 88: 316–319.

Kimura, T., Dunn, W.J., and Taloumis, L.J. (2004). Effect of fluoride varnish on the in vitro bond strength of orthodontic brackets using a self-etching primer system. *American Journal of Orthodontics and Dentofacial Orthopedics* 125(3): 351–356.

Kjær, I. (2015). Sella turcica morphology and the pituitary gland—a new contribution to craniofacial diagnostics based on histology and neuroradiology. *European Journal of Orthodontics* 37(1): 28–36.

Krishnan, V., Zahrowski, J.J., and Davidovitch, Z. (2021). The effect of drugs, hormones, and diet on orthodontic tooth movement. In: V. Krishnan, A.M. Kuijpers-Jagtman, and Z. Davidovitch (eds.), *Biological Mechanisms of Tooth Movement*, 3rd ed. Chichester: Wiley, pp. 199–216.

Krueger, R.H. (1969). Some long-term effects of severe malnutrition in early life. *Lancet* 2: 514–517.

Kühnisch, J., Anttonen, V., Duggal, M.S. et al. (2020). Best clinical practice guidance for prescribing dental radiographs in children and adolescents: An EAPD policy document. *European Archives of Paediatric Dentistry* 21(4): 375–386.

Kumar, P. (2008). Dysmorphology. In: P. Kumar and K. Barbara (eds.), *Congenital Malformations: Evidence Based Evaluation and Management*. New York: McGraw-Hill, p. 6.

Lamster, I.B., Lalla, E., Borgnakke, W.S. et al. (2008). The relationship between oral health and diabetes mellitus. *Journal of*

the American Dental Association 139(5 Suppl): 19–24.

Laurikainen, K., and Kuusisto, P. (1998). Comparison of the oral health status and salivary flow rate of asthmatic patients with those of nonasthmatic adults – results of a pilot study. *Allergy* 53: 316–319.

Leukefeld, C.G., Battjes, B.J., and Amsel, Z. (1990). *AIDS and intravenous drug use: Future directions for community-based prevention research*. NIDA Research Monograph 93. Washington, DC: US Government Printing Office.

Lifshitz, F. (ed.) (2007). *Pediatric Endocrinology: Growth, Adrenal, Sexual, Thyroid, Calcium, and Fluid Balance Disorders, 5e*. Boca Raton, FL: CRC Press. 10.3109/9781420042726.

Lip, G.Y.H., and Beevers, D.G. (2005). Hypertensive emergencies and urgencies. In: D.A. Warrell, T.M. Cox, J.D. Firth et al. (eds.), *Oxford Textbook of Medicine*, vol 2, 4th ed. Oxford: Oxford University Press, p. 1194.

Litonjua, L.A., Andreana, S., Bush, P.J. et al. (2003). Noncarious cervical lesions and abfractions: A re-evaluation. *Journal of the American Dental Association* 134(7): 845–850.

Little, J.W. (2002). Eating disorders: Dental implications. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* 93: 138–143.

Litton, S.F. (1974). Orthodontic tooth movement during an ascorbic acid deficiency. *American Journal of Orthodontics* 65(3): 290–302.

Long, R.E., Jr., and Kharbanda, O.P. (1999). Improving treatment outcomes for patients with cleft lip and palate – an historical perspective of the team concept. *Journal of the Indian Orthodontic Society* 32: 1–4.

Lopes, C., Lira, S.S., da Silva Oliveira, J.C. et al. (2021). Occlusal disorders in patients with sickle cell disease: Critical literature review. *Journal of Clinical Pediatric Dentistry* 45(2): 117–122.

Lux, C.J., Kugel, B., Komposch, G. et al. (2005). Orthodontic treatment in a patient with Papillon-Lefèvre syndrome. *Journal of Periodontology* 76: 642–650.

Mannucci, P.M., Duga, S., and Peyvandi, F. (2004). Recessively inherited coagulation disorders. *Blood* 104: 1243–1252.

Marik, P.E., and Varon, J. (2007). Hypertensive crises: Management and challenges. *Chest* 131: 1949–1962.

Matfin, G. (2009). Disorders of endocrine control of growth and metabolism. In: R.A. Hannon, C. Pooler, and C.M. Porth (eds.), *Porth Pathophysiology: Concepts of Altered Health States*. Philadelphia, PA: Lippincott Williams & Wilkins, p. 986.

McConkey, E.H. (2004). Therapy of genetic disorders. In: E.H. McConkey (ed.), *How the Human Genome Works*. Burlington, MA: Jones and Bartlett, p. 66.

McCoy, G. (1982). The etiology of gingival erosion. *Journal of Oral Implantology* 10: 361–362.

McNab, S., Battistutta, D., Taverne, A. et al. (1999). External apical root resorption of posterior teeth in asthmatics after orthodontic treatment. *American Journal of Orthodontics and Dentofacial Orthopedics* 116: 545–551.

Michalak, I., Kuśmierczyk, D., Bluj-Komarnitka, K. et al. (2019). Radiological imaging and orthodontic treatment in the case of growing patients after oncological treatment: Case reports. *Dental and Medical Problems* 56(2): 209–215.

Mitchell, L. (1996). *An Introduction to Orthodontics*. Oxford: Oxford University Press.

Moraschini, V., Calasans-Maia, J.A., and Calasans-Maia, M.D. (2018). Association between asthma and periodontal disease: A systematic review and meta-analysis. *Journal of Periodontology* 89(4): 440–455.

Morrison, N.A., Yeoman, R., Kelly, P.J. et al. (1992). Contribution of transacting factor alleles to normal physiological variability:

Vitamin D receptor gene polymorphism and circulating osteocalcin. *Proceedings of the National Academy of Sciences of the United States of America* 89: 6665–6669.

Mulimani, P., Ballas, S.K., Abas, A.B. et al. (2019a). Treatment of dental complications in sickle cell disease. *Cochrane Database of Systematic Reviews* 12(12): CD011633. 10.1002/14651858.CD011633.pub3.

Mulimani, P., Abas, A.B., Karanth, L. et al. (2019b). Treatment of dental and orthodontic complications in thalassaemia. *Cochrane Database of Systematic Reviews* 8(8): CD012969. doi: 10.1002/14651858.CD012969.pub3.

Mupparapu, M., and Singer, S.R. (2004). A rare presentation of dens invaginatus in a mandibular lateral incisor occurring concurrently with bilateral maxillary dens invaginatus: Case report and review of literature. *Australian Dental Journal* 49: 90–93.

Murphy, E., and Williams, G.R. (2004). The thyroid and the skeleton. *Clinical Endocrinology* 61: 285–298.

Nadimi, H., Bergamini, J., and Lilien, B. (1993). Uremic mixed bone disease. A case report. *International Journal of Maxillofacial Surgery* 22: 268–270.

Najeeb, S., Siddiqui, F., Qasim, S.B. et al. (2017). Influence of uncontrolled diabetes mellitus on periodontal tissues during orthodontic tooth movement: A systematic review of animal studies. *Progress in Orthodontics* 18(1): 5.

Nasman, M., Forsberg, C.M., and Dahllof, G. (1997). Disturbances in dental development in long-term survivors after pediatric malignant diseases. *European Journal of Orthodontics* 19: 151–159.

Nasstrom, K. (1996). Dentin formation after corticosteroid treatment. A clinical study and an experimental study on rats. *Swedish Dental Journal* 115: 1–45.

Nasstrom, K., Forsberg, B., Petersson, A. et al. (1985). Narrowing of the dental pulp chamber in patients with renal diseases. *Oral*

Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology 59: 242–246.

Neela, P.K., Tatikonda, V.K., Syed, M.W. (2021). Influence of orthodontic brackets and permanent retainers on the diagnostic image quality of MRI scans: A preliminary study. *Dental and Medical Problems* 58(4): 499–508.

Neelapu, B.C., Kharbanda, O.P., Sardana, H.K. (2017). Craniofacial and upper airway morphology in adult obstructive sleep apnea patients: A systematic review and meta-analysis of cephalometric studies. *Sleep Medicine Reviews* 31: 79–90.

Neeley, W.W., Kleumper, G.T., and Hays, L.R. (2006a). Psychiatry in orthodontics. Part I: Typical adolescent psychiatric disorders and their relevance to orthodontic practice. *American Journal of Orthodontics and Dentofacial Orthopedics* 129: 176–184.

Neeley, W.W., Kleumper, G.T., and Hays, L.R. (2006b). Psychiatry in orthodontics. Part II: Substance abuse among adolescents and its relevance to orthodontic practice. *American Journal of Orthodontics and Dentofacial Orthopedics* 129: 185–193.

Neville, D.W., Damm, D.D., Allen, C.M. et al. (2005). Abnormalities of teeth. In: D.W. Neville, D.D. Damm, C.M. Allen et al. (eds.), *Oral and Maxillofacial Pathology*. Philadelphia, PA: Elsevier, pp. 49–89.

Neyaz, Z., Gadodia, A., Gamanagatti, S. et al. (2008). Radiographical approach to jaw lesions. *Singapore Medical Journal* 49(2): 165.

Okada, H., Davies, J.E., and Yamamoto, H. (2000). Brown tumor of the maxilla in a patient with secondary hyperparathyroidism: A case study involving immunohistochemistry and electron microscopy. *Journal of Oral and Maxillofacial Surgery* 58: 233–238.

Orbak, R., Simsek, S., Orbak, Z. et al. (2008). The influence of type-1 diabetes mellitus on dentition and oral health in children and adolescents. *Yonsei Medical Journal* 49: 357–365.

Park, J.H., Park, J.J., Papademetriou, M. et al. (2019). Anterior open bite due to idiopathic condylar resorption during orthodontic retention of a Class II Division 1 malocclusion. *American Journal of Orthodontics and Dentofacial Orthopedics* 156(4): 555–565.

Patel, A., Burden, D.J., and Sandler, J. (2009). Medical disorders and orthodontics. *Journal of Orthodontics* 36(Suppl): 1–21.

Poley, G.E., Jr, and Slater, J.E. (2000). Latex allergy. *Journal of Allergy and Clinical Immunology* 105: 1054–1062.

Portelli, M., Matarese, G., Militi, A. et al. (2009). Myotonic dystrophy and craniofacial morphology: Clinical and instrumental study. *European Journal of Paediatric Dentistry* 10(1): 19–22.

Prasad, K.C., Sreedharan, S., Prasad, S.C. et al. (2007). Tuberculosis of the temporomandibular joint and parotid secondary to tuberculous otitis media. *Otolaryngology Head and Neck Surgery* 137(6): 974–975.

Prendergast, B.D. (2006). The changing face of infective endocarditis. *Heart* 92: 879–885.

Proctor, R., Kumar, N., Stein, A. et al. (2005). Oral and dental aspects of chronic renal failure. *Journal of Dental Research* 84: 199–208.

Pucciarelli, V., Gibelli, D., Mastella, C. et al. (2020). 3D facial morphology in children affected by spinal muscular atrophy type 2 (SMAII). *European Journal of Orthodontics* 42(5): 500–508.

Quiroga, T., Goycoolea, M., Panes, O. et al. (2007). High prevalence of bleeders of unknown cause among patients with inherited mucocutaneous bleeding. Prospective study of 280 patients and 299 controls. *Haematologica* 92: 356–364.

Rajendran, R. (2009). Diseases of skin. In: R. Rajendran and B. Sivapathasundharam (eds.), *Shafer's Textbook of Oral Pathology*, 6th ed. New Delhi: Elsevier, pp. 797–843.

Ren, Y., Maltha, J.C., and Kuijpers-Jagtman, A.M. (2003). Optimum force magnitude for orthodontic tooth movement: A systematic

literature review. *Angle Orthodontist* 73: 86–92.

Rivkees, S.A., Bode, H.H., and Crawford, J.D. (1988). Long-term growth in juvenile acquired hypothyroidism: The failure to achieve normal adult stature. *New England Journal of Medicine* 318: 599–602.

Roomaney, I.A., and Chetty, M. (2021). Sella turcica morphology in patients with genetic syndromes: A systematic review. *Orthodontics & Craniofacial Research*, 24(2), 194–205.

Rosten, A., Cunningham, S., and Newton, J.T. (2018). Body dysmorphic disorder: A guide to identification and management for the orthodontic team. *Journal of Orthodontics* 45(3): 163–168.

Ruiz-Roca, J.A., Berini-Aytes, L., and Gay-Escoda, C. (2005). Pyostomatitis vegetans: Report of two cases and review of the literature. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* 99: 447–454.

Sadowsky, P.L., Bernreuter, W., Lakshminarayanan, A.V. et al. (1988). Orthodontic appliances and magnetic resonance imaging of the brain and temporomandibular joint. *Angle Orthodontist* 58(1): 9–20.

Salerno, F., Cocchi, D., Lampertico, M. et al. (1982). Growth hormone response to thyrotropin-releasing hormone in liver cirrhosis: Unique alteration in anterior pituitary responsiveness to hypothalamic hormones. *Hormone Metabolism Research* 14: 482–486.

Sennimalai, K., Singhal, M. (2022). *History* Taking and Clinical Assessment of a Newborn with a Cleft Lip and Palate. In: O.P. Kharbanda (ed.), Cleft Orthodontics: A Holistic and Interdisciplinary Approach, 1st ed, New Delhi, India: Thieme India, pp. 78

Semlali, S., Nassar, I., Fikri, M. et al. (2004). Candida arthritis of the TM joint complicating chronic otitis media. *Journal of Radiology* 85(11): 1953–1955.

Setian, N.S. (2007). Hypothyroidism in children: Diagnosis and treatment. *Jornal de pediatria* 83(Suppl 5), S209–S216.

Sheller, B. (2004). Orthodontic management of patients with seizure disorders. *Seminars in Orthodontics* 10: 247–251.

Shepard, C.W., Simard, E.P., Finelli, L. et al. (2006). Hepatitis B virus infection: Epidemiology and vaccination. *Epidemiologic Reviews* 28: 112–125.

Sheth, R.D. (2004). Metabolic concerns associated with antiepileptic medications. *Neurology* 63(10 Suppl 4): S24–S29.

Shimano, T. (1995). Radiographic diagnosis of systemic diseases in dentistry. *Oral Radiology* 11(2): 1–19.

Shirazi, M., Dehpour, A.R., and Jafari, F. (1999). The effect of thyroid hormone on orthodontic tooth movement in rats. *Journal of Clinical Pediatric Dentistry* 23: 259–264.

Sidell, F.R., and Kaminskis, A. (1975). Temporal intrapersonal physiological variability of cholinesterase activity in human plasma and erythrocytes. *Clinical Chemistry* 21:1961–1963.

Sonis, S. (2004). Orthodontic management of selected medically compromised patients: Cardiac disease, bleeding disorders, and asthma. *Seminars in Orthodontics* 10: 277–280.

Sonneveld, M.J., and Janssen, H.L.A. (2010). Pros and cons of peginterferon versus nucleos(t)ide analogues for treatment of chronic hepatitis B. *Current Hepatitis Reports* 9: 91–98.

Sperber, G.H., Gutterman, G.D., and Sperber, S.M. (eds.) (2001). *Craniofacial Development*, vol. 1. Toronto: B.C. Decker.

Sulieman, M. (2005). An overview of tooth discoloration: Extrinsic, intrinsic and internalized stains. *Dental Update* 32(8): 463–471.

Suter, V.G., Morger, R., Altermatt, H.J. et al. (2008). Oral erythroplakia and erythroleukoplakia: Red and red-white dysplastic lesions of the oral mucosa—part 1: Epidemiology,

etiology, histopathology and differential diagnosis. *Schweizer Monatsschrift für Zahnmedizin* 118(5): 390–397.

Task Force on Infective Endocarditis of the European Society of Cardiology (2004). Guidelines on prevention, diagnosis and treatment of infective endocarditis: Executive summary. *European Heart Journal* 25: 267–276.

Teng, L., Bui, H., Bachrach, L. et al. (2004). Catch-up growth in severe juvenile hypothyroidism: Treatment with a GnRH analog. *Journal of Pediatric Endocrinology and Metabolism* 17: 345–354.

Tinuper, P., Plazzi, G., Provini, F. et al. (1992). Facial asymmetry in partial epilepsies. *Epilepsia* 33(6): 1097–1100.

Torlińska-Walkowiak, N., Majewska, K.A., Kędzia, A. et al. (2021). Clinical implications of growth hormone deficiency for oral health in children: A systematic review. *Journal of Clinical Medicine* 10(16): 3733.

Tramontana, M., Bianchi, L., Hansel, K. et al. (2020). Nickel allergy: Epidemiology, pathomechanism, clinical patterns, treatment and prevention programs. *Endocrine, Metabolic & Immune Disorders Drug Targets* 20(7): 992–1002.

Trujillo, R., Jr., Fontão, F.N., and de Sousa, S.M. (2002). Unilateral masseter muscle hypertrophy: A case report. *Quintessence International* 33(10): 776–779.

Tsai, C.Y., Yang, L.Y., Chen, K.T. et al. (2010). The influence of masticatory hypofunction on developing rat craniofacial structure. *International Journal of Oral Maxillofacial Surgery* 39(6): 593–598.

Tuddenham, E.G.D., and Cooper, D.N. (1994). *The Molecular Genetics of Haemostasis and Its Inherited Disorders. Oxford Monograph on Medical Genetics No. 25*. Oxford: Oxford University Press.

Turkkahraman, H., and Sarıoglu, M. (2006). Oculo-facio-cardio-dental syndrome: Report of a rare case. *Angle Orthodontist* 76:

184–186.

Vandersluis, Y.R., and Suri, S. (2020). Infective endocarditis and orthodontic implications in children: A review of the literature. *American Journal of Orthodontics and Dentofacial Orthopedics* 157(1): 19–28.

Van Erum, R., Mulier, G., Carels, C. et al. (1998). Craniofacial growth and dental maturation in short children born small for gestational age: Effect of growth hormone treatment. Own observations and review of the literature. *Hormone Research* 50: 141–146.

van Venrooy, J.R., and Proffit, W.R. (1985). Orthodontic care for medically compromised patients: Possibilities and limitations. *Journal of the American Dental Association* 111: 262–266.

Verna, C., Dalstra, M., and Melsen, B. (2000). The rate and the type of orthodontic tooth movement is influenced by bone turnover in a rat model. *European Journal of Orthodontics* 22: 343–352.

Vernillo, A.T. (2001). Diabetes mellitus: Relevance to dental treatment. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* 91(3): 263–270.

Villa, A., Mariani, U., and Villa, F. (2010). T-cell lymphoma of the oral cavity: A case report. *Australian Orthodontic Journal* 55(2): 203–206.

Vitral, R.W., Tanaka, O.M., Fraga, M.R. et al. (2006). Acromegaly in an orthodontic patient. *American Journal of Orthodontics and Dentofacial Orthopedics* 130: 388–390.

Vogel, R.I. (1975). Intrinsic and extrinsic discoloration of the dentition (a literature review). *Journal of Oral Medicine* 30(4): 99–104.

Vucic, S., Korevaar, T., Dhamo, B. et al. (2017). Thyroid function during early life and dental development. *Journal of Dental Research* 96(9): 1020–1026.

Walker, M.R., Lovel, S.F., and Melrose, C.A. (2007). Orthodontic treatment of a patient with a renal transplant and drug-induced

gingival overgrowth: A case report. *Journal of Orthodontics* 34(4): 220–228.

Warburton, G., and Caccamese, J.F., Jr. (2006). Valvular heart disease and heart failure: Dental management considerations. *Dental Clinics of North America* 50(4): 493–512.

Williams, D.A. (2008). Drug metabolism. In: T.L. Lemke and D.A. Williams (eds.), *Foye's Principles of Medicinal Chemistry*, 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins, p. 253.

Wittmann, A.L. (1977). Macroglossia in acromegaly and hypothyroidism. *Virchow's Archives* 373: 353–360.

Wolford, L.M. (2001). Idiopathic condylar resorption of the temporomandibular joint in teenage girls (cheerleaders' syndrome). *Proceedings (Baylor University. Medical Center)* 14(3): 246–252.

Yagi, T., Kawakami, M., and Takada, K. (2004). Surgical orthodontic correction of acromegaly with mandibular prognathism. *Angle Orthodontist* 74: 125–131.

Yasny, J. (2010). The importance of oral health for cardiothoracic and vascular patients. *Seminars in Cardiothoracic and Vascular Anesthesia* 14: 38–40.

Zhang, X., Yi, J., and Li, Y. (2020). Effects of nutrition and hormones on functional appliance treatment outcome in patients with skeletal Class II malocclusion. *Journal of the World Federation of Orthodontists* 9(1): 9–12.

3

Psychosocial Factors in Orthodontics: Patient Perceptions, Motivation, and Expectations

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Summary

Every patient has individual perceptions, behaviors, and needs, some of which are outside the usual experience of most orthodontists. Clear communication is critical when discussing orthodontic problems, proposed treatment, and treatment alternatives and expectations. In addition, the clinician must become completely familiar with the patient's medical and psychosocial history, needs, and perceptions. In this way, many problems can be minimized, and the treatment outcome can be most successful. This chapter will explore the patient's perspective on orthodontic treatment, both in patients with a typical range of perspectives as well as in patients whose character is influenced by atypical situations such as jaw deformities, craniofacial anomalies, or abnormal psychology.

Orthodontic patients present with a variety of malocclusions, but also with an even greater variety of motivations, perceptions, and expectations. Motivations and expectations can also be different between patients and their parents. Managing these intangible factors is not typically taught in detail during orthodontic education, but orthodontists must learn to address them because they may significantly influence treatment success.

Motivation for orthodontic treatment

Learning about patients' motivations for orthodontic treatment is the key to meeting their needs and expectations. Research into the motivation of patients and their parents for orthodontics has typically been carried out through questionnaires administered at the beginning of treatment. Wędrychowska-Szulc and Syryńska (2010) gathered information from 674 children aged 7–18, a parent or guardian of each, and 86 adult patients in Poland to explore their reasons for seeking orthodontic treatment. Each questionnaire had nine options and the respondent could select multiple reasons for treatment. Examples of reasons included "I want to correct my appearance," "I have been referred by my dentist," and "my parents want me to be treated." These reasons were reworded for the parental questionnaire. The main motivational factor reported was "I have irregular teeth," checked by 50–70% of each age group. Another significant factor for patients younger than 16 years was "my parents wanted me to be treated." Females more than males checked "I want to correct my appearance" and the percentage of both genders indicating this increased with age. Geoghegan et al. (2019) carried out a similar study of patients in private practices in the UK. They administered a different questionnaire to 238 patients aged 8–20 (with nearly half aged 11–13) at the screening appointment. Their results were similar in that esthetic concerns played a major role. Over 80% were concerned about the appearance of their teeth. The top three concerns were "crookedness," "sticking out," and "bite."

Daniels et al. (2009) compared the motivation and cooperation of patients aged 7–16 and their parents before and during treatment. They surveyed 83 patients at the screening visit and 144 during treatment at a university clinic. Like previous studies, esthetic concerns were by far the most important motivating factor for treatment, with >90% of both parents and patients giving this response. Interestingly, however, the parents were always more motivated than the children for treatment, particularly during treatment, while the children's responses did not change during treatment. It was found that children who were more highly motivated for treatment also had greater cooperation. Ernest et al. (2019) studied a group of 100 children aged 7–17 years in Nigerian

public hospitals both before and during orthodontic treatment. The patients and their parents completed similar surveys regarding motivation and expected cooperation. In contrast to Daniels' study, Ernest et al. (2019) found that before treatment, children were more motivated than their parents to have treatment. However, as Daniels et al. (2009) reported, the parents had more motivation than the children during treatment. Ernest did find that the children's motivation decreased slightly during treatment, although the percentage of children who agreed that braces were important increased significantly. Clinicians should realize that although parents are responsible for bringing their children to the orthodontist, the child's motivation is important for the success of treatment.

Bauss and Vassis (2023) investigated the influence of bullying on the motivation for and expectations of orthodontic treatment. They surveyed 1020 children with a mean age of 11.8 years. Based on their responses to a questionnaire, the subjects were divided into three groups: those who reported being bullied due to dentofacial features, those who were bullied due to other physical features, and a control group who had not been bullied. Overall, 23.7% reported being bullied. Being bullied due to dentofacial features distinguished this group in several ways. They were significantly more likely to initiate treatment for themselves (as opposed to parents or their dentist), and had a greater desire for orthodontic treatment than those who were bullied for other physical features. In addition, although esthetics was the main motivation throughout the sample, this group said they had "ugly teeth," in contrast to the other groups' stated reason of wanting "to look pretty."

Tristão et al. (2020) carried out a systematic review to evaluate the relationship between malocclusion and bullying in children and adolescents. They found numerous methodological shortcomings that prevented them from drawing firm conclusions. For example, of the nine articles ultimately reviewed, six studies used the term "bullying" while four used "teasing" and one other used "harassment" to describe the unwanted behavior; in addition, five different questionnaires were used to elicit the patient's experiences. In the end, the quality of evidence given in the studies was judged to be "very low," and only two studies were classified as

methodologically sound. However, the authors still concluded that severe malocclusion may be related to bullying.

Clearly, being bullied specifically for the appearance of their teeth and mouth makes children with significant malocclusion particularly motivated for orthodontic treatment. Clinicians should be sensitive to the perception of all patients, including children.

Treatment expectations

Several authors explored the expectations of patients and their parents about orthodontic treatment. Geoghegan et al. (2019) included several questions about what treatment required on his questionnaire discussed previously. Nearly 100% of the patients knew that they would need to alter their diet and that oral hygiene would be very important, but only 24% knew how often they should brush their teeth. Half of the parents thought treatment would take 1–2 years, and an additional 40% thought it would take less than 1 year. Michelogiannakis et al. (2021) used a validated questionnaire from a European study to explore the expectations of 70 prospective patients and their parents in a university setting. Comparing patients and parents, they learned that patients expected less discussion and diagnosis at the screening appointment and more dietary restrictions than parents. Parents more than patients expected a better smile and more social confidence after treatment. Examining sociodemographic factors, those parents with more than 12 years of education expected more problems with eating, less improvement in mastication, and more discussion about treatment than those parents with 12 years of education or less. The more educated group also expected more improvement in social confidence. Expectations should be probed, with both patients and parents being asked detailed questions to identify and clarify the specific features they dislike and how they would like to have them changed. The patient and parent may be guided toward realistic expectations using photos and questions that elicit detailed responses.

Perception of malocclusion

Patients' perceptions of their malocclusion are influenced by personal factors, perhaps due to the deeply personal significance of the mouth and teeth. In addition to determining patients' motivation and expectations, exploring how they perceive their condition is also useful when formulating a treatment plan so that their concerns can be addressed.

Several research approaches can give insight into how patients see their malocclusion. One key method is to show the patient profiles. By altering one aspect of the profile in successive photographs or silhouettes and asking the patient to indicate which profile is most like theirs, it is possible to determine how accurately patients perceive profiles (Tufekci et al., 2008). A version of this is the Perceptometrics technique developed by Giddon et al. (1996), in which computer alterations are made to photographic images, with the feature of interest moved back and forth in one dimension at gradual, predetermined intervals. By clicking on the image, the range of photographs can be traversed. Patients can then indicate the acceptable range of profiles, and they can also indicate which profile is most attractive. This tool enables clinicians to determine the range of what patients consider acceptable.

Many studies have been done using the Perceptometrics method. Kitay et al. (1999) found that orthodontic patients are less tolerant of variations in their profiles than are nonorthodontic patients. To determine their range of acceptability, 16 patients and 14 nonorthodontic adult patients were asked to respond to computer-animated profiles that distorted the lower third of their own faces using the Perceptometrics program. Both groups of subjects were equally accurate in identifying their own profiles. However, the orthodontic patients had a smaller zone of acceptability (ZA) in features in a control face, with a significant disparity between one feature in their own profile and the most pleasing position for that feature. This suggests that orthodontic patients are motivated to seek treatment by specific features in their own face that they perceived as undesirable.

Using the Perceptometrics technique, Arpino et al. (1998) compared the acceptable profiles selected by orthognathic surgery patients with those of their "significant others," orthodontists, and oral surgeons. Patients with both Class II and Class III jaw discrepancies evaluated their own photographs with the upper lip, lower lip, both lips together, and chin altered horizontally and one feature, lower facial height, altered vertically. Although there was some variation, the ZA was smallest for the patient, followed by the surgeon, the significant other, and finally the orthodontist. Whereas the patient and the significant other groups differed in only two instances, the orthodontists and oral surgeons had significantly different ZAs for all but the Class II bimaxillary relationship. These results show that orthodontists are most tolerant of different profiles, while the patients themselves are least tolerant.

Hier et al. (1999) used the same technique to compare the preferences for lip position between orthodontic patients and untreated subjects of the same age. They found for both males and females that the untreated subjects preferred fuller lips than did orthodontically treated subjects, which is greater than Ricketts's ideal measurement of lip protrusion.

Miner et al. (2007) compared the self-perception of pediatric patients with the perceptions of their mothers and their treating orthodontists. Using the Perceptometrics technique, the upper lip, lower lip, and chin were distorted as the images moved from retrusive to protrusive extremes. The patients, mothers, and clinicians were asked to indicate the ZA for each feature and the most accurate representation of the child's profile, as well as to indicate the ZA for a neutral female face. Both patients and mothers were found to overestimate the protrusiveness of the child's actual mandible, and both groups preferred a more protrusive profile for both the child and the neutral face. In addition, the mothers had the smallest tolerance for change in the soft tissue profile. These studies are valuable for pointing out the potential inaccuracies of patients' perceptions as well as their differing preferences.

These techniques are also useful for exploring the perceptions of different racial and ethnic groups. In a study by Mejia-Maidl et al. (2005), 30 Mexican Americans and 30 white people of varying age,

sex, education, and acculturation indicated their perceptions of four profiles of individuals of Mexican descent. Using the Perceptometrics program, the authors found that in general Mexican Americans preferred less protrusive lips than did white people. In addition, there was a wider ZA for male lip positions and female lower-lip positions among the white people than among the Mexican Americans of low acculturation. These observations were not true of highly acculturated Mexican Americans, who may have assimilated white American esthetic preferences. Park et al. (2006) compared the perceptions of Korean American orthodontic patients with those of white orthodontists and Asian American orthodontists. Statistically significant differences were found between the Korean American patients and the white orthodontists for the acceptable and preferred positions of the female nose and the male chin, finding that the Korean Americans preferred a more protrusive nose for females and a more retrusive chin for males. McKoy-White et al. (2006) compared the ZA for Black females among Black female patients, Black orthodontists, and white orthodontists. The patients were also asked to identify their most accurate pretreatment and posttreatment profile. It was found that the white orthodontists preferred flatter profiles than did the Black women, who in turn preferred fuller profiles than the Black orthodontists. Although the patients could correctly identify their own posttreatment profile, they all recalled a fuller pretreatment profile than they actually had.

Another method of assessing patients' perception of their own malocclusion or facial disharmony is by assessing their oral health-related quality of life (QOL). QOL is defined as individuals' perception of their position in life in the context of the culture and value system in which they live and in relation to their goals, expectations, standards, and concerns (de Avila et al., 2013). The oral cavity is the center of much of life – eating, speaking, esthetics – that any problem may significantly influence a patient's overall feeling of well-being. In the past few years, the effect of malocclusion on patients' QOL has been studied.

Several studies were carried out at Boston University to explore the oral health-related QOL in teens and adults. A specific Teen Oral Health-Related Quality of Life (TOQOL) instrument (Wright et al., 2017) was developed that probed the oral health-related QOL in five

domains: role (everyday functioning), oral health, social, emotional, and physical. Each item in each domain is explored by asking a question beginning “Due to problems with your teeth and mouth, how often in the past 3 months have you…?” Rich et al. (2015) surveyed 161 parent–teen pairs from diverse ethnic backgrounds and no previous orthodontic treatment. The severity of malocclusion was determined using the Index of Orthodontic Treatment Need (IOTN; Brook and Shaw, 1989) and those teens with mild to moderate malocclusions were compared with those with severe malocclusions. Parents were also surveyed as to their perception of the effect of their child’s malocclusion on the QOL. Children with severe malocclusion had poorer oral health-related QOL in the esthetic domain, while their parents reported worse QOL in the emotional, physical, and role domains. Neely et al. (2017) compared these scores with those of 146 adults with a mean age of 32. In general, scores overall and by domains were higher for adults than for teens, signifying a greater effect on QOL. Mean TOQOL scores were worse (17.55) in adults than in teens (11.92, $p < 0.01$); emotional domain scores were 16.54 in adults compared with 9.39 in teens ($p < 0.01$); and the social domain score was 35.29 for adults compared with 21.59 for teens ($p < 0.01$). It can be concluded that both teens and adults can be greatly affected by their malocclusions, and specific areas of influence can be identified.

Multiple authors (Dimberg et al., 2015; Kragt et al., 2016; Sun et al., 2017, 2018; Alrashed and Alqerban, 2021) have carried out systematic reviews or meta-analyses exploring the relationship between malocclusion and the patient’s perceived oral health-related QOL. All analyses revealed a negative impact of malocclusion on oral health-related QOL, and some detected more nuanced associations. Sun et al. (2018) evaluated 11 qualifying studies and found that while malocclusion had an impact on all subscale scores of the Oral Health Impact Profile survey instrument, patients with severe malocclusion had worse QOL in the areas of physical disability, physical pain, psychological discomfort, psychological disability, and social disability. Kragt et al. (2016) discovered significant findings in two areas. First, the age of the patient had an influence in the impact of malocclusion on oral health-related QOL. Although younger adolescents (age 11–14) were more likely to be affected by

malocclusion, teens older than 14 years had a more severe impact on their oral health-related QOL. Second, the outcomes from the different countries represented in the studies suggested that cultural differences may influence the impact of malocclusion on oral health-related QOL. This is consistent with the definition of QOL as the individual's perception of his/her position in life. In addition, the local healthcare system and the presence or absence of other significant oral disease may place malocclusion in a very different context for the individual.

Because of the wide variation in patient perception and the effect of the malocclusion on the patient's life, it is critical for the orthodontist to explore the patient's ideas and expectations when discussing treatment. Here, education of the patient and the parents, if applicable, is important, because most have a limited understanding of what are reasonable treatment goals and procedures.

Patients do not always understand or remember what they have been told about their malocclusion or the orthodontic treatment. Mortensen et al. (2003) interviewed 29 patients aged 6–12 years and their parents 30 minutes after obtaining informed consent. Both the children and their parents were asked about the reasons for treatment, risks, and responsibilities mentioned during the discussion. It was discovered that although an average of 4.7 risks were mentioned during each discussion, the parents remembered on average 1.5 risks and the children remembered less than 1. Similarly, 2.3 reasons for treatment were mentioned by the orthodontist, but the parents and children remembered on average 1.7 and 1.1, respectively. Clearly, patients and parents do not remember all the information told to them. Clinicians need to convey such information to patients in writing or graphic form.

Patients with psychological disorders

In addition to physical problems, many orthodontic patients may have preexisting psychological disorders when they present for orthodontic treatment. Although these patients are usually controlled, it is important to recognize how these disorders may be manifested. In addition, orthodontists should be aware of side effects of medications that may have implications for oral health.

Common psychological conditions are delineated by the American Psychiatric Association in the *Diagnostic and Statistical Manual of Mental Disorders*, or *DSM-5-TR* (American Psychiatric Association, 2022). The most common conditions that orthodontists may encounter are attention-deficit/hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD), body dysmorphic disorder (BDD), bipolar disorder, panic disorder, and depression. In addition, there are some personality disorders and other psychological conditions, such as eating disorders, that may acutely affect adolescents.

ADHD is a chronic disorder characterized by inattention, impulsivity, and hyperactivity. A survey carried out in 2013 reported that 8.8% of children aged 3–17 were diagnosed with ADHD (Friedlander et al., 2007). Some diagnostic criteria, however, are nonspecific and the disorder may be overdiagnosed. Nevertheless, the main criterion is that the behavior must cause impairment in the individual's life for a prolonged period of time (American Psychiatric Association, 2022). Hyperactivity and the inability to focus can be problems during orthodontic treatment. Patients with ADHD may have trouble sitting still during procedures and may not be compliant in maintaining good hygiene, wearing elastics, or performing other tasks because of inattentiveness. These patients can be best managed by giving short, clear instructions and written instructions or reminders to them or their parents, with follow-up questions to determine their comprehension and rewards for successful compliance. Dental prophylaxis may be needed more frequently to avoid decalcification and caries. To increase the likelihood of treatment success, it may be wise to avoid treatment plans that require a high degree of patient compliance. During treatment, it is often helpful to give the patient breaks during prolonged procedures.

OCD (Zohar, 1999), depression (Kessler and Walters, 1998; Neely et al., 1998; Friedlander and Mahler, 2001), panic disorder (Becker, 2008), and bipolar disorder (Friedlander et al., 2002) may all present with a wide variety of symptoms, including intrusive thoughts, suicidal ideation, apathy, and anxiety, and more than one disease may coexist in the same patient. In addition, these conditions are frequently treated with serotonin reuptake inhibitors. These

medications serve to increase the amount of neurotransmitters in the postsynaptic space, but may have side effects including glossitis, xerostomia, and gingivitis (Ferguson, 2001).

BDD is characterized by an intensely negative emotional response to a minimal or nonexistent defect in the patient's appearance. Because the head and face are common foci for the disorder, orthodontists may see patients who have excessive concerns about their dentofacial appearance (Veale et al., 1996). Other characteristics of this disorder involve multiple consultations about their perceived defect, an obsessive concern with appearance, and emotional volatility (Anthony and Farella, 2014). This preoccupation may lead to stress and related disorders and behaviors. Patients with BDD will frequently see multiple providers in an effort to get treatment, but even if they receive treatment they are rarely satisfied. In some cases, these patients become violent or commit suicide (Philips, 1991).

Even if patients do not have a diagnosis of BDD, they may have excessive concerns about minimal or nonexistent deformities or malocclusion. The orthodontist can screen out patients who may have excessive concerns that are impossible to satisfy by taking a careful history on every patient, particularly probing the extent and nature of esthetic concerns. Since most patients with esthetic concerns are not significantly disfigured, these deformities would probably be considered minimal. If patients show an inordinate focus on minor problems, the orthodontist would be well advised to look further before starting treatment, or not begin treatment at all. Polo (2011) has developed questions that can be used as starting points to identify patients who may have excessive concern over esthetic problems.

Personality disorders are conditions that involve maladaptive behaviors and patterns of thinking that lead to problems at home, school, and work. Personality disorders most frequently seen are narcissistic personality, borderline personality disorder (BPD), and antisocial personality disorder (APD). It is estimated that the prevalence of these personality disorders ranges from 4.4% to 13% in the United States (Coid, 2003). Environmental influences such as prior abuse, poor family support, family disruption, and peer

influences, as well as biological causes, are important risk factors for the development of such disorders.

Patients with narcissistic personalities believe that they are special and therefore entitled to special treatment. The typical narcissistic patient has very brittle self-esteem and a strong need for approval, which are manifested as arrogance and demands for special attention. These patients are thus more intolerant of minor complications and are more likely to seek legal recourse when dissatisfied.

Patients with any form of personality disorder can be difficult to manage in an orthodontic office, and may be disruptive and challenging for clinicians. Such individuals may be hard to identify or label, even though they may not be compliant and may show some signs of depression or substance abuse and even attempted suicide. Staff members need to handle these patients with evenhandedness, not allowing them to disrupt the office procedures or abuse office personnel. Orthodontists should beware of excessively dependent or manipulative behaviors, which can cause conflict among staff members. If necessary, care can be discontinued and the patient dismissed.

In general, all demanding and needy patients should have limits placed on their behavior at the point when treatment alternatives are discussed. Orthodontists should not promise too much in describing treatment plans and outcomes. They should describe how they would address the orthodontic needs, noting potential problems and obstacles to the treatment, and explain how progress might be evaluated. In fact, some variation of the Perceptometrics method might be helpful in presenting patients with an acceptable range of suggested treatment outcomes. This will minimize the possibility that patient expectations are too high. As Groves (1978) commented, “Difficult patients are typically those patients who raise ‘difficult’ feelings within the clinician.” Orthodontists must learn to address these difficult feelings and deal with them. The orthodontist should remain friendly, unemotional, and professional at all times. Emotional outbursts should be responded to with an acknowledgment of feelings but an expectation of appropriate behavior. Noncompliance must be countered with an appropriate

alternative treatment plan. The clinician and staff must avoid being provoked and remain professional and emotionally neutral while maintaining a correct office atmosphere.

With such patients, limits on therapeutic intervention must be set. Patients should be given realistic options with definite endpoints, including the option of no treatment. Concrete comparisons and predictions should be shown to reinforce reality and not lead to unrealistic expectations. Treatment options and the final treatment plan, along with possible obstacles to ideal results, should be put in writing. If the patient is already undergoing orthodontic treatment, it should be stopped and/or the patient referred to other health professionals.

Orthognathic patients

Psychosocial aspects of orthognathic surgery patients deserve special consideration, because their treatment often involves changes in appearance that may or may not be the motivation for treatment. In addition, surgery entails risks beyond those of orthodontics alone.

Motivation

When considering the success of combined surgical–orthodontic treatment, the patient's motivation must be considered. Is their decision a normal reaction to a debilitating dentofacial deformity, or do they have an abnormal perception that surgery will not correct?

Yu et al. (2013) used QOL instruments to determine motivations for orthognathic surgery in Chinese patients. In this study, 210 healthy patients completed a questionnaire that included self-esteem measures as well as oral health QOL items. Their responses were compared with those from 219 individuals not undergoing surgery. Both genders listed improvement of their facial appearance as the primary reason for having orthognathic surgery. Men listed occlusion second and self-confidence third, whereas women reversed the positions of these two motivations. Self-esteem was significantly lower in the patient group.

Ryan et al. (2012b) interviewed 18 patients, 18–40 years old, before orthognathic surgery. The interviews revealed that the deformity affected the patients in either practical or psychological ways, or both. Practical effects included functional problems, such as difficulty eating or speaking, or structural problems, such as asymmetries or overjet. Psychological problems included feeling helpless about their appearance or avoiding social situations. Patients coped with these problems by either avoiding confronting the problem (including social isolation) or continuing normal activities while modifying their behavior to minimize the impact of their condition. Motivation for treatment is traditionally classified as external or internal, but this study discussed the practical and psychological motivations that led from the impacts described. Both factors resulted in the patients deciding that they wanted a change in their lives, whether that meant feeling more confident about themselves or being able to chew more effectively. The authors stressed that both external and internal motivations were present, and many patients reported combined external/internal motivation. This study very clearly demonstrated that the degree of impact deformities can have on a person's life is not necessarily proportional to the physical deformity, and that the problem as perceived by the patient may be quite different from that observed by the clinician.

Quality of life

Considerable research has studied the effect of dentofacial deformity on QOL. Lee et al. (2007) asked 76 patients referred for orthognathic surgery to complete three different questionnaires: a generic health-related questionnaire, a generic oral health-related questionnaire, and a condition-specific QOL measure. Their responses were compared with those from a control group of patients who were referred for the removal of third molars. No differences were observed in any domain of general health, such as physical functioning, pain, mental health, vitality, and social functioning. However, they found significant differences in the overall oral health-related QOL questionnaire in areas of functional limitation, psychological discomfort, psychological disability, and handicap, with specific problems in areas such as being able to pronounce words properly, being self-conscious or embarrassed because of the

mouth or teeth, and feeling that life in general was less satisfying because of problems with the teeth or mouth. Finally, the condition-specific QOL inventory demonstrated significant differences in five areas, including reporting more problems while biting and chewing and reporting disliking having their photograph taken or being seen on video. Clearly, these results indicate that patients with dentofacial deformities have a poorer QOL in a variety of aspects.

De Avila et al. (2013) also assessed 50 patients one year before undergoing orthognathic surgery to determine if they exhibited signs of depression in greater frequency than a nonsurgical population. The patients were given modified QOL questionnaires as well as a depression inventory. The patient was judged either to have some degree of depression or not depending on the total score. Using this method, 19 patients were judged to have some degree of depression. De Avila noted that the diagnosis of depression was positively correlated with a lack of energy ($p < 0.001$), less social activity ($p = 0.011$), and poorer mental health ($p = 0.008$). This study emphasizes the interrelationships between physical and mental health and underscores the necessity of carefully screening potential orthognathic patients.

Lee et al. (2008) tracked changes in QOL in 36 patients preoperatively as well as six weeks and six months postoperatively. A significant increase in QOL was revealed immediately after surgery as well as in the long term. Both general mental and physical scores improved after six weeks as well as specific improvements in facial esthetics, psychological discomfort, and social functioning. Clearly, patients benefit in a variety of ways from orthognathic surgery.

Phillips et al. (2008) more closely evaluated patients' postoperative course by asking 170 patients to complete a 20-item health-related QOL survey each postoperative day for 90 days. At least 30 days of questionnaires were completed by 170 patients, who brought them to clinic visits at 1, 4–6, and 12 weeks. By the end of the first postoperative week, most patients had few postoperative sequelae. Under 7% reported any significant problems after two weeks. The return to daily activities followed a similar pattern, with 85% reporting no substantial problems with their daily life by the end of the first month. The problem that lasted the longest was oral

function. By 64 days postoperatively, 75% of patients reported no or slight problems with opening the mouth and eating, but the same level of recovery was not reported for chewing until day 70.

Brouns et al. (2022) carried out a systematic review and meta-analysis to evaluate the impact of preoperative orthodontic treatment on oral health-related QOL. They evaluated six studies and found that all had a serious risk of bias. Only two studies measured the oral health-related QOL during each phase of treatment, which enabled the effects from the preoperative orthodontic and surgical phases to be distinguished. Nonetheless, their results suggested that there was a decrease in oral health-related QOL during the preoperative orthodontic treatment, but an improvement after surgery. They recommended that future studies employ a standardized method to document these changes.

The use of "surgery first" treatment enables the clinician to compare the effect of each stage of orthognathic treatment on the patient's QOL. Pelo et al. (2017) administered two questionnaires to 30 consecutive patients, 15 of whom received bimaxillary surgery before any orthodontic treatment and 15 patients whose treatment followed the traditional sequence of orthodontic preparation ranging from 18 to 24 months before the bimaxillary surgery. The oral health-related QOL instruments were completed before bracket placement (which was three days preoperatively for the surgery-first group), one month preoperatively (for the control group only), and one month postoperatively for both groups. Both groups had similar QOL scores at the time of bracketing, but by one month preoperatively the control group reported poorer QOL. One month postoperatively, both groups' scores had improved dramatically. However, the final oral health-related QOL score for the surgery-first group was significantly better than for controls, even though they were just beginning their orthodontic treatment. Although both groups demonstrated a similar improvement in QOL after surgery, it should be remembered that the surgery-first group experienced this improvement after only one month, whereas the control group had been in treatment for more than one year. These benefits for QOL are real and significant, and provide validation for this procedure.

Expectations and satisfaction with treatment results

Regardless of patients' motivations for orthognathic treatment, their ultimate satisfaction is related to their expectations from treatment. Ryan et al. (2012a) interviewed 18 adult patients and found two broad categories of expectations: those related to physical changes, and those related to the effect these changes had on patients' lives. Patients were found to fall into four categories earlier delineated by Ritchie et al. (2003): metamorphosizers, pragmatists, shedders, and evolvers. *Metamorphosizers* had expectations of both physical and psychological problems being fully corrected by the surgery. These patients will be more likely to be dissatisfied and may require more exploration of their expectations. *Pragmatists* expect a physical but not psychological change, since they see the deformity as totally physical. However, these patients may be dissatisfied, because the physical changes may not happen to the extent expected, and unforeseen emotional changes may trouble the patient. A third type of patient, *shedders*, expect little physical change but profound psychological change. These patients also require careful counseling to determine their true motivations and expectations. Finally, *evolvers* have very low expectations for both physical and psychological changes. This, too, poses some risk of dissatisfaction, because there may be more changes, both physical and emotional, than the patient was ready for.

Ryan et al. (2012b) made no distinction between realistic and unrealistic expectations. However, clinicians need to discuss with the patient what their expectations are and judge whether those expectations are realistic. This requires the clinician to spend the necessary time with patients discussing their perceptions and motivations.

Another method of examining expectations was used by Bullen et al. (2014), who constructed a profile altered with incremental movements of the lips to create a 13-photo sequence. Then 85 patients who were either in orthodontic treatment or considering surgery were given a photo of their own profile as well as the series of constructed profiles. The patients were first asked how satisfied they

were with their current profile, and then were asked to choose which of the profiles in the constructed series most closely matched their own. The profile chosen was compared to the individual's profile to measure the difference between the patient's real and perceived profiles. The authors found that while the younger patients (15–25 years) thought that their lips were more retrusive than they actually were, patients over 25 years of age thought that their lips were more protrusive than they actually were. The authors concluded that older patients may need additional efforts to make sure that they have an accurate view of their facial profile, and thus have an accurate expectation of treatment outcomes.

The ultimate goal of orthognathic surgery is patient satisfaction. Even with a technically successful procedure, success has not been achieved without a satisfied patient. Thus, the factors determining patient satisfaction need to be determined so that, where possible, they can be optimized.

Kiyak et al. (1982) gave questionnaires to 74 consecutive orthognathic surgery patients at six time points, from before surgery to 24 months postoperatively. They found that at 1 month and 4 months postoperatively, those who experienced less pain and numbness than expected had higher self-esteem and were overall more satisfied than those who had more pain and numbness than expected. However, although the levels of satisfaction and self-esteem rose after surgery to 4 months, the levels were lower at 9 months. The authors hypothesized that by 9 months patients might see their results as permanent, so that any remaining problems would decrease their sense of satisfaction (Kiyak et al., 1982). By 24 months, however, the various categories of self-esteem had rebounded and patient satisfaction was at its highest level. The authors concluded that satisfaction in the orthognathic surgery may evolve for at least two years and suggested that clinicians work with patients' over the long term to make sure they have adapted well to the surgical outcome (Kiyak et al., 1984).

Finlay et al. (1995) evaluated the satisfaction of 61 orthognathic patients to determine whether the surgery had any influence on the patients' self-esteem. Preoperatively, patients were given three questionnaires that assessed their extroversion/introversion status,

general health, and feelings toward their bodies. They were also asked questions surrounding their motives and expectations with regard to the surgery. At three time points postoperatively, the patients were given some or all of these questionnaires once again to examine changes. The researchers found that 87% of the patients were satisfied with their result. Those who were not satisfied had neuroticism scores on the personality tests that were significantly higher. No associations between satisfaction and general health, gender, extroversion, or self-esteem were found. All dissatisfied patients reported experiencing more pain, swelling, numbness, and scarring than expected, in contrast to the majority of the group.

Cunningham et al. (1996a) conducted a similar study, querying 83 preoperative and 110 postoperative patients to determine self-esteem and level of postoperative satisfaction. They found that 95% of patients were satisfied with their treatment at least 9 months after surgery. The reasons given for dissatisfaction were inadequate preparation for postoperative problems and one case of not having as great a change as expected. There was no significant difference in self-esteem between the pre- and postoperative groups. The authors concluded by recommending that preoperative patients be given information regarding the postoperative course and potential problems to help prevent dissatisfaction that may persist.

Perhaps the ultimate indicator of treatment success is the long-term benefit experienced by patients. Motegi et al. (2003) evaluated 93 patients who had received mandibular surgery for a Class II malocclusion preoperatively as well as 2 and 5 years postoperatively. They evaluated health-related abilities, daily activities, and current symptoms. They found that after both 2 and 5 years, there was significant improvement in all areas.

Lazaridou-Terzoudi et al. (2003) also looked at long-term benefits in 117 patients 11–14 years after orthognathic surgery and compared the results with two control groups: one group waiting for orthodontic treatment, and a group of comparably aged adults not seeking treatment. They found a linear improvement in all four subscales of function, health, interpersonal relations, and appearance from the preoperative time point to the present. Compared with both control groups, the orthognathic surgery group reported current functioning

higher than either control group, but their reported level of functioning before surgery was lower than the nontreatment controls. The authors also asked the patients to rate their feelings toward different aspects of their physical appearance. In contrast to the improved functioning reported in the earlier subscales, the orthognathic patients had lower overall facial body image than either control group, but similar assessments of total body image. The authors also found that the youngest patients, who had undergone surgery in their teens, were less likely to be satisfied with the overall result and were least satisfied with their current appearance. This is consistent with a report by Cunningham et al. (1996b) that patients in their 30s are more satisfied with their appearance after surgery.

Soh and Narayanan (2013) carried out a systematic review of 21 studies assessing patient motivations, perceptions, or changes in QOL. Their conclusions can serve to summarize all the studies discussed here:

- During the presurgical orthodontic treatment phase, oral health-related QOL decreases but orthognathic surgery improves the overall QOL, with the biggest improvements in the social/emotional and psychological areas.
- Using validated questionnaires improved clinicians' ability to determine the effect of surgery on patients.
- Esthetics and occlusion are the main motivations for patients to undergo orthognathic surgery.
- Most causes of postoperative dissatisfaction are due to short-term surgical sequelae, which can take months to resolve. However, unrealistic expectations can also cause dissatisfaction.

Patients with orofacial clefts and craniofacial anomalies

The most common facial deformity that orthodontists will see is cleft lip and palate. Considerable research has been done examining the psychological aspect of this congenital anomaly. Kapp-Simon (1986) explored whether primary school-age children with clefts have

negative self-concepts by using the Primary Self-Concept Inventory and compared the results from tests administered to 172 children without clefts. She found that the children with clefts had low self-concepts in the areas of social self, emotional state, and helpfulness. It is apparent that this group of children feels stigmatized by their cleft from a very early age and therefore can be expected to have a very different attitude toward orthodontic treatment to those without clefts.

More recently, Broder et al. (2014) assessed the QOL of patients with clefts using the Child Oral Health Impact Profile scale. This instrument was given to patients aged 7–19 years around the United States. It asks the degree to which the patient has difficulty with oral symptoms, functional well-being, social–emotional well-being, school/environment, and self-esteem. Patients who needed surgery had a lower QOL in all aspects except for self-esteem, which is consistent with earlier reports (Hunt et al., 2005) that the majority of patients with clefts do not "appear to experience major psychosocial problems." Broder also found that with increasing age, girls had a greater reduction in QOL than boys. This was thought to be due to the greater importance of attractiveness for girls during adolescence, and underscores the importance of listening carefully to patients' concerns during orthodontic visits.

In their practice orthodontists also see patients with craniofacial anomalies (CFAs), and these patients will be fundamentally different psychologically from patients who have no such deformity. Pertschuk and Whitaker (1988) compared a group of 43 patients with CFAs between the ages of 6 and 13 with children matched for age, sex, intelligence, and family income to determine differences in psychological functioning before surgery. They studied levels of anxiety, self-concept, social experiences, intelligence, and personality characteristics, and found that the craniofacial patients were more anxious, more introverted, and had a poorer self-concept. By 12–18 months after surgery, patients demonstrated reduced levels of anxiety but more negative social interactions, possibly because their social skills had not developed as the patients grew. The authors thus concluded that modest improvements in psychological adjustment were due to craniofacial surgery.

Volpicelli et al. (2017, 2020) carried out two important studies on children with CFAs and orofacial clefts, divided into three age groups: 8–10 years, 11–13 years, and 14–17 years. The first explored differences in the level of anger, anxiety, depression, and problems with peer relationships in a group of 99 patients aged 8–17 years. There were significant differences in each category, and in all categories except anger the youngest age children had the highest levels. The authors concluded that these young children were at high risk for psychosocial problems and needed to be closely monitored. In a follow-up study the scores of these children were compared with the scores given by their parents (Volpicelli et al., 2020). Surprisingly, the parents' perceptions of their child's functioning were often very different from the child's self-reported functioning. Whereas the youngest children reported the worst psychosocial functioning, their parents perceived lower depression and better peer relationships, and the parents of the 14–17-year-olds perceived higher anxiety and depression compared to the self-reports. Clearly, self-reporting of psychosocial issues is extremely important.

Sarwer et al. (1999) examined body image dissatisfaction, self-esteem, and QOL in 24 adults born with a CFA (hemifacial microsomia and orbital hypertelorism) and compared them with a control group who were not disfigured. The adults with craniofacial disfigurement reported significantly greater dissatisfaction with their facial appearance, lower self-esteem, and a lower QOL than the control group. It is interesting to note that dissatisfaction with facial appearance was correlated with the degree of residual facial deformity.

These studies point out the psychological differences in patients whose self-image is intrinsically different. Clinicians should realize that these patients may have a very different perspective on orthodontic treatment. Their expectations of treatment outcome may therefore also be quite different, and this should be explored when orthodontic treatment is discussed.

Patients with acquired deformities

An important subset of patients with facial deformities includes those who acquired their deformities after birth from trauma, tumor,

or disease. Because these patients had normal faces or occlusions prior to the insult, they may have more psychological stress in adapting to their acquired dysmorphic appearance than those patients who have never known any other morphology. Patients who have congenital anomalies have had time to incorporate the defect into their body image (Pruzinsky and Edgerton, 1997), but patients who suddenly lose their normal appearance have a much more difficult time coping with their deformity. Consequently, their expectations from treatment may be quite different from those patients who have never had a “normal” face.

De Sousa reviewed the psychological issues that may arise with reconstructive oral and maxillofacial surgery (De Sousa, 2008). In addition to CFAs, mentioned earlier, facial trauma can create significant problems for patients, not only because of the adaptation required to abrupt changes in facial appearance, but also due to posttraumatic stress disorder. Between 20% and 30% of patients with facial injuries may experience intrusive and disturbing thoughts, reexperiencing the trauma, sleep disturbances, irritability, or depression related to the original injury. These patients may need management by a team of specialists to help the patient cope with and recover from the past trauma. It has been found that a patient’s personality, coping ability, and social and family support are significantly related to how well the patient adjusts to their disease (Broder et al., 2014).

Because of the issues raised in these reports, it is critical that the patient’s expectations be discussed in detail and that the orthodontist outlines realistically what can be achieved. It is also important to discuss potential outcomes with other caregivers and, if appropriate, the patient’s family.

Conclusions

It is clear from the discussion in this chapter that patients may see their malocclusion very differently from clinicians. It is also obvious that patients may be significantly affected by their malocclusion in ways that have profound impacts on their life, from physical effects to bullying to damaged self-esteem. Patients who are born with physical deformities or CFAs may have effects that are different but

no less intense; patients who suddenly acquired facial deformities will have still different effects psychologically. The key to successful treatment of patients with these varied psychological situations and perceptions is frequent and detailed communication that includes listening on the part of the clinician as well as probing with detailed questions.

References

Alrashed, M., and Alqerban, A. (2021). The relationship between malocclusion and oral health-related quality of life among adolescents: A systematic literature review and meta-analysis. *European Journal of Orthodontics* 43(2): 173–183. doi: 10.10903/ejo/cjaa051.

American Psychiatric Association (2022). *The Diagnostic and Statistical Manual of Mental Disorders*, 5th ed., Text Revision (DSM-5-TR). Arlington, VA: American Psychiatric Association. doi: 10.1176/appi.books.9780890425596.

Anthony, M.T., and Farella, M. (2014). Body dysmorphic disorder and orthodontics – an overview for clinicians. *Australian Orthodontic Journal* 30(2): 208–213.

Arpino, V.J., Giddon, D.B., BeGole, E.A. et al. (1998). Presurgical profile preferences of patients and clinicians. *American Journal of Orthodontics and Dentofacial Orthopedics* 114(6): 631–637. doi: 10.1016/s0889-5406(98)70194-5.

Bauss, O., and Vassis, S. (2023). Prevalence of bullying in orthodontic patients and its impact on the desire for orthodontic therapy, treatment motivation, and expectations of treatment. *Journal of Orofacial Orthopedics* 84(2): 69–78. doi: 10.1007/s00056-021-00343-w.

Becker, D.E. (2008). Psychotropic drugs: Implications for dental practice. *Anesthesia Progress* 55(3): 89–99. doi: 10.2344/0003-3006-55.3.89.

Broder, H.L., Wilson-Genderson, M., Sischo, L., et al. (2014). Examining factors associated with oral health-related quality of life for youth with cleft. *Plastic and Reconstructive Surgery* 133(6): 828–834e. doi: 10.1097/PRS.0000000000000221.

Brook, P.H., and Shaw, W.C. (1989). The development of an index of orthodontic treatment priority. *European Journal of Orthodontics* 11(3): 309–320. doi: 10.1093/oxfordjournals.ejo.a035999.

Brouns, V.E.H.W, de Waal, A.-L.M.L., Bronkhorst, E.M. et al. (2022). Oral health-related quality of life before, during, and after orthodontic-orthognathic treatment: A systematic review and meta-analysis. *Clinical Oral Investigations* 26(3): 2223–2235. doi: 10./1007/s00784-021-04288-7.

Bullen, R.N., Kook, Y.-A., Kim, K. et al. (2014). Self-perception of the facial profile: An aid in treatment planning for orthognathic surgery. *Journal of Oral and Maxillofacial Surgery* 72(4): 773–778. doi: 10.1016/j.joms.2013.09.015.

Coid, J. (2003). Epidemiology, public health and the problem of personality disorder. *British Journal of Psychiatry* 44(suppl): S3–S10. doi: 10.1192/bjp.182.44.s3.

Cunningham, S.J., Crean, S.J., Hunt, N.P. et al. (1996). Preparation, perceptions, and problems: A long term follow-up study of orthognathic surgery. *International Journal of Adult Orthodontics and Orthognathic Surgery* 11(1), 41–47.

Cunningham, S.J., Hunt, N.P., and Feionmann, C. (1996). Perceptions of outcome following orthognathic surgery. *British Journal of Oral and Maxillofacial Surgery* 34(3): 210–213. doi: 10.1016/s0266-4356(96)90271-5.

Daniels, A.S., Seacat, J.D., and Inglehart, M.R. (2009). Orthodontic treatment motivation and cooperation: A cross-sectional analysis of adolescent patients' and parents' responses. *American Journal of Orthodontics and Dentofacial Orthopedics* 136(6): 780–787. doi: 10.1016/j.ajodo.2007.11.031.

de Avila, E.D., de Molon, R.S., Monteiro Loffredo, L.C. et al. (2013). Health-related quality of life and depression in patients with dentofacial deformity. *Oral and Maxillofacial Surgery* 17(3): 187–191. doi: 10.1007/s10006-012-0338-5.

De Sousa, A. (2008). Psychological issues in oral and maxillofacial surgery. *British Journal of Oral and Maxillofacial Surgery* 46(8): 661–664. doi: 10.1016/j.bjoms.2008.07.192.

Dimberg, L., Arnrup, K., and Bondemark, L. (2015). The impact of malocclusion on the quality of life among children and adolescents: A systematic review of quantitative studies. *European Journal of Orthodontics* 37(3): 238–247. doi: 10.1093/ejo/cju046.

Ernest, M.A., DaCosta, O.O., Adegbite, K. et al. (2019). Orthodontic treatment motivation and cooperation: A cross-sectional analysis of adolescent patients' and parents' responses. *Journal of Orthodontic Sciences* 8: 12. doi: 10.4103/jos.JOS_36_17.

Ferguson, J.M. (2001). SSRI antidepressant medications: Adverse effects and tolerability. *Primary Care Companion to the Journal of Clinical Psychiatry* 3(1): 22–27. doi: 10.4088/pcc/v03n0105.

Finlay, P.M., Atkinson, J.M., and Moos K.F. (1995). Orthognathic surgery: Patient expectations; psychologic profile and satisfaction with outcome. *British Journal of Oral and Maxillofacial Surgery* 33(1): 9–14. doi: 10.1016/0266-4356(95)90078-0.

Friedlander, A.H., Friedlander, I.K., and Marder, S.R. (2002). Bipolar I disorder: Psychopathology, medical management, and dental implications. *Journal of the American Dental Association* 133(9): 1209–1217. doi: 10.14219/jada.archive.2002.0362.

Friedlander, A., and Mahler, M. (2001). Major depressive disorder: Psychopathology, medical management, and dental implications. *Journal of the American Dental Association* 132(5): 629–638. doi: 10.14219/jada.archive/2001.0240.

Friedlander, A.H., Yagiela, J.A., Mahler, M.E. et al. (2007). The pathophysiology, medical management, and dental implications

of adult attention-deficit/hyperactivity disorder. *Journal of the American Dental Association* 138(4), 475–482. doi: 10.14219/jada.archive.2007.0199.

Geoghegan, F., Birjandi, A.A., Machado Xavier, G. et al. (2019). Motivation, expectations and understanding of patients and their parents seeking orthodontic treatment in specialist practice. *Journal of Orthodontics* 46(1): 46–50. doi: 10.1177/1465312518820330.

Giddon, D.B., Sconzo, R, Kinchen, J.A. et al. (1996). Quantitative comparison of computerized discrete and animated profile preferences. *Angle Orthodontist* 66(6): 441–448. doi: 10.1043/0003-3219(1996)066<0441:QCOCDA>2.3.CO;2.

Groves, J.E. (1978). Taking care of the hateful patient. *New England Journal of Medicine* 298(16): 883–887. doi: 10.1056/NEJM197804202981605.

Hier, L.A., Evans, C.A., BeGole, E.A. et al. (1999). Comparison of preferences in lip position using computer animated imaging. *Angle Orthodontist* 69(3): 231–238. doi: 10.1043/0003-3219(1999)069<0231:COPILP>2.3.CO;2.

Hunt, O., Burden, D., Hepper, P. et al. (2005). The psychosocial effects of cleft lip and palate: A systematic review. *European Journal of Orthodontics* 27(3): 274–285. doi: 10.1093/ejo/cji004.

Kapp-Simon, K. (1986). Self-concept of primary-school-age children with cleft lip, cleft palate, or both. *Cleft Palate Journal* 23(1): 24–27.

Kessler, R., and Walters, E. (1998). Epidemiology of DSM-III-R major depression and minor depression among adolescents and young adults in the National Comorbidity Survey. *Depression and Anxiety* 7(1): 3–14. doi: 10.1002/(sici)1520-6394(1998)7:1<3::aid-da2>3.0.co;2-f.

Kitay, D., BeGole, E.A., Evans, C.A. et al. (1999). Computer animated comparison of self perception with actual profiles of orthodontic

and nonorthodontic subjects. *International Journal of Adult Orthodontics and Orthognathic Surgery* 14(2): 125–134.

Kiyak, H.A., Hohl, T., West, R.A. et al. (1984). Psychologic changes in orthognathic surgery patients: A 24 month follow up. *Journal of Oral and Maxillofacial Surgery* 42(8): 506–512. doi: 10.1016/0278-2391(84)90009-0.

Kiyak, H.A., West, R.A., Hohl, T. et al. (1982). The psychological impact of orthognathic surgery: A 9-month follow-up. *American Journal of Orthodontics* 81(5): 404–412. doi: 10.1016/0002-9416(82)90078-1.

Kragt, L., Dhamo, B., Wolvius, E.B. et al. (2016). The impact of malocclusions on oral health-related quality of life in children – a systematic review and meta-analysis. *Clinical Oral Investigations* 20(8): 1881–1894. doi: 10.1007/s00784-015-1681-3.

Lazaridou-Terzoudi, T., Kiyak, H.A., Moore, R. et al. (2003). Long-term assessment of psychologic outcomes of orthognathic surgery. *Journal of Oral and Maxillofacial Surgery* 61(5), 545–552. doi: 10.1053/joms.2003.50107.

Lee, S., McGrath, C., and Samman, N. (2007). Quality of life in patients with dentofacial deformity: A comparison of measurement approaches. *International Journal of Oral and Maxillofacial Surgery* 36(6): 488–492. doi: 10.1016/j.ijom.2007.01.011.

Lee, S., McGrath, C., and Samman, N. (2008). Impact of orthognathic surgery on quality of life. *Journal of Oral and Maxillofacial Surgery* 66(6): 1194–1199. doi: 10.1016/j.joms.2008.01.006.

McKoy-White, J., Evans, C.A., Viana, G. et al. (2006). Facial profile preferences of black women before and after orthodontic treatment. *American Journal of Orthodontics and Dentofacial Orthopedics* 129(1): 17–23. doi: 10.1016/j.ajodo.2004.08.019.

Mejia-Maidl, M., Evans, C.A., Viana, G. et al. (2005). Preferences for facial profiles between Mexican Americans and Caucasians. *Angle*

Orthodontist 75(6): 953–958. doi: 10.1043/0003-3219(2005)75[953:PFFPBM]2.0.CO;2.

Michelogiannakis, D., Gajendra, S., Pathagunti, S.R. et al. (2021). Patients' and parents' expectations of orthodontic treatment in university settings. *American Journal of Orthodontics and Dentofacial Orthopedics* 159(4): 443–452. doi: 10.1016/j.ajodo.2020.02.009.

Miner, R.M., Anderson, N.K., Evans, C.A. et al. (2007). The perception of children's computer-imaged facial profiles by patients, mothers, and clinicians. *Angle Orthodontist* 77(6): 1034–1039. doi: 10.2319/080306-314.1.

Mortensen, M.G., Kiyak, H.A., and Omnell, L. (2003). Patient and parent understanding of informed consent in orthodontics. *American Journal of Orthodontics and Dentofacial Orthopedics* 124(5): 541–550. doi: 10.1016/s0889-5406(03)00639-5.

Motegi, E., Hatch, J.P., Rugh, J.D. et al. (2003). Health-related quality of life and psychosocial function 5 years after orthognathic surgery. *American Journal of Orthodontics and Dentofacial Orthopedics* 124(2): 138–143. doi: 10.1016/s0889-5406(03)00391-3.

Neely, M.L., Miller, R., Rich, S.E. et al. (2017). Effect of malocclusion on adults seeking orthodontic treatment. *American Journal of Orthodontics and Dentofacial Orthopedics* 152(6): 778–787. doi: 10.1016/j.ajodo.2017.04.023.

Neely, W.W., II, Kluemper, G.T., and Hays, L.R. (1998). Psychiatry in orthodontics. Part I: Typical adolescent psychiatric disorders and their relevance to orthodontic practice. *American Journal of Orthodontics and Dentofacial Orthopedics* 129(2): 176–184. doi: 10.1016/j.ajodo.2005.11.009.

Park, Y.S., Evans, C.A., Viana. G. et al. (2006). Profile preferences of Korean American orthodontic patients and orthodontists. *World Journal of Orthodontics* 7(3): 286–292.

Pelo, S., Gasparini, G., Garagiola, U. et al. (2017). Surgery-first orthognathic approach vs traditional orthognathic approach: Oral health-related quality of life assessed with 2 questionnaires. *American Journal of Orthodontics and Dentofacial Orthopedics* 152(2): 250–254. doi: 10.1016/j.ajodo.2016.12.022.

Pertschuk, M.J., and Whitaker, L.A. (1988). Psychosocial outcome of craniofacial surgery in children. *Plastic and Reconstructive Surgery* 82(5): 741–746. doi: 10.1097/00006534-198811000-00001.

Phillips, C., Blakey, G., III, and Jaskolka, M. (2008). Recovery after orthognathic surgery: Short-term health-related quality of life outcomes. *Journal of Oral and Maxillofacial Surgery* 66(10): 2110–2115. doi: 10.1016/j.joms.2008.06.080.

Phillips, K.A. (1991). Body dysmorphic disorder: The distress of imagined ugliness. *American Journal of Psychiatry* 148(9): 1138–1149. doi: 10.1176/ajp.148.9.1138.

Polo, M. (2011). Body dysmorphic disorder: A screening guide for orthodontists. *American Journal of Orthodontics and Dentofacial Orthopedics* 139(2): 170–173. doi: 10.1016/j.ajodo.2010.09.025.

Pruzinsky, T., and Edgerton, M.T. (1997). Psychologic understanding and management of the plastic surgery patient. In: G.S. Georgiade, R. Riefkohl, and L.S. Levin (eds.), *Plastic, Maxillofacial, and Reconstructive Surgery*. Baltimore, MD: Williams and Wilkins, pp. 1189–1197.

Rich, S.E., Miller, R., Will, L.A. et al. (2015). Teens with worse malocclusion report worse OHQL, abstract, International Association of Dental Research Meeting. Boston, MA, March.

Ritchie, J., Lewis, J., Nicholls, C.M. et al. (2003). *Qualitative Research Practice*, 2nd ed. Beverley Hills, CA: Sage.

Ryan, F.S., Barnard, M., and Cunningham, S.J. (2012a). Impact of dentofacial deformity and motivation for treatment: A qualitative

study. *American Journal of Orthodontics and Dentofacial Orthopedics* 141(6): 734–742. doi: 10.1016/ajodo.2011.12.026.

Ryan, F.S., Barnard, M., and Cunningham, S.J. (2012b). What are orthognathic patients' expectations of treatment outcome – a qualitative study. *Journal of Oral and Maxillofacial Surgery* 70(11): 2648–2655. doi: 10.1016/j.joms.2012.01.002.

Sarwer, D.B., Bartlett, S.P., Whitaker, L.A. et al. (1999). Adult psychological functioning of individuals born with craniofacial anomalies. *Plastic and Reconstructive Surgery* 103(2): 412–418. doi: 10.1097/000066534-199902000-00008.

Soh, C.L., and Narayanan, V. (2013). Quality of life assessment in patients with dentofacial deformity undergoing orthognathic surgery – a systematic review. *International Journal of Oral and Maxillofacial Surgery* 42(8): 974–980. doi: 10.1016/j.ijom.2013.03.023.

Sun, L., Wong, H.M., and McGrath, C.P. (2017) Relationship between the severity of malocclusion and oral health related quality of life: A systematic review and meta-analysis. *Oral Health and Preventive Dentistry* 15(6), 503–517. doi: 10.3290/j.ohpd.a38994.

Sun, L., Wong, H.M., and McGrath, C.P. (2018). Association between the severity of malocclusion, assessed by occlusal indices, and oral health related quality of life: A systematic review. *Oral Health and Preventive Dentistry* 16(3): 211–223. doi: 10.3290/j.ohpd.a40761.

Tristão, S.K.P.C., Magno, M.B., Pintor, A.V.B. et al. (2020). Is there a relationship between malocclusion and bullying? *A systematic review. Progress in Orthodontics* 21(1): 26–38. doi: 10.1186/s40510-020-00323-7.

Tufekci, E., Jahangiri, A., and Lindauer, S.J. (2008). Perception of profile among laypeople, dental students, and orthodontic patients. *Angle Orthodontist* 78(6): 983–987. doi: 10.2319/102207-503.1.

Veale, D., Boocock, A., Gournay, K. et al. (1996). Body dysmorphic disorder. A survey of fifty cases. *British Journal of Psychiatry* 169(2): 196–201. doi: 10.1192/bjp.169.2.196.

Volpicelli, E.J., Pfaff, M.J., Hakimi, K. et al. (2017). Age-related differences in psychosocial function of children with craniofacial anomalies. *Plastic and Reconstructive Surgery* 140(4): 776–784. doi: 10.1097/PRS.0000000000003687.

Volpicelli, E.J., Pfaff, M.J., Potemra, H.M.K. et al. (2020). Discrepancies in parent perceptions and patient-reported psychosocial function in children with craniofacial anomalies. *Plastic and Reconstructive Surgery* 145(1): 175–183. doi: 10.1097/PRS.0000000000006388.

Wędrychowska-Szulc, B., and Syryńska, M. (2010). Patient and parent motivation for orthodontic treatment—a questionnaire study. *European Journal of Orthodontics* 32(4): 447–452. doi: 10.1093/ejo/cjp131.

Wright, W.G., Spiro, A., 3rd, Jones, J.A. et al. (2017). Development of the teen oral health-related quality of life instrument. *Journal of Public Health Dentistry* 77(2): 115–124. doi: 10.1111/jphd.12181.

Yu, D., Wang, F., Wang, X. et al. (2013). Presurgical motivations, self-esteem, and oral health of orthognathic surgery patients. *Journal of Craniofacial Surgery* 24(3): 743–747. doi: 10.1097/SCS.0b013e318285d5a4.

Zohar, A.H. (1999). The epidemiology of obsessive-compulsive disorder in children and adolescents. *Child and Adolescent Psychiatric Clinics of North America* 8(3), 445–460.

4

Integrated Clinical Genetics/Syndromology for the Orthodontist

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Summary

The purpose of this chapter is to educate dental clinicians, especially those who see children and adolescents such as orthodontists and pediatric dentists, in the valuable role that a clinical geneticist can play in the diagnosis and treatment of their patients. The question of when a patient case should be referred to a clinical geneticist is discussed, followed by a review of selected syndromes that may affect the craniofacial region and the oral tissues. The chapter closes with lists of selected syndromes that may be associated with traits such as premature tooth exfoliation, delayed tooth eruption, hypodontia/oligodontia, supernumerary teeth, taurodontism, mandibular deficiency, cleft lip and palate, cleft palate, median cleft lip, midface deficiency, mandibular prognathism, long anterior facial height, facial asymmetry, ocular hypertelorism, amelogenesis imperfecta and enamel hypoplasia, dentinogenesis imperfecta, and other dentin anomalies.

In the field of dentistry, and specifically within orthodontics, patients with notable or unique skeletal and/or craniofacial features are occasionally identified. A study to investigate the knowledge of rare diseases among general and specialist dentists, including orthodontists, showed that most of the practitioners had little or no knowledge about rare diseases, especially among those outside of the university setting compared to those within (Cazzolla et al., 2022). As craniofacial growth and development specialists, orthodontists must be familiar with many of the medical conditions/syndromes their patients may have and understand how these may affect a patient's treatment. Since approximately 15% of "rare diseases" have orofacial manifestations (Jackowski and Hanisch, 2012), the orthodontist should recognize when a patient has an unusual pattern, two or more signs, that may represent an undiagnosed syndrome (Vig, 1990; Hanisch et al., 2019).

With notable or unique cases, consultation with a clinical geneticist can provide valuable insight into a patient's condition, particularly when the less common conditions or cases with multiple

complexities are encountered in the clinic. The benefits of such a consultation can include: (i) having a previously unrecognized or developing genetic condition diagnosed with appropriate further referral and counseling; and (ii) the clinician orthodontist gaining a better understanding of the patient's condition and how it may affect their dental and/or orthodontic treatment (Roberts and Hartsfield, 1997). A comparison was done of the orthodontic treatment of 56 patients with a variety of "rare disorders" to a control group of 96 systemically healthy orthodontic patients matched by sex and age range. The rare disorders group required more desensitization sessions, and were treated with mixed appliances (fixed and removable) more often and for longer periods. They also had more frequent complications, such as gingivitis, caries, mucosal ulcers, and recurrent debonding (Arriagada-Vargas et al., 2022).

Interaction with the clinical geneticist

A referral may be made for evaluation by a clinical geneticist found in the American College of Medical Genetics website after searching for a board-certified geneticist or genetics clinic (see "Additional resources" at the end of the chapter). Although the orthodontist's staff may schedule the appointment, unless the patient or parent is present at the time of scheduling the availability of the family for appointments may not be known. Alternatively, the phone number of the clinical geneticist or genetics clinic may be given to the family. Family members, however, may not be able to fully convey what the patient is being referred for, and with internet accessibility prevalent, any condition mentioned (even as a clinical possibility to rule out) may be read about in detail, possibility leading to misunderstanding and excess anxiety.

Perhaps the best approach is for the orthodontist's staff to call the clinical geneticist/genetics clinic to make the referral, giving pertinent information as to your name and address, the patient's name and address, and the reason for the referral. This does not necessarily have to be to rule out a named syndrome. A list of your concerns or findings, including reported medical history like a heart defect, hearing deficit, special classes, growth delay, and so on, along with family history, will be most helpful to the clinical geneticist

preparing for the appointment beforehand. Clinical geneticists and genetics clinics may vary in their preappointment needs, and as you interact with your local professionals you will become familiar with their intake protocols. In addition to, or instead of, you or your patient interacting with a clinical geneticist, it is not unusual for a genetic counselor, or a physician assistant or nurse with experience in genetics, to be involved. These individuals, along with laboratory geneticists who perform molecular and biochemical tests, can act together as a genetics team in the care of your patient.

It is suggested for convenience and confidentiality that you or your office tell the clinical geneticist/genetics clinic that you will give their number to the patient/family for them to call for an appointment, and provide any additional information such as family history, primary or other physicians and dentists involved in their care, and insurance coverage. Some clinical geneticists/genetics clinics will call the patient/family for an appointment themselves, just be sure the patient/family know to expect a call. The clinical geneticist/genetics clinic may send out a family questionnaire form to the patient and/or family to ask about medical history, and to construct a family tree called a "pedigree." If this is not done beforehand, it is expected that it will be done at the time of the visit to the clinical geneticist/genetics clinic, which will typically take an hour or more for an initial visit (not including waiting time).

The clinical geneticist/genetics clinic may ask for your radiographs, and/or may request medical records from others taking care of the patient. As most physicians and clinical PhDs do not routinely look at panoral, periapical, or cephalometric radiographs, providing a brief description of pertinent findings like those described in this chapter for some of the syndromes, especially pathology or deviations from normal, may be useful to them.

Following your patient's visit to the clinical geneticist/genetics clinic, you should expect a letter summarizing the family history, medical history, examination, discussion, diagnosis or differential diagnosis, genetic counseling if given, and recommendations. The latter are more likely to be for any genetic testing or further medical referral (e.g. ophthalmology and cardiology examination for a patient suspected of having Marfan syndrome because of the associated

developmental eye abnormalities and aortic dissection risk) than for any specific type of orthodontic treatment.

Evolution of the clinical geneticist specialist

The American Board of Medical Genetics (ABMG) originally defined a “clinical geneticist” as an individual who held a clinical degree (MD, DO, DDS, or DMD); had a certificate from a residency program such as but not limited to pediatrics, maternal fetal medicine, oral pathology, or orthodontics; had also completed the required ABMG-certified clinical genetics residency education and training; and had passed the ABMG Clinical Geneticist examination, consisting of the general genetics exam and a clinically focused exam. Clinical geneticists, who see patients and examine them for unusual physical features, particularly those that may occur with a congenital abnormality or in a pattern recognized as some syndrome, may be referred to as dysmorphologists.

One of the initial members of the ABMG was Dr. Robert J. Gorlin, DDS, MS (1923–2006), a dentist and well-known author, oral pathologist, and clinical geneticist/dysmorphologist. A few other dentists were also early diplomates of the ABMG, including Dr. David Bixler, DDS, PhD (1929–2005), the first president of the Society of Craniofacial Genetics (now the Society of Craniofacial Genetics and Developmental Biology). Thus, at the inception of the ABMG, dentists along with physicians played key roles in defining and establishing the functions of a geneticist in patient care. At that time both dental and medical professionals could be accepted into ABMG approved clinical genetics fellowship (“residency”) programs and could achieve ABMG Diplomate status. These programs were stipulated by the ABMG to be at least two years in length with a wide range of clinical experience in genetics, not just of the craniofacies. There were a handful of dentists who pursued this goal and become Diplomates of the ABMG as clinical geneticists.

Early on, one goal of the ABMG was to become recognized as a member of the American Board of Medical Specialties (ABMS), thus helping to recognize and legitimize the specialty, as well as to foster improved reimbursement for services provided. Once this goal was achieved and the ABMG become a member of the ABMS in 1991, the

stand was taken that the ABMS is involved in medical specialties and therefore in the certification of medical doctors (physicians and osteopaths), not the certification of dentists. Today, to be an active candidate for certification in clinical genetics and genomics by what is now named the American Board of Medical Genetics and Genomics (ABMGG), the individual must hold a US or Canadian MD, DO, or equivalent degree before undertaking the required additional minimum five years of education. Thus, even if a dentist with another specialty wished to go into the now ABMS-recognized specialty of Clinical Genetics and Genomics, he or she could not become a Diplomate of that specialty. Unfortunately, what was a move forward for the ABMGG proved to be exclusionary for dentists who wished to go into this specialty.

Clinical geneticists, genetic counselors, physician assistants, and nurses who provide clinical genetics services are generally located at major medical centers, especially children's hospitals. While they will typically have a wide range of experience in genetic conditions, including craniofacial anomalies, they may not be as familiar with pertinent findings of the oral cavity. Among dentists in general, oral pathologists may have greater knowledge of genetic conditions, but may not have the experience of conditions that manifest to some degree in areas in addition to the oral cavity, and probably do not have the education and experience in making referrals and doing genetic counseling that the clinical geneticist or genetics team member would have.

If the clinical geneticist/genetics team can make or rule out a diagnosis, then the knowledge of the orthodontist, perhaps with some reading in the literature on the condition (see "Additional resources"), can fill in what the clinical geneticist cannot tell you about the effect of the condition on craniofacial growth and other aspects of the orthodontic care. Likewise, referral to a specific oral pathologist, pediatric dentist, or specialist in oral medicine, or another practitioner who has the interest and experience to be of help, may also be supplemented by the orthodontist's knowledge.

When to refer

How do you recognize when you should seek this referral? All humans vary from one another, without it usually being a concern. One of the difficult tasks faced by any practitioner, whether orthodontist or clinical geneticist, is how to discern normal variation from a minor anomaly (Vig, 1990). A minor anomaly is a structural feature seen in less than 4% of the general population, which is of no cosmetic or functional significance that may be considered serious to the affected individual. Minor anomalies may or may not have diagnostic significance.

Even major anomalies or signs (those that require medical/surgical intervention) vary among individuals with the same etiological syndrome, meaning that clinical diagnosis is generally made based on an overall pattern of signs or anomalies. Advancements in genetic testing for those conditions that, because of their etiology, are amenable can certainly help and in some conditions make/confirm the diagnosis. The clinical geneticist will order or recommend such tests to be done when indicated. In addition, with technological advancements, next-generation sequencing of the DNA exomes that code for proteins (whole-exome sequencing, WES), or the whole-genome sequence (WGS), may be done for further detailed investigation, often in cases where the condition/syndrome is not recognized.

In medical genetics, minor anomalies have been useful in three ways. First, some minor anomalies have been external markers of specific “occult” or hidden major anomalies. In addition, most malformation syndromes in medical genetics are recognizable as patterns of minor anomalies. Finally, although 15% of normal newborns have one or more minor anomalies, the finding of three or more minor anomalies is unusual, occurring in 0.5% of newborns. The risk of having a major “hidden” abnormality increases proportionately with the number of minor anomalies present, with three or more signaling a 90% risk of one or more major structural defect, which is an evaluation indication (Hoyme, 1993; Jones et al., 2021).

Minor anomalies may occur in any part of the body. While it would not be expected for the orthodontist to physically examine all body

areas, he or she is expected to examine the craniofacies as well as intraorally and may readily observe the hands as well. Thus the orthodontist can examine/observe the areas (craniofacies and hands) where most minor anomalies occur (Jones et al., 2021). A familial pattern may be superficially ascertained promptly by asking if anyone else in the family has a similar feature of interest, or by asking who in the family the patient most resembles and in what way (stature, similar eyes, jaw profile, etc.). In addition, subjective evaluation of the patient's ability to function, as well a general medical surgery history and questions about the patient being or having been in "special" classes, may indicate that a medical genetics referral is warranted. This may require some explanation to the patient and/or family members, as the orthodontist is typically not able to make a diagnosis or answer all the questions that inevitably follow. One way to approach this is a general discussion of how the orthodontist needs to know about everything that may affect treatment, and that you noticed a few things that could be ruled out by consultation with a specialist in medical genetics. Depending on the patient's insurance, this will often be covered at least partially by medical (not dental) insurance, but may require the orthodontist to call or send a letter to the primary physician explaining your concern, and that you would like a referral for your patient in common to the medical geneticist because of the listed signs, and perhaps also to rule out a specific syndrome.

The primary physician may already have some diagnostic information that will be of use to the orthodontist, but do not be surprised if this person has no more familiarity with medical genetics than you. The reason for your call is that you are trying to do the best for each of your patients, not just the majority who, although they may vary to some degree one from the other, are not markedly affected by a genetic condition.

Artificial intelligence and facial analysis

The use of artificial intelligence (AI) and its integration into modern science by way of multiple medical specialties, including genetics, has helped transform the next generation of clinical practice (Bijarnia-Mahay and Arora, 2019). AI is increasingly used for clinical

diagnosis, including with facial analysis as part of recognizing a variety of developmental/genetic conditions. Many genetic syndromes have characteristic facial features, which may be considered in the differential diagnosis.

Face2Gene (FDNA, Sunrise, FL, USA) is an AI-based software that uses facial image analysis to help diagnose genetic syndromes. It is a national online tool for the identification of phenotypes based on next-generation phenotyping (NGP; Liehr et al., 2021). The free Face2Gene app is available to healthcare professionals on the iOS or Android platform, or as software for desktop or laptop computers (https://www.face2gene.com/startclinic). Face2Gene is available to verified US healthcare workers with activation for use by noting your profession, specialty, and if applicable institutional email (Hurst, 2018).

Using a two-dimensional (2D) facial portrait, each region of the face is scaled to a fixed size and converted to grayscale. The software uses cascaded deep convolutional neural network methodology and facial landmarks that are geometrically analyzed and compared to a database of facial characteristics of various genetic syndromes (Gurovich et al., 2019). These “dysmorphic” features as identified by Face2Gene may be reported to the clinical geneticist/genetics clinic for their use, or with subject permission you can supply the geneticist/genetics clinic with the digital portrait if they use Face2Gene. A list of several of the most likely syndromes is generated.

DeepGestalt is the neural network that drives Face2Gene (Gurovich et al., 2019; Pantel et al., 2020). It utilizes a dataset of over 17,000 images representing over 200 genetic syndromes (Gurovich et al., 2019). In a study of the accuracy of DeepGestalt, using pictures of 323 individuals who had 17 different genetic syndromes and a matched control group also consisting of 323 pictures, there was 91% sensitivity in analysis of the images (Pantel et al., 2020). Like other AI systems, DeepGestalt cannot identify which facial features supported the clinical diagnosis. However, the use of heat map visualization in the app software to identify the fit between areas and suggested syndromes can be used to identify the contributory areas (Gurovich et al., 2019).

It is also important to note that ethnic differences and variations play an important role. Most studies involve the use of Caucasian images for analysis. One study investigated facial morphology in African children with and without intellectual disability (Lumaka et al., 2017). Using Face2Gene resulted in a 37% syndrome diagnosis accuracy rate in Africans. However, with utilization of training techniques, this increased to 94%. Thus, training of the system may be required for increased accuracy in other ethnic groups.

When using Face2Gene to analyze a patient who may or may not have a syndrome, the list of possible syndromes generated should be refined by entering pertinent positive and negative patient history, attributes, or findings. Careful consideration of the characteristics of each listed syndrome compared to the patient must be done before a refined differential diagnosis or final diagnosis is entertained. This may be best left to the geneticist and not shared with the patient or family without review and confirmation by the geneticist.

Selected syndromes and conditions

Table 4.1 is a *selective and incomplete* survey of conditions/syndromes with brief descriptions (and others on which more information may be gathered from the "Additional resources"), sorted by particular signs, adapted from a number of different references (Babic et al., 1993; Bailleul-Forestier et al., 2008; Cohen, 1980; Fleming et al., 2010; Hartsfield, 1994; Jones et al., 2021; Schulman et al., 2005; Suri et al., 2004) and other references as cited in the text.

Most of the conditions are rare, and some are only relatively rare, although any of them may be presently recognized or unrecognized in a practice. The tables and online resources noted later – Online Mendelian Inheritance in Man (OMIM), GeneReviews Genetic Testing Registry, Registry of Orofacial Manifestations in People with Rare Diseases, or reference texts (Hennekam et al., 2010; Jones et al., 2021) – may also be of use if a patient comes to you with a particular diagnosis already made. Although not every patient is going to follow what is expected of someone with a particular diagnosis because of inherent variability, the practitioner can better

understand a patient's condition and how it may affect treatment, and also how treatment may affect the patient.

Table 4.1 Selected traits in selected syndromes and conditions.

Source: Adapted from Andreadis et al. (2004); Babic et al. (1993); Bailleul-Forestier et al. (2008); Cohen (1980); Ernst et al. (2007); Fleming et al. (2010); Hartsfield (1994); Hennekam et al. (2010); Jones et al. (2021); Kikuiri et al. (2018); Papapanou et al. (2018); Schulman et al. (2005); Suri et al. (2004).

Note: A syndrome or condition listed under a trait may not always, or even often, show the trait in every affected individual. Some syndromes/conditions are listed under more than one trait, which may help in forming a differential diagnosis if the patient has more than one trait and two or more are found in the same condition. Many of these conditions are too severe to be found in patients who are likely to be seen in most orthodontic practices, but may be seen in craniofacial clinics. Some of these conditions are lethal early in life, but are included to illustrate the wide range of conditions that may be associated with the selected traits. This is not intended to be an exhaustive list. Face2Gene, OMIM, and Smith's Recognizable Patterns of Human Malformation (Jones et al., 2021) are excellent additional resources.
Premature tooth exfoliation Occurs often Coffin–Lowry syndrome Early-onset periodontitis (aggressive periodontitis, stage III grade C, with rapid rate of progression) Hajdu–Cheney syndrome Hypophosphatasia Mandibulofacial dysplasia Pachyonychia congenita Papillon–Lefèvre syndrome Singleton–Merten syndrome Occurs occasionally Chédiak–Higashi syndrome Cherubism Down syndrome Ehlers–Danlos syndrome type VIII (periodontitis type) Hypophosphatemia Oculodentodigital syndrome Yunis Varón syndrome

Delayed tooth eruption Aarskog syndrome Acrodysostosis Albright hereditary osteodystrophy Apert syndrome Amelo-onychohypohydrotic dysplasia Brachmann–de Lange syndrome Carpenter syndrome Cherubism Chondroectodermal dysplasia (Ellis–van Creveld syndrome) Cleidocranial dysplasia (dysostosis) Cockayne syndrome Coffin–Lowry syndrome Coffin–Siris syndrome Congenital hypertrichosis lanuginosa Cross syndrome (has gingival fibromatosis)
Dentin dysplasia DeLange syndrome Down syndrome
Dyskeratosis congenita Ectodermal dysplasias (some types) Ekman–Westborg–Julin syndrome Enamel agenesis and nephrocalcinosis Epidermolysis bullosa Finlay–Marks syndrome Frontometaphyseal dysplasia GAPO syndrome (growth retardation, alopecia, “pseudoanodontia,” and optic atrophy) Gardner syndrome Gaucher disease Gingival fibromatosis with sensorineural hearing loss Gingival fibromatosis with growth hormone deficiency Goltz syndrome Hallermann–Streiff syndrome Hemifacial microsomia (Goldenhar syndrome, oculoauriculovertebral spectrum) Hurler Scheie syndrome (a type of mucopolysaccharidosis, abbreviated MPS I-H/S)

Hurler syndrome ((MPS I-H) Hunter syndrome (MPS II) Hyperimmunoglobulinemia E (Buckley syndrome) I-cell disease (mucolipidosis II) Incontinentia pigmenti (Bloch–Sulzberger syndrome) Killian/Teschler–Nicola syndrome Laband syndrome (has gingival fibromatosis) Levy–Hollister syndrome Maroteaux–Lamy syndrome (MPS IV) McCune–Albright syndrome (polyostotic fibrous dysplasia) Menkes kinky hair syndrome Miller–Dieker syndrome Murray–Puretic–Drescher syndrome (has gingival fibromatosis) Neurofibromatosis Nevoid basal cell carcinoma (Gorlin) syndrome Osteoglophonic dysplasia Osteopathia striata with cranial stenosis Osteopetrosis (marble bone disease) Osteogenesis imperfecta (variable) Otodental dysplasia Parry–Romberg syndrome (progressive hemifacial atrophy) Progeria (Hutchinson–Gilford syndrome) Pyknodysostosis
Rutherford syndrome (has gingival fibromatosis) Ramon syndrome (has gingival fibromatosis) Rothmund–Thompson syndrome Sclerosteosis SHORT syndrome
Singleton–Merten syndrome Trichodentoosseous syndrome Velocardiofacial syndrome XXXY and XXXXY syndrome (occasionally)
Supernumerary teeth Chondroectodermal dysplasia (Ellis–Van Creveld syndrome) Cleidocranial dysplasia Ehlers–Danlos vascular type IV Fabry disease Familial adenomatous polyposis (Gardner syndrome)

Incontinentia pigmenti (Bloch–Sulzberger syndrome) Nance–Horan syndrome Oral-facial-digital syndrome Saethre–Chotzen syndrome Trichorhinophalangeal syndrome type I (occasionally)
Taurodontism Down syndrome (occasionally) Ectodermal dysplasias (some occasionally) Lowe syndrome (occasionally) Oral-facial-digital II syndrome (occasionally) Otodental dysplasia Sex chromosome aneuploidies/anomalies with one or more extra X chromosome (e.g. Klinefelter syndrome) Seckel syndrome (occasionally) Trichodentoosseous syndrome Trisomy 18 (occasionally) Williams syndrome X-linked hypophosphatemic rickets (occasionally) XXXXX syndrome XXX and XXXX syndrome (occasionally) XXXY and XXXXY syndrome (occasionally)
Odontoma Encephalocraniocutaneous lipomatosis Gardner syndrome Odontoma-dysphagia syndrome SATB2-associated syndrome Schimmelpenning–Feuerstein–Mims (SFM) syndrome (linear sebaceous nevus syndrome)
Mandibular deficiency Achondrogenesis types IA and IB Amyoplasia congenita disruptive sequence Aniridia–Wilms tumor association Atelosteogenesis type I Baller–Gerold syndrome Boomerang dysplasia Brachmann–de Lange syndrome Branchio-oculo-facial syndrome Campomelic dysplasia

Catel–Manzke syndrome
Cat-eye syndrome
Cerebro-costco-mandibular syndrome
Cerebro-oculo-facio-skeletal syndrome
Cohen syndrome
Cranioectodermal dysplasia
Diamond Blackfan anemia (DBA)
Escobar syndrome
Femoral hypoplasia–unusual facies syndrome
Fetal aminopterin/methotrexate syndrome
Frontometaphyseal dysplasia
Fryns syndrome
GAPO syndrome (growth retardation, alopecia, “pseudoanodontia,” and optic atrophy)
Hajdu–Cheney syndrome
Hallermann–Streiff syndrome
Hemifacial microsomia (Goldenhar syndrome, oculoauriculovertebral spectrum)
Langer–Giedion syndrome
Lethal multiple pterygium syndrome
Loeys–Dietz syndrome
Mandibuloacral dysplasia
Mandibulofacial dysostosis with microcephaly
Marden–Walker syndrome
Marshall–Smith syndrome
Matthew–Wood syndrome
Meckel–Gruber syndrome
Meier–Gorlin syndrome
Melnick–Needles syndrome
Microcephalic primordial dwarfing syndrome
Microdeletion 2q31.1 syndrome
Microdeletion 22q11.2 syndrome
Miller syndrome
Miller–Dieker syndrome
Moebius (Möbius) syndrome
Mohr syndrome
Mucopolysaccharidosis I H, I H/S
Mycophenolate mofetil embryopathy

Nablus mask-like facial syndrome Nager acrofacial dysostosis Neu–Laxova syndrome Opitz G/BBB syndrome Oral-facial-digital syndrome Oromandibular-limb hypogenesis spectrum Oto-palato-digital syndrome Type II Pallister–Hall syndrome Pena Shokeir phenotype Peters-plus syndrome Progeria syndrome Pyknodysostosis Restrictive dermopathy Retinoic acid embryopathy Roberts syndrome Robin sequence (nonsyndromic, or may be syndromic, e.g. Stickler syndrome, velocardiofacial syndrome Russell–Silver syndrome Schwartz–Jampel syndrome SHORT syndrome Shprintzen–Goldberg syndrome Smith–Lemli–Opitz syndrome Stickler syndrome Toriello–Carey syndrome Treacher Collins syndrome Trichorhinophalangeal syndrome type I and type II (Langer–Giedion syndrome) Diploid/triploid mixoploidy syndrome Turner (45X and variants) syndrome Weaver syndrome Wildervanck–Smith syndrome Velocardiofacial syndrome Vici syndrome XXX and XXXX syndrome Yunis Varón syndrome Zellweger syndrome
Cleft lip and or cleft palate (Note: there are over 300 “clefting syndromes”)

Amnion rupture sequence
Apert syndrome
Branchio-oculo-facial syndrome (pseudocleft)
Cleidocranial dysostosis (dysplasia)

Deletion 4p syndrome
Diastrophic dwarfism
Ectrodactyly–ectodermal dysplasia–clefting (EEC) syndrome
Fetal alcohol syndrome (cleft palate occasionally)
Fetal hydantoin syndrome
Fetal valproate syndrome
Fryns syndrome
Hay–Wells ectodermal dysplasia
Hemifacial microsomia (Goldenhar syndrome, oculoauriculovertebral spectrum; occasionally)
Larsen syndrome (cleft palate occasionally)
Marfan syndrome (cleft palate occasionally)
Miller syndrome
Mycophenolate mofetil embryopathy
Nager acrofacial dysostosis (cleft palate)
Nevoid basal cell carcinoma (Gorlin) syndrome
Oral-facial-digital syndrome I
Oral-facial-digital syndrome II
Otopalatodigital syndrome
Popliteal pterygium syndrome (lower lip pits frequent)
Rapp–Hodgkin ectodermal dysplasia
Roberts syndrome
Single median maxillary central incisor (SMMCI)
Stickler syndrome (cleft palate)
Treacher Collins syndrome (cleft palate)
Van der Woude syndrome (variable paramedian lip pits, cleft lip, cleft palate)
Velocardiofacial syndrome (cleft palate)
Waardenberg syndrome (occasionally)
Median Cleft Lip (In the middle of the upper lip, developmentally between the medial nasal prominences, in contrast to the more common cleft lip that is paramedian (lateral) to the mid-sagittal plane)
Frontonasal dysplasia

Holoprosencephaly sequence Mohr syndrome Short rib-polydactyly syndrome, type II (Majewski type) Oral-facial-digital syndrome I Oral-facial-digital syndrome II Premaxillary agenesis syndrome 18p-karyotype
Midface (malar) deficiency Aarskog syndrome Achondroplasia Atelosteogenesis type I Cleidocranial dysplasia (dysostosis)
Coffin–Lowry syndrome Craniosynostoses (including Apert, Crouzon, Pfeiffer, Muenke, and Saethre–Chotzen syndromes) Down syndrome Hajdu–Cheney syndrome Marshall syndrome Maxillonasal dysplasia (Binder syndrome) Miller syndrome Mohr syndrome Singleton–Merten syndrome Stickler syndrome Treacher Collins syndrome Trichorhinophalangeal syndrome I Velocardiofacial syndrome
Mandibular prognathism (may be, at least partially, maxillary hypoplasia) Aarskog syndrome Axenfeld–Rieger syndrome (maxillary hypoplasia) Beckwith–Wiedemann syndrome Chondroectodermal dysplasia (Ellis–van Crevald syndrome, occasionally) Cleidocranial dysplasia (dysostosis) Coffin–Lowry syndrome Down syndrome Fabry disease (occasionally) Fragile X syndrome

Klinefelter syndrome (and other sex chromosome aneuploidies in males) Marfan syndrome Maxillonasal dysplasia (Binder syndrome) Nevoid basal cell carcinoma (Gorlin) syndrome Osteogenesis imperfecta (types III and IV often) Papillon–Lefèvre and Haim–Munk syndromes Singleton–Merton syndrome (occasionally) Smith–Magenis syndrome Sotos syndrome Tricho-dento-osseous syndrome Waardenburg syndrome
Long anterior facial height (may be with open bite tendency) Amelogenesis imperfecta Beckwith–Wiedemann syndrome (associated with macroglossia) Fragile X syndrome Klinefelter syndrome (and other sex chromosome aneuploidies in males) Marfan syndrome Velocardiofacial syndrome
Facial asymmetry Hemifacial microsomia (Goldenhar syndrome, oculoauriculovertebral spectrum) Hemihypertrophy Neurofibromatosis (occasionally) Parry–Romberg syndrome Saethre–Chotzen syndrome (nasal deviation common) Velocardiofacial syndrome
Ocular hypertelorism (increased distance between the eyes, real or apparent) Aarskog syndrome Apert syndrome Cardio-facio-cutaneous syndrome Coffin–Lowry syndrome Crouzon syndrome Fetal face syndrome Frontonasal dysplasia

Hajdu–Cheney syndrome Hypertelorism–hypospadias syndrome Leopard syndrome Marshall syndrome Nevoid basal cell carcinoma (Gorlin) syndrome Noonan syndrome Oral-facial-digital syndrome I Pfeiffer syndrome Saethre–Chotzen syndrome Sotos syndrome Weaver syndrome Waardenberg syndrome
Syndromes associated with dental dysplasias (amelogenesis imperfecta, dentinogenesis imperfecta, and dentin dysplasia) Albright hereditary osteodystrophy Amelogenesis imperfecta with nephrocalcinosis (McGibbon syndrome) Autoimmune polyendocrinopathy Cleidocranial dysplasia (dysostosis) Cone–rod dystrophy and amelogenesis imperfecta Ehlers–Danlos syndrome (some types) Familial hypophosphatemic vitamin D–resistant rickets Goldblatt syndrome Hypophosphatasia Hyperphosphatemic familial tumoral calcinosis (HFTC) Kohlschütter–Tönz syndrome Oculodentodigital syndrome
Osteogenesis imperfecta (some in type I, mostly in types III and IV) Schimke immunoosseous dysplasia (SIOD) Seckel syndrome Tricho-dento-osseous syndrome Tuberous sclerosis Vitamin D–dependent rickets Vitamin D–resistant rickets Williams syndrome
Supernumerary teeth (hyperdontia) Cleidocranial dysplasia (dysostosis)

Fabry disease (occasionally) Familial adenomatous polyposis (FAP) Gardner syndrome Nance–Horan syndrome
Dental agenesis (besides the third molars; avoid the term congenital absence as the teeth are typically absent at birth anyway, at least clinically, and most radiographically as well. Can variably be in families or just one family member. Being associated with some other anomaly, especially in more than one family member is an indication for clinical genetics referral.) Aarskog syndrome Axenfeld–Rieger malformation and Rieger syndrome Cancer (colorectal, epithelial ovarian, rare?) Chondroectodermal dysplasia (Ellis–van Crevald syndrome) Coffin–Lowry syndrome Down syndrome Ectodermal dysplasias Fabry disease (occasionally) Hallermann–Strieff syndrome Hypohidrotic ectodermal dysplasia (HED) Hypohidrotic ectodermal dysplasia and immune deficiency (HED-ID) Incontinentia pigmenti Johansson–Blizzard syndrome Kallmann syndrome Lacrimo-auriculo-dento-digital syndrome Oculo-facio-cardio-dental syndrome p63 mutation-related syndromes Single median maxillary central incisor (SMMCI) Tricho-dento-osseous syndrome Williams syndrome Wolf–Hirschhorn syndrome

As an educator I have often been asked by students: “What do we need to know?” My response has been: “Tell me about all the patients you will ever see, and then we can start from there.” No one knows every condition or syndrome that any of our patients may present to us, but we can be aware of when something seems out of

the usual range of variation, particularly if more than one unusual feature is present. While typically no single malformation or sign is pathognomonic, each can often point us in the direction of what to consider in the referral and differential diagnosis (Babic et al., 1993).

Today, understanding a patient's medical/genetic condition may help the orthodontist to understand how to help and what to expect from that patient. A more common application of genetics to orthodontic practice in the future may be in how nonsyndromic complex traits – such as external apical root resorption (EARR) associated with orthodontic treatment, Angle Class III malocclusion, or Angle Class II division 2 malocclusion, for example palatally displaced canines – occur and respond to different orthodontic treatment protocols (Hartsfield et al., 2021). Other areas that also require more investigation include the application of genetics for better prediction of individual growth during puberty, and when the orthodontist should send a patient with hypodontia to the medical geneticist for cancer risk evaluation (Bader, 1967; Jaspers and Witkop, 1980; Hartsfield, 2005, 2008, 2009; McLain et al., 1983).

Knowing the diagnosis and characteristics of a genetic condition, or using an evaluation of genetic factors to better anticipate an individual's risk of disease or developmental abnormality as opposed to the general population, or their growth pattern and/or likely response to a treatment, has been called personalized or precision medicine. Application of this principle to orthodontic practice is known as "personalized or precision orthodontics" (Hartsfield, 2005, 2008, 2009; Hartsfield et al., 2021).

Radiographic signs

Odontoma

The presence of an odontoma should alert the practitioner to inquire about the concurrent presence of dysphagia (difficulty in swallowing) or a family history of dysphagia, which is perhaps due to hypertrophy of the smooth muscles of the esophagus as part of the rare autosomal dominant odontoma–dysphagia syndrome (Bader, 1967).

Taurodontism

Taurodontism is found in about 2.5% of Caucasian adults as an isolated (nonsyndromic) trait (Jaspers and Witkop, 1980). Individuals with nonsyndromic hypodontia are more likely to show taurodontism of the permanent first molar teeth than children with nonsyndromic supernumerary teeth (Kan et al., 2010). It can also be found in several conditions and syndromes, including the following.

Tricho-dento-osseous syndrome

Tricho-dento-osseous (TDO) syndrome is characterized by variably kinky curly hair at birth that straightens about half of the time after infancy, thin-pitted enamel, taurodontism, and in approximately 80% of affected individuals thickening of cortical bone (including of the skull). The natural straightening of the hair during infancy complicates the diagnosis of TDO and makes differentiating between TDO and amelogenesis imperfecta with taurodontism difficult in many cases. While TDO is caused by mutations in the *DLX3* gene, it is not clear whether at least some cases of amelogenesis imperfecta with taurodontism are also caused by mutations in the *DLX3* gene, or actually represent milder cases of TDO (Visinoni et al., 2009; Bloch-Zupan and Goodman, 2006).

Teeth are typically small, and often have a slight yellow-brown coloration, although there can be considerable variability in the clinical appearance of the teeth in affected individuals even within the same family. The teeth range from mildly affected with normal color and a slight size reduction to severe enamel hypoplasia and markedly reduced size. The incidence of dental abscesses is increased, and hypodontia may be present (Wright et al., 1997). The eruption of teeth may also be delayed (Suri et al., 2004).

Detailed cephalometric analysis of the craniofacial structures in individuals with TDO did not establish a distinct craniofacial phenotype, although the cranial base length, cranial base angle, and length of the body of the mandible were all increased compared with unaffected relatives (Lichtenstein et al., 1972).

Otodental dysplasia

Features of otodental dysplasia include grossly enlarged molar teeth (globodontia), taurodontism, high-frequency sensorineural hearing deficit, and eye coloboma (part of the eye does not form due to failure of fusion of the intraocular fissure, which may be apparent externally as a "notch" in the iris). Tooth eruption may also be delayed (Suri et al., 2004). Dental management has been described as interdisciplinary and complex, including regular follow-up, extraction of teeth as indicated, and orthodontic treatment (Bloch-Zupan and Goodman, 2006).

Sex chromosome aneuploidies/anomalies

These are a deviation from the normal XY chromosomes in males and XX chromosomes in females. Studies on tooth crown size and structure in families and in individuals with various sex chromosome anomalies have demonstrated differential direct effects of the human X and Y chromosome genes on growth. The Y chromosome promotes both enamel and dentin growth, whereas the effect of the X chromosome on crown growth seems to be restricted to enamel formation (Alvesalo, 2009; Krusinskiene et al., 2005).

The positive predictive value for Klinefelter syndrome (47,XXY; i.e. a male with an extra X chromosome, which affects approximately 1.2 in 1000 males), given a male patient with taurodontism and a learning disability, is 84% (Schulman et al., 2005). In addition to tall stature for the family, a tendency toward mandibular prognathism and decreased facial height may also be present.

In contrast to the increase in taurodontism with an extra X chromosome, females lacking an X chromosome (Turner syndrome, 45,X and variations, which occurs in 1 out of 2500 females) appear not to have an increased incidence of taurodontism, although they may show increased variation in root morphology, including short roots (Midtbo and Halse, 1994; Varrela et al., 1990). Turner syndrome shows variable short stature, low hairline, low-set ears, and a broad neck. These patients typically experience gonadal dysfunction (nonworking ovaries), which results in amenorrhea (absence of menstrual cycle; Babic et al., 1993).

Depending on the sex, lack of an X chromosome or the presence of an extra X chromosome produces opposite effects on cranial-base flexion, jaw displacement, and maxillary and mandibular inclination relative to the anterior cranial base. An extra X chromosome in males affects the jaw relationship in the sagittal plane, typically increasing the length of the mandible, while an extra X chromosome in females results in shorter lengths of the anterior and posterior cranial bases, the calvarium, mandibular ramus, and posterior and upper anterior face.

The lack of an X chromosome in females (Turner syndrome) results predominantly in cranial base changes, so that the mandible is short in the sagittal plane, whereas the maxilla is of normal length. The extra Y chromosome in 47,XYY males results in larger craniofacial dimensions than in normal males, without substantial effects on dimensional ratios and plane angles. In general, there is a skeletal height- and craniofacial growth-promoting effect from an extra Y chromosome, and a delaying effect from an extra X chromosome (Alvesalo, 2009; Babic et al., 1993; Krusinskiene et al., 2005). Face2Gene facial analysis had good to excellent accuracy in discriminating individuals with Turner syndrome from healthy controls and individuals with Noonan syndrome, who share some phenotypic features with Turner syndrome (Kruszka et al., 2020).

Williams syndrome

Physical features of this condition include characteristic facial features with full prominent cheeks, wide mouth, long philtrum, small nose with depressed nasal bridge, heavy orbital ridges, medial eyebrow flare, dental abnormalities, hoarse voice, growth retardation, and cardiovascular abnormalities (most commonly supravalvular aortic stenosis and/or peripheral pulmonary artery stenosis). The cognitive profile is distinctive, consisting of strengths in auditory memory, language, and face processing, but extreme weakness in visual-spatial, numerical, and problem-solving abilities.

Cephalometric analysis shows that the anterior and posterior cranial bases are shorter in individuals with Williams syndrome, although the cranial base angle is normal. The frontal and occipital bones are thicker, and the shape of the sella turcica may be unusual. Marked

deficiency of the bony chin in combination with a large mandibular plane angle can give the impression of a retrusive mandible. Hypodontia is frequent, and the teeth tend to be small. Maxillary and mandibular incisors in both jaws are often tapered toward the incisal edge (screwdriver shaped). Most of the molars deemed to be taurodontic had short total tooth lengths and could thus be defined as having taurodontism without meeting the classic definition (Axelsson, 2005).

Other conditions in which taurodontism is seen more commonly then in the general population include trisomy 18, some types of ectodermal dysplasia, Down syndrome, Mohr (oral-facial-digital, type II) syndrome, Seckel syndrome, Lowe syndrome, and X-linked hypophosphatemic rickets (X-linked hypophosphatemia; see under conditions in which premature tooth exfoliation may occur occasionally; Cichon and Pack, 1985; Kan et al., 2010).

History of premature tooth exfoliation

A history of primary teeth exfoliation prior to the age of 5 years in the absence of trauma is an indication that further investigation should be made, as several conditions may be of concern to the orthodontist, including a risk of additional tooth loss. The early exfoliation of primary teeth resulting from periodontitis has been observed occasionally in children. Along with hypophosphatasia, early-onset periodontitis appears to be the most common cause of premature exfoliation of the primary teeth, especially in girls (Hartsfield, 1994).

Hypophosphatasia

Hypophosphatasia is characterized by improper mineralization of bone caused by deficient tissue-nonspecific alkaline phosphatase activity in serum, liver, bone, and kidney. Increased levels of urinary phosphoethanolamine are also seen. Diagnostic tests should include determination of serum alkaline phosphatase levels for parents and siblings (Hu et al., 1996).

The typical dental finding diagnostic of hypophosphatasia in children is premature exfoliation of the anterior primary teeth associated with deficient cementum. The loss of teeth in the young child may be

spontaneous or may result from a slight trauma. Early exfoliation of the primary teeth is usually associated with the juvenile type of hypophosphatasia, although such a history may also be present in the adult type. Severe gingival inflammation will be absent. The loss of alveolar bone may be limited to the anterior region. Treatment of patients with hypophosphatasia may be problematic because of the risk of permanent tooth loosening during orthodontic procedures (Macfarlane and Swart, 1989).

Early-onset periodontitis

Early-onset periodontitis may occur in the primary dentition (prepubertal periodontitis), develop during puberty (juvenile periodontitis, JP), or be characterized by exceedingly rapid loss of alveolar bone (rapidly progressive periodontitis). Because several forms of early-onset periodontitis (e.g. localized prepubertal periodontitis, localized JP, and generalized JP) can be found in the same family, the expression of the underlying genetic etiology appears to have the potential to be influenced by other genetic and environmental factors (Schenkein, 1998). An updated classification of periodontitis previously recognized as “chronic” or “aggressive” is now referred to as periodontitis with a staging and grading system. The staging (I–IV) is largely dependent on the severity of disease at its presentation, as well as on the complexity of disease management. Grading provides supplemental information about biological features of the disease. These include a history-based analysis of the rate of disease progression (A slow, B moderate, C rapid), and the presence of modifiers such as diabetes and smoking. This updated classification now refers to early-onset periodontitis as aggressive periodontitis, stage III grade C, with a rapid rate of progression (Papapanou et al., 2018).

The early onset of alveolar bone loss may occur by itself (nonsyndromic) or as part of a syndrome. For example, leukocyte adhesion deficiency (LAD) type I and type II are autosomal recessive disorders of the leukocyte adhesion cascade. LAD type I has abnormalities in the integrin receptors of leukocytes leading to impaired adhesion and chemotaxis, which results in increased susceptibility to severe infections and early-onset (prepubertal)

periodontitis (Meyle and Gonzales, 2001). LAD type II is also an autosomal recessive disorder in which the severity of the general infectious episodes is much milder than those observed in LAD type I, although there is chronic severe periodontitis. Furthermore, patients with LAD type II present other abnormal features, such as growth retardation and intellectual disability (Etzioni and Tonetti, 2000).

Orthodontic movement of teeth into previously affected areas has been reported to be successful after a short healing period following extractions secondary to aggressive periodontal disease or crowding, to correct antero-posterior discrepancies, or to reduce bimaxillary protrusion. Teeth that have lost periodontal support may be indicated in particular for extraction. For example, it has been claimed that after orthodontic space closure, bony contours and attachment levels on repositioned second and third molars will be superior to those possible if the periodontally affected first molars were retained and treated.

As for any patient each case is unique, and the treatment plan depends on close collaboration with the periodontist, the stability of the remaining teeth, and possible substitutions that would result in a functional occlusion. Periodontal evaluations should be scheduled as often as orthodontic appointments to monitor the condition during tooth movement (McLain et al., 1983).

Papillon–Lefèvre and Haim–Munk syndromes

Two of the many different types of palmoplantar keratoderma (thickened skin over the palms and soles of the feet that may appear to be darkened or “dirty”) differ from the others by the occurrence of severe early-onset periodontitis with premature loss of the primary and permanent dentition as a characteristic sign. Lateral cephalometric analysis of eight patients with Papillon–Lefèvre syndrome revealed a tendency toward a Class III skeletal relationship with maxillary retrognathia, decreased lower facial height, retroclined mandibular incisors, and upper lip retrusion (Bindayel et al., 2008).

It has been reported that following successful combined mechanical and antibiotic therapy of periodontitis associated with Papillon–Lefèvre syndrome, moderate orthodontic tooth movements may be possible within a complex interdisciplinary treatment regimen (Lux et al., 2005). Haim–Munk syndrome is characterized in addition to features seen in Papillon–Lefèvre syndrome by arachnodactyly (long and thin fingers and toes), acroosteolysis (destruction of the digit tips, including the bone), and onychogryphosis (hypertrophy and curving of the nails, giving them a claw-like appearance; Hart et al., 1997).

Singleton–Merten syndrome

Singleton–Merten syndrome is a rare condition with dentin dysplasia and poor dental root development, progressive calcification of the thoracic aorta, calcific aortic stenosis, osteoporosis, and expansion of the marrow cavities in hand bones like that observed in anemia. Generalized muscle weakness and atrophy may also be present. Maxillary hypoplasia has also been noted (Singleton and Merten, 1973; Feigenbaum et al., 1988).

Hajdu–Cheney syndrome

Hajdu–Cheney syndrome (HCS) is a heritable, rare disorder of bone metabolism, associated with acroosteolysis, short stature, distinctive craniofacial and skull changes, periodontitis, and premature tooth loss.

A 22-year-old female presented with the characteristic clinical features of HCS, including short stature, small face, prominent epicanthal folds, thin lips, small mouth, and short hands. Biochemical, hematological, and hormonal parameters were normal. Tests for bone mineral density were indicative of osteoporosis. Cephalometric analysis revealed hypoplasia of the mid-face and increased cranial base angle; the maxilla and the mandible were positioned posteriorly. The sella turcica was enlarged, elongated, and wide open with slender clinoids (Bazopoulou-Kyrkanidou et al., 2007; Figure 4.1). The mandible may be underdeveloped as well as the maxilla and mid-face. Le Fort III maxillary distraction

osteogenesis and advancement genioplasty followed by orthodontia have been successfully performed for the mid-facial retrusion and to eliminate severe snoring during sleep in one case (Satoh et al., 2002).

Conditions in which premature tooth exfoliation may occur occasionally

Ehlers–Danlos syndrome

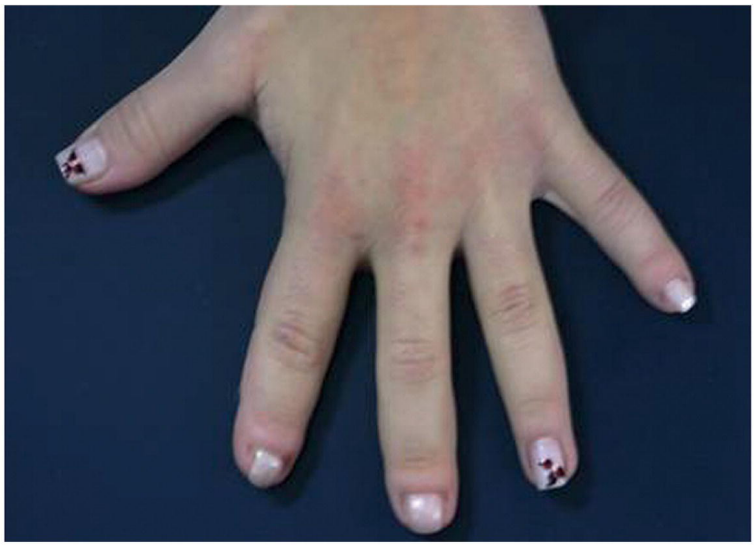
See under “Connective tissue dysplasia.”

X-linked hypophosphatemic rickets (X-linked hypophosphatemia)

In X-linked hypophosphatemia, addition to short stature and bowing of the lower extremities, there are often dental manifestations including apical radiolucencies, abscesses (that may result in premature exfoliation of teeth), and fistulas associated with pulp exposures in the primary and permanent teeth. The pulp exposures relate to the pulp horns extending to the dentino-enamel junction or even to the external surface of the tooth. The thin, hypomineralized enamel may abrade easily, exposing the pulp. Dental radiographs show rickety bone trabeculations and absent or abnormal lamina dura (Hartsfield, 1994; Smith and Steinhauser, 1971).

There are other types of hypophosphatemia with overlapping clinical features and different modes of inheritance and genes involved. Generally, the more severe and earlier the onset, the more severe will be the dental manifestations. In contrast, vitamin D–deficient rickets does not show the dental abnormalities found in X-linked hypophosphatemic rickets (Hartsfield, 1994). Dental abnormalities in patients with familial hypophosphatemic vitamin D–resistant rickets were prevented or diminished by early treatment with 1-hydroxyvitamin D (Chaussain-Miller et al., 2003). Successful treatment has been reported of a relatively mild case with Class II Division 2 malocclusion with severe anterior crowding and lack of mandibular growth with a functional appliance, followed by the

extraction of four premolars and the use of edgewise appliances. No unfavorable root resorption or bone defect occurred (Kawakami and Takano-Yamamoto, 1997).



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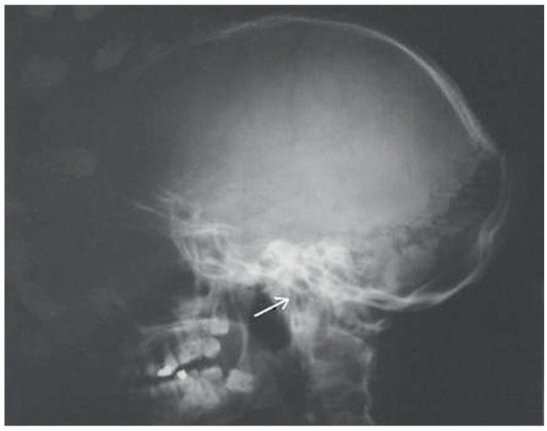

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Figure 4.1 Hajdu–Cheney syndrome. (a) Patient's left hand demonstrating its small size and the clubbing of the fingertips. (b) Hand–wrist radiographs of the patient demonstrating osteolysis of the distal phalanges and clinodactyly (arrow) of the fifth left finger. (c) Lateral skull radiograph demonstrating bathrocephaly, wormian bones in lambdoid suture, and basilar invagination (arrow). Cephalometric analysis reveals hypoplasia of the midface anteroposteriorly and vertically, with the maxilla and the mandible being set posteriorly. The cranial base is increased (two standard deviations) and the sella turcica is enlarged, elongated, and wide open with slender clinoids.

Source: Bazopoulou-Kyrkanidou et al. (2007) / with permission from John Wiley & Sons.

Coffin–Lowry syndrome

This X-linked condition typically affects boys (although girls may be affected less severely), with developmental delay/usually severe mental deficiency, hypotonia (muscle weakness), laterally downslanting palpebral fissures (eye openings), maxillary hypoplasia, prominent lips and anterior open bite tendency, short stature, and thick, soft hands with tapering fingers (Figure 4.2). Sensorineural hearing deficit, cataracts, and retinal changes are occasional abnormalities. In addition to hypodontia with dental spacing and large maxillary central incisors, late eruption and premature loss of primary teeth are common (Babic et al., 1993; Hartsfield et al., 1993). Face2Gene facial analysis had excellent accuracy in the diagnosis of Coffin–Lowry syndrome in Chinese patients, with their composite photo similar to the Face2Gene composite photo based on Caucasian, African, and Hispanic Coffin–Lowry patients (Fung et al., 2019).

Down syndrome

Down syndrome results from trisomy of all or a large part of chromosome 21, occurring in 1/660 births. There are many variable features associated with Down syndrome, including laterally upslanting palpebral fissures, flat facial profile (euryprosopic with brachycephaly), hypotonia (which tends to improve with age), joint hyperflexibility, developmental delay/some degree of mental deficiency, and excess nuchal (neck) skin.

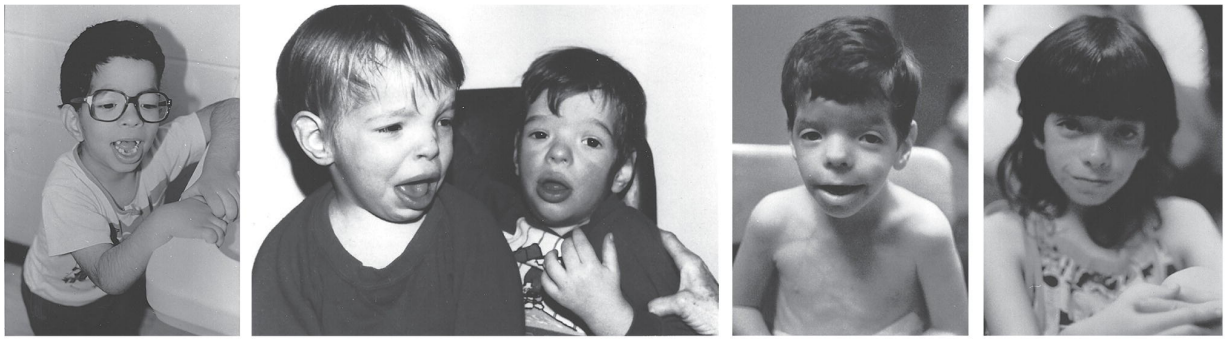


Figure 4.2 (a–d) Patients with Coffin–Lowrey syndrome.

Periodontal disease is common in the older patient, especially in the anterior mandibular region. Paradoxically they may have fewer dental caries, although baby bottle caries may be a concern. The tongue is often positioned partially outside the mouth (particularly when young), giving the impression that it is enlarged, although it is likely to be a posture secondary to hypotonia of the tongue and the facial musculature, and the relatively small size of the oral cavity (Hartsfield, 1994; Hennequin et al., 1999; Babic et al., 1993).

It has been claimed that almost all individuals with Down syndrome have a significant malocclusion, typically a maxillary hypoplasia Class III with anterior open bite, often with hypodontia, tooth size discrepancy, and occasionally with impacted or transposed teeth. Considerations in the treatment of individuals with Down syndrome include a two-phase or multiphase plan to assist in early correction of maxillary transverse deficiency and Class III malocclusion.

As with any individual with developmental delay/mental deficiency, they must be able to cooperate and tolerate the discomfort associated with braces and orthodontic procedures to be treated effectively (Hennequin et al., 1999; Musich, 2006). This is a case-by-case evaluation. Working with them may be effective after some initial difficulty, but sometimes it is just not possible. Some procedures may be done in the operating room, but obviously this is not practical on any continuing basis for orthodontic treatment.

Treatment considerations include taking impressions using quick-set materials with flavors that may reduce the tendency to gag frequently experienced with Down syndrome patients, bonding brackets instead of banding, using a self-etching primer with a glass ionomer cement

that can be used in the oral environment when it is difficult to maintain a dry field for several minutes at a time, using nickel–titanium wires when and for as long as possible allowing a longer interval between appointments, and the use of implants in treatment planning to replace agenic teeth and temporary anchorage devices to minimize the need for compliance (Musich, 2006).

The stages of eruption and development of teeth are often delayed in children with Down syndrome. It has been recommended that regular radiographic screening, to intervene as indicated to guide impacted teeth to their appropriate locations, might prevent or diminish malocclusion and lead to optimal bone height. It is also important to note that stature growth is slower than usual during childhood, the adolescent period is shorter, and skeletal maturation is delayed, taking place around 15–17 years of age (Reuland-Bosma et al., 2010).

Down syndrome patients who underwent rapid maxillary expansion showed a reduction in hearing deficit; the yearly rate of ear, nose, and throat infections; and parentally assessed symptoms of upper airway obstruction compared with Down syndrome children who received no treatment. It was concluded that these findings were probably related to increased oronasal space secondary to the expansion (de Moura et al., 2008).

Chédiak–Higashi syndrome

This rare autosomal recessive disorder has frequently been linked with severe periodontitis (Meyle and Gonzales, 2001). It is characterized by oculocutaneous hypopigmentation, severe immunological deficiency with neutropenia and lack of natural killer cells, a bleeding tendency, and neurological abnormalities (Nagle et al., 1996).

Cherubism

Cherubism is a rare childhood disease in which the expression may be so variable that a clinically normal-appearing parent may have a history of prominent facial swellings or radiographic evidence of abnormal bone pattern in the mandible. Although the progression of

bone destruction typically stabilizes or even regresses after puberty, a few very aggressive cases, sometimes producing morbid results, have been reported (Ayoub and El-Mofty, 1993; Silva et al., 2002; Timosca et al., 2000). Teeth in the involved area are frequently exfoliated prematurely from the loss of support or root resorption or, in permanent teeth, because of interference in the development of roots. Spontaneous loss of the teeth may occur, or the child may pick the teeth out of the soft tissue (McDonald et al., 2011). Delay of tooth eruption may also occur (Suri et al., 2004).

Reossification of the cystic areas within the jaws therefore usually spontaneously occurs, and dislocated teeth have subsequently been realigned orthodontically. Advancements in virtual three-dimensional (3D) reconstruction of anatomical structures based on computed tomography (CT) or cone beam CT (CBCT) data have provided for more predictable individual treatment planning (Holst et al., 2009; Pierce et al., 1996).

Supernumerary teeth and hypodontia (oligodontia)

It is rare to find *multiple* supernumeraries in individuals with no other associated disease or syndrome, although some individual cases have been reported (Fleming et al., 2010). Thus, the presence of multiple supernumerary teeth is a strong indication for further diagnostic evaluation, especially if any other anomalies are present.

Cleidocranial dysplasia (dysostosis)

Cleidocranial dysplasia or dysostosis (CCD) is characterized by agenesis or hypoplasia of the clavicles (allowing the shoulders to be rolled to the body midline in the more severe cases), delayed and imperfect ossification of the cranium (with variable persistence of open fontanels and sutures), moderately short stature, and a variety of other skeletal abnormalities, although clinical variation may be seen even in affected members of the same family (Farronato et al., 2009; Golan et al., 2002).

As the frontal, parietal, and occipital bones are prominent, the skull tends to be brachycephalic, with the face appearing small relative to the cranium with hypoplastic maxillary, lachrymal, nasal, and zygomatic bones. The maxillary and or paranasal sinuses may be underdeveloped. The maxillary hypoplasia results in a relative mandibular protrusion. Occasionally cleft palate has been reported. The dental manifestations are a delayed exfoliation of primary teeth, a lack of or delayed eruption of the permanent dentition that may appear without radiography to be hypodontia, and multiple supernumerary teeth (Farronato et al., 2009).

Referral to a clinical geneticist to confirm the diagnosis and follow-up as indicated, as well as from the clinical geneticist to the orthodontist for treatment planning and case treatment/management at the best age of development, is important. Patients with cleidocranial dysostosis benefit from a team approach with good cooperation and communication within the team and with the patient and family (Farronato et al., 2009). As with any patient with a hypoplastic/retrusive maxilla, timing of a dentofacial orthopedic intervention to bring the maxilla ventral is critical, usually before the age of 10 years depending on skeletal maturation (Macfarlane and Swart, 1989; Clocheret et al., 2003).

The most effective therapeutic approach for the early treatment of the dentofacial problems in CCD is to start with the protraction of the maxilla, followed by orthodontic and surgical treatments as indicated. Further orthodontic treatment and surgery may be required following the pubertal growth spurt. Although there is an abundance of teeth present, sometimes they cannot be moved or placed in an acceptable position, which may necessitate prosthetics with or without surgery as needed.

Several methods, surgical and/or prosthetic, have been put forth for the oral-facial treatment of CCD. An early diagnosis is helpful so that early surgical intervention may be undertaken, typically in a more aggressive fashion than previously to facilitate dental eruption. Although application of a protocol depends on the individual needs of a patient, it has been stated that the “Jerusalem” protocol is recommended as an initial consideration. This involves two surgeries (anterior and posterior) under general anesthesia at the stage when

the root development of unerupted teeth is at least two-thirds of their final estimated length. The first surgery is performed at the chronological age of 10–12 years, which with the usual dental development delay in CCD corresponds to a dental age of 7–8 years. In addition to the extraction of deciduous incisors and supernumerary unerupted teeth in both arches, unerupted permanent incisors are exposed and have attachments bonded to them, followed by primary closure of the surgical flaps. The immature posterior permanent teeth are not exposed, nor their dental follicles disturbed at this stage.

In the second operation (chronological age of at least 13 years; dental age of 10–11 years), deciduous canines and molars are extracted, permanent canines and premolars are exposed in both arches, attachments are bonded, and the surgical flap is closed. Care should be taken in the extraction of supernumerary unerupted teeth and the exposure of permanent unerupted teeth to maintain the integrity of vestibular and lingual/palatal bone plates. Bone is only removed around the crowns of the permanent teeth as needed for the bonding of attachments. To encourage healing by first intention, the flap is repositioned so as to completely cover the wound, without compresses/pressure.

Traction is placed by the application of low extrusion forces using rigid upper and lower arches, and anterior box elastic between the two arches to oppose the possible distortions caused by the excess of space in the arch and the resistance to extrusion. Further details of the treatment protocol may be found in D'Alessandro et al. (2010) and Becker et al. (1997a, 1997b).

Nance–Horan syndrome

Nance–Horan syndrome is an X-linked condition typically affecting males, although as with many X-linked recessive conditions females may be affected to some degree. The typical pattern is the presence of congenital cataracts (with vision impairment, particularly in males), anteverted (folded outward) external ears, shortened metacarpal bones, and dental anomalies including screwdriver-shaped incisors (crown form tapering toward the incisal edge resembling a flat screwdriver head), maxillary midline dental diastema, mesiodens,

and mulberry (multilobed crown) molars (Figures 4.3 and 4.4). There is some mental impairment in 30% of those affected. Although some affected males do not have mesiodens, there appears to be a positive correlation in severity between the eye and dental findings (Bixler et al., 1984; Toutain et al., 2002).

Chondroectodermal dysplasia (Ellis–van Crevald syndrome)

Chondroectodermal dysplasia is an autosomal recessive disorder with diagnostic criteria including postaxial polydactyly (extra digit on the little finger side) of the hands, short limb dwarfism, dysplastic (small and or misshaped) fingernails, and prominent and additional oral frenula with serrations of the alveolar ridge (Figure 4.5). There may be neonatal teeth, hypodontia, small teeth, or delayed eruption of teeth. The upper lip may be short and more tightly bound to the alveolar ridge because of the frenula (Varela and Ramos, 1996; Babic et al., 1993).

Malocclusions are said to be common in Ellis–van Creveld syndrome, but they are not of any consistent type (Figure 4.6). Many of these patients show cephalometric parameters within the normal range, although hypoplasia of the anterior maxilla with relative prognathism of the mandible has been found in some individuals. A large gonial angle with increased anterior lower face height has also been shown in this syndrome (Prabhu et al., 1978; Varela and Ramos, 1996). Other syndromes that have short stature, polydactyly, and orofacial abnormalities include oral-facial-digital syndromes I and II, and asphyxiating thoracic dystrophy (Varela and Ramos, 1996; Babic et al., 1993).

Gardner syndrome (familial adenomatous polyposis)

See under “Supernumerary teeth or hypodontia (oligodontia) and cancer.”

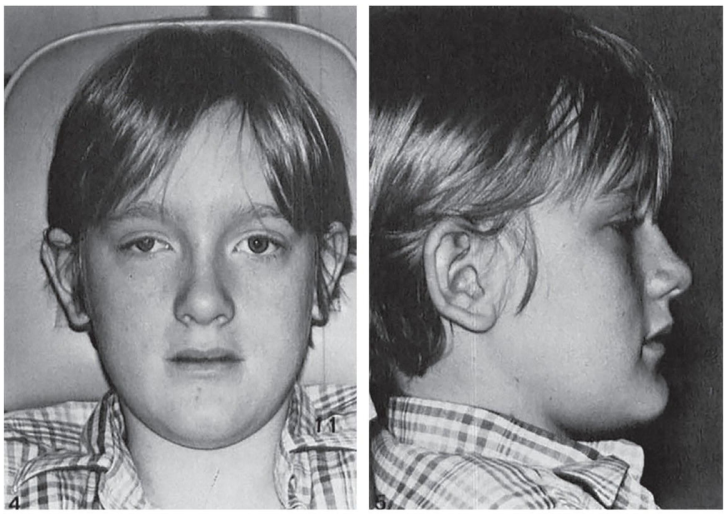
Fabry disease

Fabry disease is an X-linked metabolic disorder caused by a deficiency of the lysosomal enzyme alpha-galactosidase A. The deficit of this catabolic enzyme causes a progressive accumulation of glycosphingolipids containing alpha-galactosyl residues in multiple organs. Although some patients may be diagnosed as adults, the first symptoms of Fabry disease are usually noticed during childhood, when the patient typically experiences febrile episodes, painful acroparesthesia (burning feeling of the hands and feet), and gastrointestinal upset.

Figure 4.3 Intraoral picture showing incisors of a Nance–Horan syndrome family proband.

The accumulation of glycophospholipids leads to numerous systemic manifestations, including cutaneous angiokeratomas (lesions of capillaries, resulting in small marks of red to blue color and characterized by hyperkeratosis), fever from anhidrosis (lack of sweating) due to sweat gland failure, stroke at a young age, cardiovascular disease, renal dysfunction, and corneal dystrophy (Baccaglini et al., 2001).

Malocclusion has been reported to be common, with variable skeletal bimaxillary protrusion, and molar Class III, I, or rarely II. Both supernumerary teeth, and less commonly hypodontia, have been present in affected individuals. Diastemata may be present. Xerostomia has been reported, which if present may complicate oral hygiene during orthodontic treatment (Baccaglini et al., 2001).



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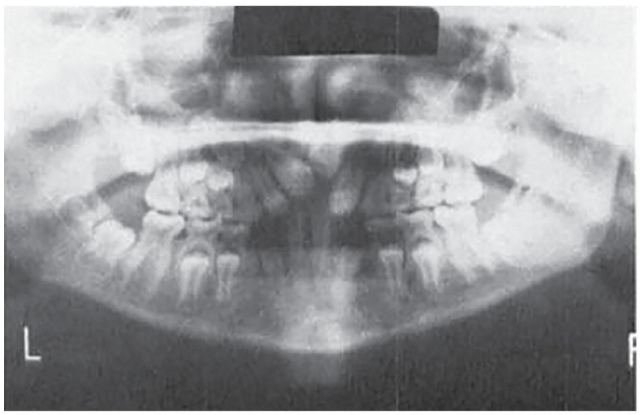

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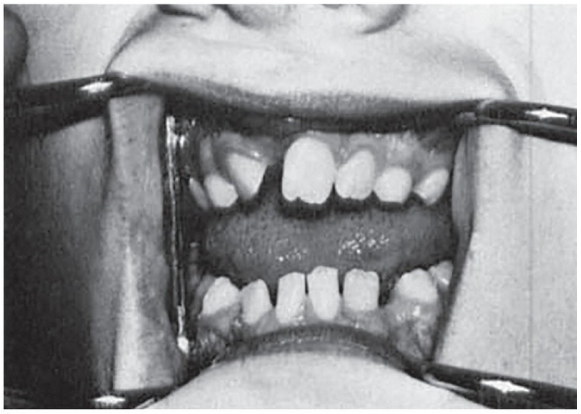

(c)

Figure 4.4 (a) Facial photos of a Nance–Horan syndrome family proband. (b) Panoramic radiograph of the same patient. (c) Intraoral picture showing incisors of the same patient.

(a)

(b)

Figure 4.5 (a, b) A patient with Ellis–Van Creveld syndrome exhibiting polydactyly in both hands, as well as severe nail dysplasia.

Source: Pena-Cardelles et al. (2019) / Medicina Oral S.L / CC BY.

Figure 4.6 (a–e) The intraoral features of the patient in Figure 4.5 exhibiting agenesis of lateral maxillary and mandibular incisors, conical-shaped mandibular incisors and canines, fusion of maxillary incisor, and a supernumerary tooth (mesiodens). Concerning soft tissues, multiple frenum, macroglossia, and glososquissis can be found. Retention of maxillary incisors was present, due to the presence of a central supernumerary tooth.

Source: Pena-Cardelles et al. (2019) / Medicina Oral S.L / CC BY.

Incontinentia pigmenti (Bloch–Sulzberger syndrome)

Incontinentia pigmenti is a genodermatosis that segregates as an X-linked dominant disorder and is usually lethal prenatally in males. In affected females it causes highly variable abnormalities of the skin, hair, nails, teeth, eyes, and central nervous system (Smahi et al.,

2000). In the fully developed disease, the skin shows swirling patterns of melanin pigmentation, especially on the trunk, although this may fade with age. Hypodontia and peg-shaped teeth are characteristic, with some cases exhibiting delayed dental eruption as well. The lack of vertical support from hypodontia of the posterior arches may result in forward rotation of the mandible. A combined orthodontic and prosthetic treatment plan is often needed. Treatment may be complicated by the ability of the patient to cooperate, which can vary (Yamashiro et al., 1998; Babic et al., 1993).

Trichorhinophalangeal syndrome type I

Impacted supernumerary teeth have occasionally been described in this condition (Karacay et al., 2007; Gorlin et al., 1969). Individuals with trichorhinophalangeal syndrome (TRPS) type I have characteristic facies with sparse scalp hair, bulbous tip of the nose, long flat philtrum, thin upper vermilion border, and protruding ears. Axial skeletal abnormalities include cone-shaped epiphyses at the phalanges, hip malformations, and short stature (Momeni et al., 2000). A lateral cephalometric study found them to have a shortened posterior face height associated with a short mandibular ramus, as well as a reduced and superiorly deflected posterior cranial base. These craniofacial findings were associated with a steep inclination of the lower border of the mandible (King and Frias, 1979). Midface hypoplasia has also been noted (Hennekam et al., 2010).

Syndromic hypodontia

A search on missing permanent teeth and oligodontia/anodontia on the POSSUMweb subscription syndrome identification program (Murdoch Childrens Research Institute, Royal Childrens Hospital, Melbourne, Australia, www.possum.net.au) identified 288 syndromes/conditions in which this may occur, including trichodentoosseous syndrome, Williams syndrome, Coffin–Lowry syndrome, Down syndrome, Ellis–van Crevald syndrome, Fabry syndrome, incontinentia pigmenti, and many types of ectodermal dysplasia as noted.

Single median maxillary incisor

A unique form of hypodontia that may be of significant medical importance is the presence of a single primary and permanent maxillary central incisor. Although it may at first appear to be a product of fusion, if the single tooth is in the midline and symmetrical with a normal crown, root shape, and size, then it may be an isolated (nonsyndromic) finding or may be part of the solitary median maxillary central incisor (SMMCI) syndrome. This is a heterogeneous condition that may include other midline developmental abnormalities of the brain and other structures that can be due to mutation in the sonic hedgehog (*SHH*) gene, *SIX3* gene, or other genetic abnormality (Nanni et al., 2001).

SMMCI is estimated to occur in 1 in 50,000 live births. Congenital nasal malformation (choanal atresia, mid-nasal or pyriform aperture stenosis) is positively associated with SMMCI. The presence of SMMCI can predict associated anomalies, in particular the serious developmental brain anomaly holoprosencephaly, which is often, but not always, associated with ocular hypotelorism (decreased distance between the eyes). Common developmental anomalies associated with SMMCI are severe to mild intellectual disability, congenital heart disease, and cleft lip and/or palate. Less frequently, microcephaly, hypopituitarism, hypotelorism, convergent strabismus, esophageal and duodenal atresia, cervical hemivertebrae, cervical dermoid, hypothyroidism, scoliosis, absent kidney, micropenis, and ambiguous genitalia are present. Notably, short stature is present in half the children with SMMCI (Hall et al., 1997).

The SMMCI tooth itself is mainly an esthetic problem, which is ideally managed by combined orthodontic, prosthodontic, and oral surgical treatment; alternatively, it can be left untreated. The importance of the orthodontist recognizing and referring the patient and family for evaluation is primarily that SMMCI, even in the absence of any other clinical signs, can be the mildest expression of a strong family tendency to pass on developmental abnormalities that may range from just the SMMCI to other anomalies such as holoprosencephaly. The orthodontist may be in a position to diagnosis a case of SMMCI with no obvious (traumatic) cause, with

due consideration given to referral for the appropriate genetic testing and counseling (Hall et al., 1997; Kjaer et al., 2001; DiBiase and Cobourne, 2008).

Aarskog syndrome

This condition most severely affects males, although carrier females may show milder signs (especially in the facies and hands) with X-linked recessive inheritance. In males features include slight to moderate short stature, shortened fingers with mild webbing, ocular hypertelorism (increased distance between the eyes), and other findings. The midface and maxilla are often hypoplastic, resulting in a Class III malocclusion, for which orthodontic treatment is often indicated. Delayed dental development and eruption may be found, although it tends to be delayed less than height for age and bone age. In addition to an increase in malocclusion compared to the general population, these individuals have an increased prevalence of hypodontia and caries (Halse et al., 1979).

Supernumerary teeth or hypodontia (oligodontia) and cancer

The association of supernumerary teeth or hypodontia (oligodontia) with cancer may be part of a syndrome, an autosomal dominant trait by itself, or what appears to be a nonsyndromic positive but not absolute correlation.

Gardner syndrome (familial adenomatous polyposis)

Familial adenomatous polyposis (FAP) is an autosomal dominant disorder characterized by predisposition to cancer. Affected individuals usually develop hundreds to thousands of adenomatous polyps of the colon and rectum, a small proportion of which will progress to colorectal carcinoma if not surgically treated. Gardner syndrome is a variant of FAP in which desmoid tumors (fibrous neoplasms originating from musculoaponeurotic structures),

osteomas, and other neoplasms occur together with multiple adenomas of the colon and rectum (Nishisho et al., 1991).

The skull, mandible, facial bones, and paranasal sinuses are the most common sites for the associated osteomas (Ishikawa et al., 1986; Lew et al., 1999). The early detection of osteomas is critical, as they always precede the presentation of intestinal polyps, which may then lead to steps necessary in the prevention of the transformation of intestinal polyps into colorectal cancers (Katou et al., 1989; Nandakumar et al., 2004).

The dental abnormalities in Gardner syndrome include multiple ectopic teeth, impacted permanent teeth, supernumerary teeth, retained primary teeth, hypercementosis, and odontomas (Thomas and Smith, 1981; Carl and Herrera, 1987). Dental eruption may be delayed as well (Suri et al., 2004). Although panoral radiographs may be useful for early detection of osteomas, they may be of limited use. Since the size and location of odontomas may act as a complicating factor in the dental management of a case, it has been recommended that CBCT scans would be beneficial (Kamel et al., 2009).

The variation in the location and size of the osteomas requires evaluation and possibly different treatment plans for those affected, even those from the same family. Difficulty in moving teeth through bone with increased density may be ascertained by an initial stage of treatment. The hypercementosis may complicate tooth extraction. All of these factors necessitate close consultation and cooperation between the oral maxillofacial surgeon and orthodontist, along with the general dentist and/or prosthodontist as needed (Kamel et al., 2009).

Oligodontia–colorectal cancer syndrome

A striking example of autosomal dominant inheritance was reported in a Finnish family in which oligodontia and colorectal cancer were associated with each other. The oligodontia and cancer predisposition were caused by a nonsense mutation in the *AXIN2* gene. Colorectal cancer or precancerous lesions in the family were found only in association with oligodontia and the *AXIN2* mutation,

and affected all those of the oldest generation who had the mutation (Lammi et al., 2004).

Hypodontia and epithelial ovarian cancer

Further support for the proposition that hypodontia can be developmentally associated with cancer comes from the University of Kentucky report that women with epithelial ovarian cancer (EOC) are 8.1 times more likely to have hypodontia than are women without EOC. In contrast to the oligodontia reported with the specific mutations in the *AXIN2* gene, the severity of hypodontia was similar between the two groups (affected and nonaffected) in the Kentucky study, with one or two teeth being agenic. Maxillary lateral incisors followed by second premolars were the most frequently affected teeth (Chalothorn et al., 2008).

This is not to say that everyone who has hypodontia, or even oligodontia, is going to develop cancer, or is even at increased risk. To suggest so to young patients and/or their families would only lead to needless worry, unless there is a striking family history of cancer that occurs in the individuals with hypodontia/oligodontia. In this case referral to the clinical geneticist, especially one who deals with familial cancer, would be indicated because of a strong family history of cancer if the family has not previously been evaluated. Future studies into the family history and genetic analysis of individuals with hypodontia will help illustrate what the relative risk may be of individuals or family members developing cancer associated with hypodontia in the general population.

Failure of dental eruption

Primary failure of eruption (nonsyndromic)

In contrast to failure of teeth to erupt associated with mechanical failure of eruption (e.g. cysts, gingival fibromatosis, adjacent teeth) or with syndromes like cleidocranial dysplasia, “classic” (type I) primary failure of eruption (PFE) is a condition in which all teeth distal to the most mesial involved tooth do not erupt *or* respond to orthodontic force. Some cases of PFE do not follow this classic

pattern and may show partial eruption of some molars that stops. First molars are usually the type of tooth that is affected. The familial occurrence of this phenomenon in approximately one-quarter of cases facilitated the investigation and discovery of the *PTHR1* gene being involved (Decker et al., 2008; Proffit and Frazier-Bowers, 2009). An addition to diagnosis of individuals who are likely to develop or have PFE, further advancements in this area could potentially result in treatment for PFE, as well as the molecular manipulation of selective tooth eruption rates to enhance treatment protocols on an individual basis (Wise et al., 2002; Stellzig-Eisenhauer et al., 2010).

The clinical impact of PFE is frequently very severe. Alveolar bone growth is impaired in the affected areas. The affected teeth appear at the base of a large vertical defect and often present dilacerations. The result is a severe lateral open bite. Unfortunately the affected teeth typically become ankylosed as soon as orthodontic force is applied (Proffit and Vig, 1981; Raghoebar et al., 1989). It is not clear why highly variable clinical expressivity is observed in PFE, with some persons affected bilaterally and others affected unilaterally in the same family. Likewise, there is no apparent explanation for why the posterior dentition is preferentially affected. To date, there are only a few anecdotal cases of successful extrusion of teeth affected with PFE. Thus, any attempt at early orthodontic intervention involving affected teeth for these patients has been said to be futile, and may even make the situation worse if the force increases the occurrence of ankylosis (Frazier-Bowers et al., 2010).

Once growth is complete with the expected posterior open bite, single-tooth or multiple-tooth osteotomies, or selective extractions followed by implants, can often lead to a functioning occlusion. Thus, the advantage of making an early diagnosis of PFE is that it allows a clinician the assurance of providing the best care possible by initially observing the unfavorable growth changes that will inevitably take place, explaining to the patient and family that this is preferred over a useless and potentially damaging early orthodontic intervention involving those teeth. Thus, the best treatment for an accurately established early diagnosis of PFE is initially no treatment of the affected teeth, reserving the multidisciplinary options for affected

patients for a later time after the completion of growth (Frazier-Bowers et al., 2010).

Gingival fibromatosis (hyperplasia)

Generalized gingival enlargement can be caused by a variety of etiological factors. It can be inherited as a nonsyndromic trait (hereditary gingival fibromatosis, HGF), be associated with other diseases characterizing a syndrome, or most commonly be induced as a side effect of medications such as phenytoin, cyclosporin, or nifedipine. Regardless of the etiology, the increased in thickness and firmness of the overlying gingiva may impede and/or alter the course of dental eruption. Interestingly, its occurrence is coincident usually, but not always, with the eruption of teeth, particularly of the permanent dentition (Coletta and Graner, 2006; Suri et al., 2004; Hartsfield et al., 1985).

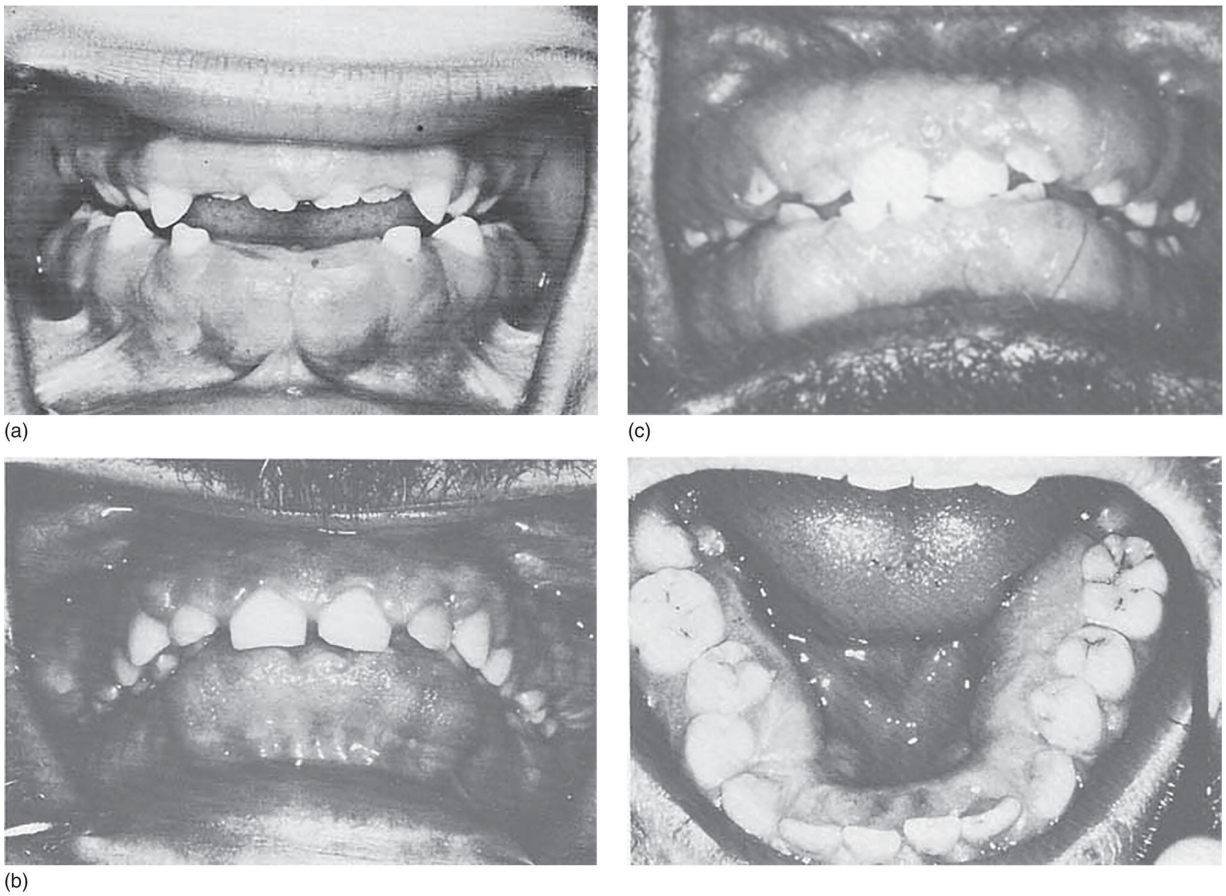

Figure 4.7 (a) Intraoral picture showing gingival fibromatosis of a proband with sensorineural hearing loss. (b) Intraoral picture showing gingival fibromatosis of the father of the proband shown in Figure 4.7a. (c) Intraoral picture showing gingival fibromatosis of the paternal uncle of the proband shown in Figure 4.7a.

Excision of the hyperplastic tissue is indicated for esthetic or functional reasons, including facilitation of tooth eruption and of good oral hygiene. Unfortunately, reports about recurrence rates are conflicting, so the long-term benefit (chance of recurrence) of gingival resection and other periodontal surgical outcomes cannot be predicted, of which the patient must be made aware prior to gingivectomy. It has been recommended that gingivectomy should only be carried out in the areas where the orthodontic treatment is about to be, or has been, initiated to reduce the chance of gingival hypertrophy recurrence. Although personal experience would indicate otherwise, it has been said that it is not clear whether the additional oral hygiene burden from fixed orthodontic appliances

increases the severity of the hyperplasia, or its postsurgical recurrence. Regardless, monthly periodontal check-ups with scaling and polishing as indicated are recommended to counteract gingival inflammation as needed (Kelekis-Cholakis et al., 2002; Clocheret et al., 2003).

Searching POSSUMweb for “thickened gingivae” yields 84 syndromes/conditions in which it may be associated, including gingival fibromatosis with sensorineural hearing loss. In this condition with autosomal dominant inheritance, all individuals with hearing loss/deafness had gingival fibromatosis (Figure 4.7), although not all who have gingival fibromatosis will have the hearing loss (Hartsfield et al., 1985).

Soft and hard tissue asymmetry

Hemifacial microsomia

(See also the discussion of hemifacial microsomia in Chapter 8.) Hemifacial microsomia is a congenital asymmetry of the lower face that may be associated with other cranial and extracranial anomalies. Clinicians realize that the assessment of facial symmetry involves a conscious or subconscious threshold above which the patient is recognized as having a functional and/or esthetic asymmetry. Recognizing the variable expression of hemifacial microsomia versus garden-variety nonsyndromic facial asymmetry can be facilitated by noting involvement of not only the face, but also the symmetrical formation of the external ears, cant of the occlusal plane, vertical position of the orbits, or eye abnormalities, as well as a medical history of skeletal, heart, kidney, or other developmental anomalies (Hartsfield, 2007). On occasion eruption of teeth may also be asymmetrically delayed (Suri et al., 2004).

The variability of asymmetry severity, and the wide range of anomalies that have been reported with the condition in some cases, has resulted in these composite manifestations being given several names. These include Goldenhar syndrome (originally described as mandibular asymmetry with preauricular skin tags, epibulbar dermoids (growths of tissue on the eye), and anomalies of the

cervical vertebrae), and oculo-auriculo-vertebral spectrum (OAVS), reflecting the wide range of associated anomalies throughout the body that may be associated with the facial asymmetry. Although reported incidence rates vary, an incidence of 1/5600 has been stated to be the best estimation. This would make hemifacial microsomia/Goldenhar syndrome/OAVS the fourth most common human craniofacial anomaly after cleft lip with or without cleft palate, cleft palate, and craniosynostosis.

The etiology is often stated to be a perturbation of embryonic blood flow in the developing region, although other factors may also play a role in some cases, as etiological can clearly be heterogeneous. In some animal models and human families there is an apparent influence of genetic factors that influence phenotype, perhaps through alteration of mesodermal development, or indirectly through increased susceptibility to vascular disruption. Depending on what are considered to be the minimum criteria for affected classification, what is often to be presumed to be a sporadic event in a family may be the more severe manifestation of a familial condition, in which family members who are minimally affected may for example have a slightly smaller ear on one side, a small preauricular tag, or slight facial asymmetry (Hartsfield, 2007).

Parry–Romberg (Romberg) syndrome

In contrast to the congenital nature of hemifacial microsomia, Parry–Romberg syndrome, also known by the more descriptive term hemifacial progressive atrophy, is characterized by a slowly progressive atrophy of the soft tissues of essentially half the face, accompanied usually by contralateral Jacksonian epilepsy, trigeminal neuralgia, and changes in the eyes and hair. The process typically begins in the first or second decade of life and may occur in association with localized scleroderma or a “coup de sabre” anomaly, with thinning of the skin and subcutaneous fat. The condition may extend to the jaws, resulting in a unilateral hypoplasia of the maxilla and mandible, producing a malocclusion with an occlusal cant (Anderson et al., 2005).

Without any orthodontic and orthopedic therapy during craniofacial growth in the patient with Parry–Romberg syndrome, the mandible

will become asymmetrical, with a longer ramus and condyle on the healthy side of the face with respect to the other side, as the maxilla is affected. Although it is not possible to arrest the progression of the atrophy in the affected area, it is possible to limit the effect secondarily caused by this process on the mandible. Thus, as vertical facial growth slows, an open bite is evident on the affected side caused by the hypoplasia of the maxilla.

A removable acrylic appliance with a maxillary labial bow that stretches the soft tissue on the affected side by keeping the maxillary and mandibular teeth apart on that side more than on the normal side, as needed, is used to counteract the asymmetrical growth pattern, as might be used in hemifacial microsomia. To be effective, the young patient must keep the appliance in place using muscular force for at least 12–14 hours per day. The treatment must be constantly maintained during the growth period until the end of puberty.

Monitoring the patient monthly, the appliance may require frequent revision by changing the thickness of the inner layer of acrylic interposed between dental arches when a lateral deviation in opening the mouth is detected because of progressive atrophy of the affected area. Groves and guiding surfaces may be placed in the appliance acrylic to allow and guide dental eruption as needed (Grippaudo et al., 2004).

Saethre–Chotzen syndrome

Although cranial and associated facial asymmetry may occur with any asymmetrical craniosynostosis (see the subsequent craniosynostosis section for a definition and further information), one type in particular, Saethre–Chotzen syndrome (caused by a mutation in the *TWIST1* gene), may result in cranial asymmetry (plagiocephaly), as well as facial asymmetry (particularly in individuals with unilateral coronal synostosis). Ironically for a condition associated with asymmetrical premature closure of some sutures, the anterior fontanel (soft spot) closure may be delayed and still open. As part of a differential diagnosis, another condition that often presents with a persistently open anterior fontanel is cleidocranial dysostosis. Saethre–Chotzen syndrome has autosomal

dominant inheritance and variable expressivity, with associated findings including ptosis (“drooping” upper eyelids), low frontal hairline, deviated nasal septum, and partial soft tissue syndactyly (Cunningham et al., 2007; Jones and Smith, 2006). Midface hypoplasia, narrow palate, and supernumerary teeth may also be present (Hennekam et al., 2010).

Maxillary hypoplasia

Maxillonasal dysplasia (Binder syndrome)

Some do not consider this a true syndrome, but rather a nonspecific abnormality of the nasomaxillary complex that may possibly be related in some cases to prenatal deficiency of vitamin K, or actually a manifestation of chondrodysplasia punctata. Clinically the nose is notably flattened, the anterior nasal spine is absent or hypoplastic, and the labial bone overlying the maxillary incisors may be thin on radiographs. Because of premaxillary hypoplasia and maxillary sagittal shortening, patients typically have a relative mandibular prognathism (Hennekam et al., 2010).

Fragile X (Martin–Bell) syndrome

X-linked intellectual disability is close in frequency to that of Down syndrome and fetal alcohol syndrome, with fragile X syndrome being the most common form of it. It is the most common inherited form of intellectual disability. As noted before for X-linked conditions, although males are affected more often and more severely than females, the latter can be affected as well. The face tends to be long and narrow in approximately 70% of postpubertal males with fragile X syndrome. The maxilla can be hypoplastic with mandibular prognathism, and crossbite and anterior open bite are relatively common. Increased occlusal wear has also been described in this condition. Although the cognitive abilities of affected males are often severely affected, the IQs of affected females can range from 50 to normal, with an average of 81. Joint laxity, recurrent middle ear infections, and prominent ears are also common in this condition (Hennekam et al., 2010; Shellhart et al., 1986).

Nevoid basal cell carcinoma (Gorlin) syndrome

This condition combines variable manifestations, including numerous basal cell cancers, epidermal cysts of the skin, odontogenic keratocysts of the jaws, other tumors and cancers, rib and vertebral anomalies, cleft lip and/or palate, with autosomal dominant inheritance, although approximately one-third to one-half of cases are the result of new mutations. Mandibular prognathism may be mild (Hennekam et al., 2010).

Craniosynostosis

Craniosynostosis is the premature closure of some or all cranial sutures, occurring in 1 in 2500 children. The discovery of mutations in the *MSX2*, *FGFR1*, *FGFR2*, *FGFR3*, *TWIST1* (as in Saethre–Chotzen syndrome discussed earlier), and *EFNB1* genes in both syndromic and nonsyndromic cases has led to considerable insights into the etiology, classification, and developmental pathology of these disorders (Morriss-Kay and Wilkie, 2005). Depending on the sutures involved, the resulting cranial shape may be long and narrow anterior to posterior (dolichocephaly or scaphocephaly), or relatively short anterior to posterior and broad transverse (brachycephaly). The latter may also be associated with a pronounced increase in the vertical face height from nasion to bregma, resulting in turricephaly. Most instances of craniosynostosis are nonsyndromic, although there over 100 craniosynostosis syndromes, the most common of which have known genetic etiology (Boyadjiev, 2007).

Craniosynostosis, particularly involving the coronal sutures, often results in maxillary hypoplasia and a Class III malocclusion secondary to the effect on craniofacial growth and development. Although as mentioned most of these are autosomal dominant traits associated with single-gene mutations, their variable expressivity (clinical variation) provides a good example of how even with the strong influence of a single gene, the phenotype can vary considerably. At one time it was presumed that a particular mutation in a particular gene would always result in a specific syndrome, but several identical mutations in the fibroblast growth factor receptor 2 (*FGFR2*) gene have been found in patients diagnosed with the three

overlapping yet different clinical craniosynostosis entities of Crouzon, Pfeiffer, and Jackson–Weiss syndromes (Mulvihill, 1995; Park et al., 1995).

Further evidence for the variable expressivity in autosomal dominant phenotypes associated with a single-gene mutation presumably resulted from the interaction of different proteins from modifying genes and environmental factors occurring when individuals with the classic phenotypes of two overlapping but clinically distinct syndromes (Pfeiffer and Apert), as well as seven other individuals with a facial resemblance to yet another syndrome (Crouzon), occurred in the same family (Escobar and Bixler, 1977).

Even with an autosomal dominant condition that typically manifests, the phenotype may be so variable that an individual may appear to be clinically normal yet have the same gene mutation associated with Crouzon syndrome as his three children and two of his grandchildren. In this case, only through cephalometry was a minimal expression of features suggestive of Crouzon syndrome evident (Everett et al., 1999).

These examples give a clear message: even a generally extreme phenotype associated with an autosomal dominant mutation is variable, even within those who are to some degree affected in a family. Simply discovering the gene mutation likely will indicate a future effect on craniofacial growth and development, but will not necessarily predict the precise effect, and the presentation of severity in any patient may be relatively mild and overlooked (Hartsfield, 2005). This overlap of clinical presentations for variable mutations and even the same mutation in one of the *FGFR* genes has led some to refer to this group of conditions, along with the conditions involving short stature that may also affect facial growth such as achondroplasia (the most common type of short-limbed “dwarfism”) that also are the result of mutations in the *FGFR* genes, as the fibroblast growth factor receptor (FGFR) syndromes.

Axenfeld–Rieger syndrome

Axenfeld–Rieger syndrome as a rare (1 in 200,000) condition with an autosomal dominant mode of inheritance with variable

expressivity characterized by ocular and nonocular manifestations (cardiovascular, mild craniofacial abnormalities, and dental anomalies). Some patients may have short stature, cognitive delay, and anomalies of the fingers (Cazzolla et al., 2022). Craniofacial malformations may include maxillary hypoplasia, cleft palate, anterior open bite, hypertelorism with a broad nasal bridge, and an enlarged sella turcica. The face appears to be flattened with a mildly prognathic profile. Dental anomalies include dental agenesis (most often maxillary incisors and canines), microdontia, short roots (reported to be the etiology when early tooth loss occurs in this condition), taurodontism, enamel hypoplasia, and a hyperplastic maxillary labial frenum (Berenstein-Aizman et al., 2011).

Functional (neoromuscular) asymmetry

Muscle function can influence facial morphology, whether from overcontraction (e.g. torticollis, sometimes called a “wry” neck, or cerebral palsy) or a lack of muscle tone/strength (hypotonia). Many syndromes, such as Down syndrome, may include hypotonia, as previously noted. If the neurological or muscular etiology of the hypotonia is central or systematic, the effect is likely to be generally symmetrical, for example in myotonic dystrophy and the muscular dystrophies that affect to some degree the muscles of mastication or facial expression, and often directly or indirectly leads to an anterior open bite. If the muscular and/or neurological abnormality is generally unilateral, as in hemifacial microsomia, then the affect will typically be an asymmetry.

A symmetrical or asymmetrical lack of facial expression and affect may be due to hypoplasia of cranial nerve ganglia affecting to a variable degree the facial, external eye, and tongue musculature, called the Moebius (Möbius) sequence (also referred to as syndrome). The cause is heterogeneous, although one mechanism may be a tendency for vascular bleeding to occur, and it may be associated with limb reduction and other developmental anomalies beyond the face (Hennekam et al., 2010).

Mandibular retrognathism

Robin sequence

A congenital retrognathic appearance may be due to mandibular micrognathia or retrognathia relative to the maxilla. If this position of the mandible was present when the palatal shelves were closing, a cleft palate (particularly of the posterior) may result. After birth, the position of the tongue secondary to the small mandible may obstruct the airway (glossoptosis). Thus, the sequence of events, mandibular size/position, and resulting cleft palate and glossoptosis are the classic triad of the (Pierre) Robin sequence. The prevalence of the Robin sequence has been estimated to be 1/3000 to 1/5000 (Jones et al., 2021). During childhood some "catch-up growth" has been reported, but appears to be variable (Figueroa et al., 1991). Cephalometric analysis at an adolescent age may show a decreased SNB angle, high mandibular plane angle, and short ramus height. The gonial angle may be increased, and the length of the mandibular body may or may not be short. There may be an increase in hypodontia, particularly of the mandibular second premolars or incisors (Matsuda et al., 2006).

The Robin sequence may be nonsyndromic or be a part of over 40 conditions, including Stickler syndrome, velocardiofacial syndrome, and the Moebius sequence (Hennekam et al., 2010). Knowing whether the Robin sequence is part of a syndrome can be investigated by the medical geneticist, and may help in the expectation of mandibular growth in the presence or lack of hypodontia. For example, children with nonsyndromic Robin sequence with mandibular hypodontia had smaller mandibles than children with nonsyndromic Robin sequence and no mandibular hypodontia. In contrast to the average growth pattern for children with the nonsyndromic Robin sequence and no mandibular hypodontia, the average growth pattern of the nonsyndromic Robin sequence subjects did not improve during adolescence, and the magnitude of differences between the two groups increased. Ultimately, orthodontic treatment with or without orthognathic surgery will depend on the individual case (Suri et al., 2006).

Cephalometric analysis of subjects with nonsyndromic and "syndromic" (Stickler, velocardiofacial, Treacher Collins, and bilateral facial microsomia in this study) Robin sequence concluded

that mandibular morphology and position are variable in the Robin sequence, based on the presence and type of associated syndromic diagnosis. The mean mandibular length was shorter than normal in nonsyndromic and syndromic Robin sequence patients, although more significantly in the latter group, and varied considerably among the different syndromes. The sagittal position of the mandible was relatively normal on average in the nonsyndromic and Stickler and velocardiofacial syndromic patients, in contrast to the Treacher Collins and bilateral facial microsomia patients, who tend to have more of an abnormal mandibular shape. Thus, it was recommended that mandibular distraction be considered for selective Robin sequence patients, such as those with Treacher Collins syndrome or bilateral facial microsomia, because they were unlikely to achieve a relatively normal mandibular growth and position. There was no analysis or mention of the possible effect hypodontia may have in these groups (Rogers et al., 2009).

Velocardiofacial (Shprintzen or del22q11) syndrome

This extremely variable spectrum of conditions has autosomal dominant inheritance of usually a relatively small deletion part of the long arm of the number 22 chromosome. It is not rare, as it accounts for 8% of cleft palate patients, and is second only to Stickler syndrome for syndrome-associated Robin sequence. However, cases do not have to have cleft palate or marked developmental delay, and may only show a mild problem with school, submucous cleft, and/or nasal speech. Facial asymmetry is not unusual along with upslanting palpebral fissures (eye openings), increased anterior vertical face height, malar hypoplasia, and mandibular retrognathia. A history of congenital heart disease may also be part of the condition (Hennekam et al., 2010).

Hallermann–Strieff syndrome

Almost all cases of this condition have been sporadic; that is, only one member in each family has been affected. It is characterized by dyscephaly, hypotrichosis, microphthalmia, congenital cataracts, beaked nose, marked retrognathia (especially of the mandible, which

may exacerbate respiratory problems), and proportionately short stature (Hennekam et al., 2010).

A report of a 19-year-old male with severe mandibular retrognathia, maxillary transverse hypoplasia, oligodontia, and ankylosed primary teeth was treated by surgical assisted rapid palatal expansion with fixed orthodontic therapy, orthognathic surgery, and prosthodontic rehabilitation with implant-retained fixed partial dentures (Abadi et al., 2009).

Diamond Blackfan anemia

Diamond Blackfan anemia (DBA) is one of a rare group of genetic disorders characterized by pro-apoptotic hematopoiesis leading to bone marrow failure, congenital anomalies, and predisposition to cancer. Craniofacial findings may include cleft lip and palate, micrognathia, microcephaly, microtia, hypertelorism, drooping eyes, flat nasal bridge, and congenital glaucoma and/or cataracts (Vlachos et al., 2008). Patients with DBA are often prescribed combined steroid/bisphosphonate therapies. Both agents are likely to affect alveolar bone modeling/remodeling after tooth extraction and orthodontic tooth movement (Sasaki et al., 2021).

Connective tissue dysplasia

Ehlers–Danlos syndromes

The Ehlers–Danlos syndromes (EDS) are a heterogeneous group of heritable connective tissue disorders characterized by joint hypermobility, skin hyperextensibility, and tissue fragility. Classification of EDS has gone from the Villefranche nosology proposed in 1998, which delineated six subtypes, to an expanded classification recognizing 13 subtypes. There is clinical overlap among the EDS, as well as other hereditary connective tissue disorders. The vast genetic heterogeneity and phenotypic variability of the EDS subtypes, except for the hypermobile type for which a genetic/molecular etiology is not known, rely on molecular confirmation with identification of (a) causative genetic variant(s). The report by the International EDS Consortium that proposed the

13 subtypes in 2017 regrouped them according to the causative proteins function within biological pathways. This report gives a concise review of the criteria and other aspects of the subtypes (Malfait et al., 2017).

A comprehensive review of the oral manifestations of EDS notes that although several EDS subtypes involve changes in some type of collagen, periodontal disease is a feature of the specific periodontal subtype of EDS (Lepperdinger et al., 2021), which is caused by variants not in collagen, but in the C1r and C1s subcomponents of the complement pathway (Kapferer-Seebacher et al., 2016). The periodontal EDS subtype, as well as the separate "aggressive periodontitis, stage III grade C, with rapid rate of progression" (early-onset periodontitis), Papillon–Lefèvre syndrome, and other conditions that may be associated with early onset of periodontal disease (refer to the "History of premature tooth exfoliation" section) are of particular interest to the unsuspecting orthodontist who may initiate treatment in younger patients prone to or in the process of losing alveolar bone.

In addition to early-onset periodontitis, periodontal EDS subtype patients have variable hyperextensibility of the skin, ecchymotic pretibial (purple discoloration of the shin) lesions of the skin (Figure 4.8), variable bruising besides the pretibial ecchymosis, minimal to moderate joint hypermobility of the digits, and "cigarette-paper" scars in which the skin looks thin and crinkled (Hartsfield and Kousseff, 1990; Stewart et al., 1977; Linch and Acton, 1979).

The outcome of orthodontic treatment in at least two cases of periodontal subtype EDS is the basis for the recommendation that these patients may be a high-risk group for orthodontia not only in respect to alveolar bone loss, but enhanced external apical root resorption as well. For example, prior to starting the orthodontic treatment, one patient had since the age of 5 years had atrophic, hyperpigmented scars on his shins, as well as bruising from mild trauma. He reportedly had suffered from gingival bleeding for many years. Four first premolars had been extracted at the beginning of the orthodontic treatment. Unfortunately, the periodontal status had deteriorated after orthodontic treatment had been started with fixed appliances (Buckel and Zaenglein, 2007; Karrer et al., 2000).

Other dental concerns in EDS have included hypermobility of the temporomandibular joint with an increased incidence of subluxation, fragile oral mucosa, early-onset periodontitis, high cusps and deep fissures on the crowns of teeth, high incidence of enamel and dental fractures, stunted roots or dilacerations, coronal pulp stones, aberrant dentinal tubules, pulpal vascular lesions and denticles, increased rate of tooth movement in response to orthodontic forces, and increased need for and duration of orthodontic retention (Norton and Assael, 1997).

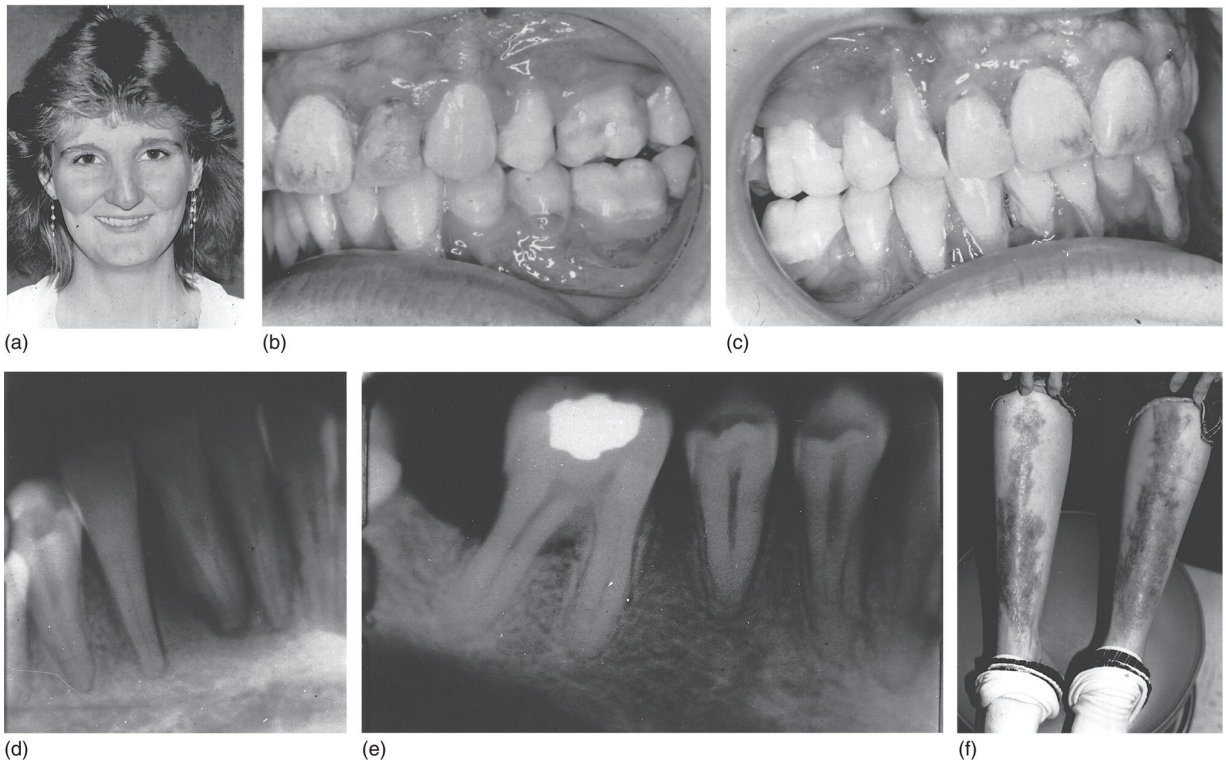

Figure 4.8 (a) Facial photograph of a proband with Ehler–Danlos syndrome. (b) Left-side intraoral view of the patient shown in Figure 4.8a. (c) Right-side intraoral view of the same patient. (d) Intraoral picture showing lower incisors of the same patient. (e) Intraoral picture showing lower right molar of the same patient. (f) The legs of the same patient.

Osteogenesis imperfecta

Osteogenesis imperfecta (OI) is a heterogeneous group of conditions affecting bone mass and fragility. It is a highly variable disease that is

usually secondary to an abnormality in type I collagen synthesis or extracellular secretion. However, some OI patients with normal type I collagen apparently have mutations affecting other bone proteins. The hallmark sign of OI ("brittle bone disease") is an increased incidence or history of bone fracture, usually resulting from minimal if any trauma. In addition to a variable decrease in bone mass, there is abnormal tissue organization and aberrant morphology (size and shape) of bones. There are associated craniofacial and dental manifestations that may include dentinogenesis imperfecta, a hypoplastic maxilla, and hypodontia, among others (Figure 4.9).

Variable expression of dentin developmental defects has been documented, with approximately one-fourth to three-fourths of cases showing some manifestation of dentinogenesis imperfecta, depending to some degree on the type of OI. To control the elevated rate of bone remodeling, some OI patients are treated with bisphosphonates, drugs that inhibit osteoclastic resorption. Bisphosphonate treatment may introduce additional problems, which have been observed in other patients, such as decreased rates of tooth movement, problems maintaining dental implant integration, or osteonecrosis following dental extractions (Hartsfield et al., 2006).

There is an information sheet for healthcare professionals and the public on "Dental Care for People with Osteogenesis Imperfecta" that is currently available online from the Osteogenesis Imperfecta Foundation (Hartsfield and Schwartz, 2007). However, because of the marked clinical variability both among and within families with OI, comprehensive statements about treatment and prognosis should be understood to be merely guidelines.

There are several types of OI, based on clinical presentation and to some degree genotype. Taking all the different types and manifestations of OI as a group, the incidence is probably between 1 in 5000 and 1 in 10,000 individuals (Byers and Steiner, 1992). Documentation of histological dentin abnormalities, in clinically and radiographically normal teeth, indicates that the effect on dentin development is a continuum. In addition to dentinogenesis imperfecta, the presence of additional dental and craniofacial manifestations has been documented: attrition of teeth and tooth

fracture (associated with dentinogenesis imperfecta), thistle-shaped pulp chambers, apically extended pulp chambers (resembling taurodontism), denticles, maxillary lateral incisor invagination, gemination, odontoma, Class II malocclusion, periapical radiolucencies in noncarious teeth, class III malocclusion (more common than class II malocclusion), maxillary hypoplasia, anterior and posterior crossbite, anterior and posterior open bite that tends to worsen with age, hypodontia, supernumerary teeth (rare), advanced or delayed dental development, mandibular cysts (rare), and lack of eruption (or ectopic eruption) of the first and/or second permanent molars (Schwartz and Tsipouras, 1984; Lukinmaa et al., 1987a, 1987b; Lund et al., 1998; Petersen and Wetzel, 1998; O'Connell and Marini, 1999; Malmgren and Norgren, 2002).

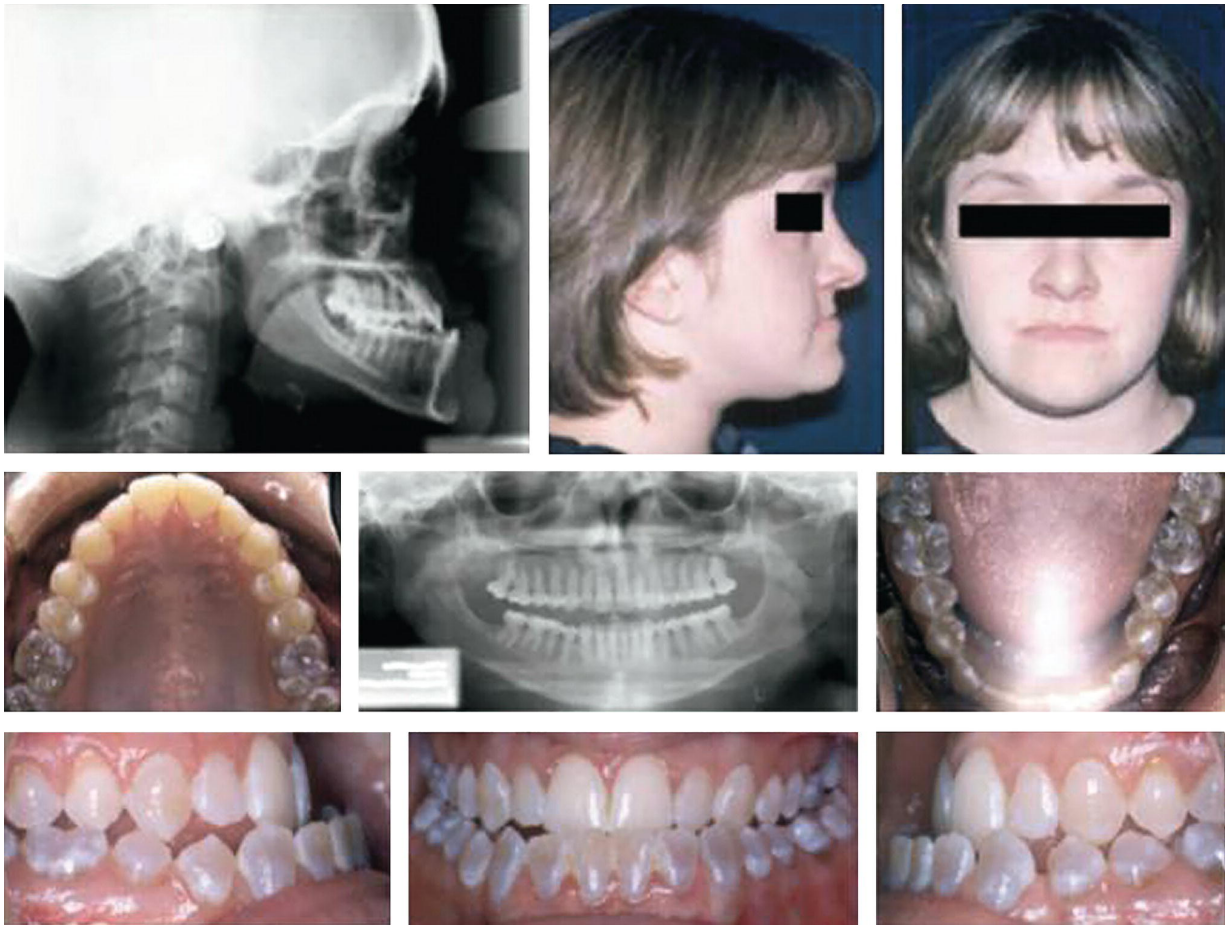

Figure 4.9 Patient with osteogenesis imperfecta type IV showing typical features of skeletal and dental class III malocclusion.

Bone continues to form during the growth period in patients with OI (Jones et al., 1999). Although all patients with OI are said to be osteoporotic, it has not been determined if bone mineralization patterns in the lumbar spine or other locations correlate well with those of the craniofacies, so bone mineral density determinations in other parts of the body may not be informative for orthognathic surgery and other treatment. Healing of fractures occurs within the time frame experienced by patients without OI (O'Connell and Marini, 1999). With regard to tooth movement, rapid palatal expansion, and orthognathic surgery, in general rapid palatal expansion and tooth movement are not a problem, although the teeth may seem relatively loose after debanding so immediate and long-term retention is advised.

When present in cases with OI, dentinogenesis imperfecta tends to affect the maxillary anterior teeth the least, and the mandibular arch the most. Care should be taken when debonding brackets from teeth with dentinogenesis imperfecta to minimize the chance of their fracture and chipping. Although banding of teeth may be contemplated if some teeth are already chipped or fractured prior to initiating orthodontic treatment, prudence may indicate no orthodontic attachments on those teeth, and possibly some restorative coverage.

The variability of the facial bone quality is so great that prediction of orthognathic surgery outcome can be uncertain until the surgeon makes the osteotomies and places the surgical fasteners. In addition, patients with OI have additional general anesthesia and possible bleeding concerns of which the anesthesiologist and surgeon should be aware.

Recommendations must be tempered by the characteristics and condition of the affected individual. It is imperative that informed consent be given, with the clear understanding by the patient and/or family (depending on patient age) that each individual with OI is unique with regard to a particular combination of genes and environmental factors. Presumed collagen or other bone protein mutation(s) may influence the expression of the OI and the response to treatment as well (Hartsfield et al., 2006, Hartsfield and Schwartz, 2007).

Marfan syndrome

Marfan syndrome is estimated to occur in 1 in 5000–10,000 individuals, has autosomal dominant inheritance, and is typically associated with mutations in *FBN1*, thereby affecting fibrillin, an important component of many connective tissues. There is a tendency for those affected to be taller than family members; to have scoliosis, pectus excavatum, or carinatum (indented or ridged sternum); and to variably have long and thin limbs, hands, and feet, an overall body build sometimes referred to as a “Marfanoid” habitus.

Not only is there often an oral facial component from affected growth, there is significant morbidity from increased likelihood of

ectopia lentis (ocular lens displacement), myopia, retinal detachment, and/or aortic dissecting aneurysm, including in those previously undiagnosed and thought to be in good health. This is a condition in which a diagnosis may not only assist in treatment of malocclusion, but also lead to medical care that may save the patient from a sudden premature death.

Malocclusion is often present in this condition, as is the incidence of a high and narrow palatal vault (transverse maxillary deficiency), mandibular retrognathia, dental crowding, and anterior overjet and open bite are increased. In one report on occlusion and cephalometrics in Marfan syndrome patients, 36% (out of a total of 76) had undergone orthodontic treatment before a diagnosis or suspicion of the condition (Westling et al., 1998). In addition to these structural concerns including dolichocephaly, there is also an increased risk for caries, local hypoplastic enamel spots (thought to possibly be related to caries history of the deciduous dentition), root deformity, abnormal pulp shape, pulpal inclusions, calculus, and elevated gingival indices and periodontal disease (De Coster et al., 2002; Utreja and Evans, 2009). Severe root resorption and temporomandibular joint derangement with some resorption of the condyles have been reported in Marfan syndrome, but it is not clear if this was a pleiotropic effect of or a coincident occurrence with the condition (Bilodeau, 2010).

Stickler syndrome

This is another connective tissue dysplasia in which the body proportions may be “Marfanoid” like with hyperextensible “loose” joints, which is usually secondary to a mutation in type 2 or 11 collagen, defining three types of Stickler syndrome: type 1, *COL2A1* mutation in 75% of cases overall; type 2, *COL11A1* mutation; and type 3, *COL11A2* mutation, generally found to be without ocular involvement. There is often a sensorineural hearing loss, and there may also be a conductive hearing loss associated with cleft palate if present and recurrent otitis (ear infections).

About 20% of type 1 patients have cleft palate or bifid uvula. As already mentioned, it is also a condition with which the Robin sequence may be associated (Hennekam et al., 2010). Preorthodontic

treatment characteristics have included malar hypoplasia (flat midface), small SNA and SNB angles, steep mandibular planes, enlarged gonial angles, and retroclined incisors of both arches (Suda et al., 2007; Kucukyavuz et al., 2006). Like in Marfan syndrome vision may be affected with high myopia (thus the patient may be wearing relatively thick eyeglasses) that may even lead to retinal detachment, but there is not typically the increased risk of mortality from aortic aneurysm.

Treacher Collins syndrome

(See also the discussion of Treacher Collins syndrome in Chapter 8.) This craniofacial syndrome can vary from being very severe to being clinically nonpenetrant (skipping a generation), with typically bilateral mandibular deficiency, downslanting palpebral fissures, malformed ears, and one-third with cleft palate. Eye abnormalities may also be present (Hennekam et al., 2010).

Cleft lip and cleft palate

In children with a cleft lip and palate, the question of etiology always arises (see also Chapter 7). Most cases will not be part of a syndrome, but some will be. This is the case in particular when the neonatologist discovers or suspects additional malformations. The orthodontist could ensure that the patient and family are referred for care and support by a cleft lip/palate craniofacial team. Most of these teams will have on them, or access to, geneticists, genetic counselors, or other individuals who could help with determining if the oral cleft is part of a syndrome.

Cleft uvula is a relatively common finding, reportedly occurring in every 1 of 75 Caucasians in one report. Although it has been reported to have a familial pattern by itself and to be a mild expression of the more severe cleft of the entire palate, care must be taken to presume a connection with cleft palate that occurs with an incidence of 1 in 2500. The presence of cleft uvula by itself is unlikely to be of any significance; its occurrence with a family history of cleft palate may suggest familial cleft palate, or other minor anomalies may suggest it is part of a syndrome (Meskin et al., 1964, 1965, 1966).

Van der Woude syndrome

Van der Woude syndrome is said to be the most common of the over 300 syndromes with oral clefting, occurring in 1 in 40,000–100,000 stillborn or live births. The other notable feature of this condition with autosomal dominant inheritance is its extreme variability. It is one of a few clefting syndromes in which a cleft lip with or without a cleft palate, or a cleft palate (which may be as mild as a submucous cleft or cleft uvula), may occur in different members of the same family. It may also skip a generation (nonpenetrance), or only manifest with small paramedian (just to one side or the other of the midsagittal plane) lower lip pits or mounds of tissue (these should not be confused with commissural lip pits located at the site of the lateral oral commissures). Thus, a family history of any of these findings should raise suspicion. It has been stated that a general skeletal pattern is not consistently found in this syndrome. This is not surprising given the wide range of clinical expression from normal to cleft lip and palate, so the skeletal pattern of each patient will be influenced by the particular malformation(s), if any, that present (Rizos and Spyropoulos, 2004; Suda et al., 2006; Lam et al., 2010).

Additional resources

Online

- American College of Medical Genetics (ACMG; https://www.acmg.net/ACMG/Directories.aspx) for a listing of board-certified geneticists (Find a Member link) or a listing of genetics clinics (Find a Genetic Service link).
- Online Mendelian Inheritance in Man (OMIM®; https://omim.org) is a US publicly funded comprehensive, authoritative, and timely compendium of human genes and genetic phenotypes that is authored and edited at the McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University School of Medicine. The full-text, referenced overviews in OMIM contain information on Mendelian

disorders and over 16,000 genes. OMIM focuses on the relationship between phenotype and genotype. It is updated daily, and the entries contain copious links to other genetics resources.

- GeneReviews® (https://www.ncbi.nlm.nih.gov/books/NBK1116) is a free international point-of-care resource owned by the University of Washington that provides clinically relevant and medically actionable information for inherited conditions in a standardized journal-style format, covering diagnosis, management, and genetic counseling for patients and their families.
- Genetic Testing Registry (https://www.ncbi.nlm.nih.gov/gtr) is a US publicly funded medical genetics information resource on clinical and research genetic testing facilities developed for physicians, other healthcare providers, and researchers, available at no cost to all interested persons.
- MedlinePlus (https://medlineplus.gov/genetics) is a US publicly funded National Institutes of Health website for patients and their families and friends that is produced by the National Library of Medicine.
- Registry of Orofacial Manifestations in People with Rare Diseases (ROMSE; https://wiki.romse.org/romsewiki/index.php/ROMSEWiki:Über_ROMSEWiki) was founded in 2013 by Univ. Prof. Dr. med. Dent. Jochen Jackowski and Dr. med. Dent. Marcel Hanisch as a freely accessible database to record orofacial manifestations in people living with rare diseases (Hanisch et al., 2017).

Printed texts

Both texts include numerous pictures, especially in *Gorlin's Syndromes of the Head and Neck*, which also has sections on most of the conditions specifically concerning the facies and oral manifestations.

Hennekam, R.C.M., Krantz, I.D., and Allanson, J.E. (2010). *Gorlin's Syndromes of the Head and Neck*, 5th ed. Oxford: Oxford University Press.

Jones, K.L., Jones, M.C., and Del Campo, M. (2021). *Smith's Recognizable Patterns of Human Malformation*, 8th ed. St. Louis, MO: Elsevier.

References

Abadi, B.J., Van Sickels, J.E., McConnell, T.A. et al. (2009). Implant rehabilitation for a patient with Hallerman-Streiff syndrome: A case report. *Journal of Oral Implantology* 35: 143–147.

Alvesalo, L. (2009). Human sex chromosomes in oral and craniofacial growth. *Archives of Oral Biology* 54(Suppl 1): S18–S24.

Anderson, P.J., Molony, D., Haan, E. et al. (2005). Familial Parry-Romberg disease. *International Journal of Pediatric Otorhinolaryngology* 69: 705–708.

Andreadis, D.A., Rizos, C.B., Belazi, M. et al. (2004). Encephalocraniocutaneous lipomatosis accompanied by maxillary compound odontoma and juvenile angiofibroma: Report of a case. *Birth Defects Research Part A: Clinical and Molecular Teratology* 70: 889–891.

Arriagada-Vargas, C., Abeleira-Pazos, M.T., Outumuro-Rial, M. et al. (2022). Rare disorders: Diagnosis and therapeutic planning for patients seeking orthodontic treatment. *Journal of Clinical Medicine* 11: 1527.

Axelsson, S. (2005). Variability of the cranial and dental phenotype in Williams syndrome. *Swedish Dental Journal Suppl*: 3–67.

Ayoub, A.F., and El-Mofty, S.S. (1993). Cherubism: Report of an aggressive case and review of the literature. *Journal of Oral and Maxillofacial Surgery* 51: 702–705.

Babic, M., Scepan, I., and Micic, M. (1993). Comparative cephalometric analysis in patients with X-chromosome aneuploidy. *Archives of Oral Biology* 38: 179–183.

Baccaglini, L., Schiffmann, R., Brennan, M.T. et al. (2001). Oral and craniofacial findings in Fabry's disease: A report of 13 patients. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* 92: 415–419.

Bader, G. (1967). Odontomatosis (multiple odontomas). *Oral Surgery, Oral Medicine, and Oral Pathology* 23: 770–773.

Bailleul-Forestier, I., Berdal, A., Vinckier, F. et al. (2008). The genetic basis of inherited anomalies of the teeth. Part 2: Syndromes with significant dental involvement. *European Journal of Medical Genetics* 51: 383–408.

Bazopoulou-Kyrkanidou, E., Vrahopoulos, T.P., Eliades, G. et al. (2007). Periodontitis associated with Hajdu-Cheney syndrome. *Journal of Periodontology* 78: 1831–1838.

Becker, A., Lustmann, J., and Shteyer, A. (1997a). Cleidocranial dysplasia: Part 1—General principles of the orthodontic and surgical treatment modality. *American Journal of Orthodontics and Dentofacial Orthopedics* 111: 28–33.

Becker, A., Shteyer, A., Bimstein, E. et al. (1997b). Cleidocranial dysplasia: Part 2—Treatment protocol for the orthodontic and surgical modality. *American Journal of Orthodontics and Dentofacial Orthopedics* 111: 173–183.

Berenstein-Aizman, G., Hazan-Molina, H., Drori, D. et al. (2011). Axenfeld-Rieger syndrome: Dentofacial manifestation and oral rehabilitation considerations. *Pediatric Dentistry* 33: 440–444.

Bijarnia-Mahay, S., and Arora, V. (2019). Next generation clinical practice – it's man versus artificial intelligence! *Indian Pediatrics* 56: 1007–1008.

Bilodeau, J.E. (2010). Retreatment of a patient with Marfan syndrome and severe root resorption. *American Journal of*

Orthodontics and Dentofacial Orthopedics 137: 123–134.

Bindayel, N.A., Ullbro, C., Suri, L.et al. (2008). Cephalometric findings in patients with Papillon-Lefevre syndrome. *American Journal of Orthodontics and Dentofacial Orthopedics* 134: 138–144.

Bixler, D., Higgins, M., and Hartsfield, J., Jr. (1984). The Nance-Horan syndrome: A rare X-linked ocular-dental trait with expression in heterozygous females. *Clinical Genetics* 26: 30–35.

Bloch-Zupan, A., and Goodman, J.R. (2006). Otodental syndrome. *Orphanet Journal of Rare Diseases* 1: 5.

Boyadjiev, S.A. (2007). Genetic analysis of non-syndromic craniosynostosis. *Orthodontics & Craniofacial Research* 10: 129–137.

Buckel, T., and Zaenglein, A.L. (2007). What syndrome is this? Ehlers-Danlos syndrome type VIII. *Pediatric Dermatology* 24: 189–191.

Byers, P.H., and Steiner, R.D. (1992). Osteogenesis imperfecta. *Annual Review of Medicine* 43: 269–282.

Carl, W., and Herrera, L. (1987). Dental and bone abnormalities in patients with familial polyposis coli. *Seminars in Surgical Oncology* 3: 77–83.

Cazzolla, A.P., Testa, N.F., Spirito, F. et al. (2022). Axenfeld–Rieger syndrome: Orthopedic and orthodontic management in a pediatric patient: A case report. *Head & Face Medicine* 18: 1–7.

Chalothorn, L.A., Beeman, C.S., Ebersole, J.L. et al. (2008). Hypodontia as a risk marker for epithelial ovarian cancer: A case-controlled study. *Journal of the American Dental Association* 139: 163–169.

Chaussain-Miller, C., Sinding, C., Wolikow, M. et al. (2003). Dental abnormalities in patients with familial hypophosphatemic vitamin D-resistant rickets: Prevention by early treatment with 1-hydroxyvitamin D. *Journal of Pediatrics* 142: 324–331.

Cichon, J.C., and Pack, R.S. (1985). Taurodontism: Review of literature and report of case. *Journal of the American Dental Association* 111: 453–455.

Clocheret, K., Dekeyser, C., Carels, C. et al. (2003). Idiopathic gingival hyperplasia and orthodontic treatment: A case report. *Journal of Orthodontics* 30: 13–19.

Cohen, M.M., Jr. (1980). Craniofacial syndromes. In: W.H. Bell, W. R. Proffit, and R.P. White (eds.), *Surgical Correction of Dentofacial Deformities*. Philadelphia, PA: Saunders, pp. 7–44.

Coletta, R.D., and Graner, E. (2006). Hereditary gingival fibromatosis: A systematic review. *Journal of Periodontology* 77: 753–764.

Cunningham, M.L., Seto, M.L., Ratisoontorn, C. et al. (2007). Syndromic craniosynostosis: From history to hydrogen bonds. *Orthodontics & Craniofacial Research* 10: 67–81.

D'Alessandro, G., Tagariello, T., and Piana, G. (2010). Craniofacial changes and treatment of the stomatognathic system in subjects with Cleidocranial dysplasia. *European Journal of Paediatric Dentistry* 11: 39–43.

Decker, E., Stellzig-Eisenhauer, A., Fiebig, B.S. et al. (2008). PTHR1 loss-of-function mutations in familial, nonsyndromic primary failure of tooth eruption. *American Journal of Human Genetics* 83: 781–786.

De Coster, P.J., Martens, L.C., and De Paepe, A. (2002). Oral manifestations of patients with Marfan syndrome: A case–control study. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics* 93: 564–572.

de Moura, C.P., Andrade, D., Cunha, L.M. et al. (2008). Down syndrome: Otolaryngological effects of rapid maxillary expansion. *Journal of Laryngology & Otology* 122: 1318–1324.

Dibiase, A.T., and Cobourne, M.T. (2008). Beware the solitary maxillary median central incisor. *Journal of Orthodontics* 35: 16–19.

Ernst, L.M., Quinn, P.D., and Alawi, F. (2007). Novel oral findings in Schimmelpenning syndrome. *American Journal of Medical Genetics Part A* 143: 881–883.

Escobar, V., and Bixler, D. (1977). On the classification of the acrocephalosyndactyly syndromes. *Clinical Genetics* 12: 169–178.

Etzioni, A., and Tonetti, M. (2000). Leukocyte adhesion deficiency II —from A to almost Z. *Immunological Reviews* 178: 138–147.

Everett, E.T., Britto, D.A., Ward, R.E. et al. (1999). A novel FGFR2 gene mutation in Crouzon syndrome associated with apparent nonpenetrance. *Cleft Palate Craniofacial Journal* 36: 533–541.

Farronato, G., Maspero, C., Farronato, D. et al. (2009). Orthodontic treatment in a patient with cleidocranial dysostosis. *Angle Orthodontics* 79: 178–185.

Feigenbaum, A., Kumar, A., and Weksberg, R. (1988). Singleton-Merten (S-M) syndrome: Autosomal dominant transmission with variable expression. *American Journal of Human Genetics* 43: A48.

Figueroa, A.A., Glupker, T.J., Fitz, M.G. et al. (1991). Mandible, tongue, and airway in Pierre Robin sequence: A longitudinal cephalometric study. *Cleft Palate Craniofacial Journal* 28: 425–434.

Fleming, P.S., Xavier, G.M., Dibiase, A.T. et al. (2010). Revisiting the supernumerary: The epidemiological and molecular basis of extra teeth. *British Dental Journal* 208: 25–30.

Frazier-Bowers, S.A., Simmons, D., Wright, J.T. et al. (2010). Primary failure of eruption and PTH1R: The importance of a genetic diagnosis for orthodontic treatment planning. *American Journal of Orthodontics and Dentofacial Orthopedics* 137: 160.e1–7.

Fung, J.L., Rethanavelu, K., Luk, H.M. et al. (2019). Coffin–Lowry syndrome in Chinese. *American Journal of Medical Genetics Part A* 179: 2043–2048.

Golan, I., Baumert, U., Wagener, H. et al. (2002). Evidence of intrafamilial variability of CBFA1/RUNX2 expression in cleidocranial dysplasia—a family study. *Journal of Orofacial Orthopedics* 63: 190–198.

Gorlin, R.J., Cohen, M.M., Jr., and Wolfson, J. (1969). Tricho-rhino-phalangeal syndrome. *American Journal of Diseases of Childhood* 118: 595–599.

Grippaudo, C., Deli, R., Grippaudo, F.R. et al. (2004). Management of craniofacial development in the Parry-Romberg syndrome: Report of two patients. *Cleft Palate Craniofacial Journal* 41: 95–104.

Gurovich, Y., Hanani, Y., Bar, O. et al. (2019). Identifying facial phenotypes of genetic disorders using deep learning. *Nature Medicine* 25: 60–64.

Hall, R.K., Bankier, A., Aldred, M.J. et al. (1997). Solitary median maxillary central incisor, short stature, choanal atresia/midnasal stenosis (SMMCI) syndrome. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics* 84: 651–662.

Halse, A., Bjorvatn, K., and Aarskog, D. (1979). Dental findings in patients with Aarskog syndrome. *Scandinavian Journal of Dental Research* 87: 253–259.

Hanisch, M., Hanisch, L., Benz, K. et al. (2017). Development of a database to record orofacial manifestations in patients with rare diseases: A status report from the ROMSE (recording of orofacial manifestations in people with rare diseases) database. *British Journal of Oral and Maxillofacial Surgery* 55: 500–503.

Hanisch, M., Hanisch, L., Kleinheinz, J. et al. (2019). Orthodontically relevant manifestations in people with rare diseases. *Medical Principles and Practice* 28: 216–221.

Hart, T.C., Stabholz, A., Meyle, J. et al. (1997). Genetic studies of syndromes with severe periodontitis and palmoplantar hyperkeratosis. *Journal of Periodontal Research* 32: 81–89.

Hartsfield, J.K., Jr. (1994). Premature exfoliation of teeth in childhood and adolescence. *Advances in Pediatrics* 41: 453–470.

Hartsfield, J.K., Jr. (2005). Genetics and orthodontics. In: T.M. Graber, R.L. Vanarsdall, and K.W.L. Vig (eds.), *Orthodontics: Current Principles and Techniques*, 4th ed. St. Louis, MO: Mosby, pp. 101–115.

Hartsfield, J.K. (2007). Review of the etiologic heterogeneity of the oculo-auriculo-vertebral spectrum (hemifacial microsomia). *Orthodontics & Craniofacial Research* 10: 121–128.

Hartsfield, J.K., Jr. (2008). Personalized orthodontics: The future of genetics in practice. *Seminars in Orthodontics* 14: 166–171.

Hartsfield, J.K., Jr. (2009). Pathways in external apical root resorption associated with orthodontia. *Orthodontics & Craniofacial Research* 12: 236–242.

Hartsfield, J.K., Jr., Bixler, D., and Hazen, R.H. (1985). Gingival fibromatosis with sensorineural hearing loss: An autosomal dominant trait. *American Journal of Medical Genetics* 22: 623–627.

Hartsfield, J.K., Jr., Hall, B.D., Grix, A.W. et al. (1993). Pleiotropy in Coffin-Lowry syndrome: Sensorineural hearing deficit and premature tooth loss as early manifestations. *American Journal of Medical Genetics* 45: 552–557.

Hartsfield, J.K., Jr., Hohlt, W.F., and Roberts, W.E. (2006). Orthodontic treatment and orthognathic surgery for patients with osteogenesis imperfecta. *Seminars in Orthodontics* 12: 254–271.

Hartsfield, J., James, K., Gudsoorkar, P. et al. (2021). Precision orthodontics: Limitations and possibilities in practice. In: V. Krishnan, A.M. Kuijpers-Jagtman, and Z. Davidovitch (eds.), *Biological Mechanisms of Tooth Movement*. Chichester: Wiley, pp. 189–198.

Hartsfield, J.K., Jr., and Kousseff, B.G. (1990). Phenotypic overlap of Ehlers-Danlos syndrome types IV and VIII. *American Journal of*

Medical Genetics 37: 465–470.

Hartsfield, J.K., Jr., and Schwartz, S. (2007). *Dental Care for People with Osteogenesis Imperfecta*. Gaithersburg, MD: Osteogenesis Imperfecta Foundation. https://www.brittlebone.org/wp-content/uploads/2022/02/87045_Dental_Care.pdf.

Hennekam, R.C.M., Allanson, J.E., Krantz, I.D. et al. (2010). *Gorlin's Syndromes of the Head and Neck*. Oxford: Oxford University Press.

Hennequin, M., Faulks, D., Veyrune, J.L. et al. (1999). Significance of oral health in persons with Down syndrome: A literature review. *Developmental Medicine & Child Neurology* 41: 275–283.

Holst, A.I., Hirschfelder, U., and Holst, S. (2009). Diagnostic potential of 3D-data-based reconstruction software: An analysis of the rare disease pattern of cherubism. *Cleft Palate Craniofacial Journal* 46: 215–219.

Hoyme, H.E. (1993). Minor anomalies: Diagnostic clues to aberrant human morphogenesis. *Genetica* 89: 307–315.

Hu, C.C., King, D.L., Thomas, H.F. et al. (1996). A clinical and research protocol for characterizing patients with hypophosphatasia. *Pediatric Dentistry* 18: 17–23.

Hurst, A.C.E. (2018). Facial recognition software in clinical dysmorphology. *Current Opinion in Pediatrics* 30: 701–706.

Ishikawa, T., Yashima, S., Hasan, H. et al. (1986). Osteoma of the lateral pterygoid plate of the sphenoid bone. *International Journal of Oral & Maxillofacial Surgery* 15: 786–789.

Jackowski, J., and Hanisch, M. (2012). Orofacial manifestations in 2006 rare diseases—a preliminary systematic review of the literature. *Journal of the German Society of Dental and Oral Medicine* 67: D10.

Jaspers, M.T., and Witkop, C.J., Jr. (1980). Taurodontism, an isolated trait associated with syndromes and X-chromosomal aneuploidy. *American Journal of Human Genetics* 32: 396–413.

Jones, K.L., Jones, M.C., and Del Campo, M. (2021). *Smith's Recognizable Patterns of Human Malformation*, 8th ed. Philadelphia, PA: Elsevier.

Jones, K.L., and Smith, D.W. (2006). *Smith's Recognizable Patterns of Human Malformation*, 6th ed. Philadelphia, PA: Elsevier Saunders.

Jones, S.J., Glorieux, F.H., Travers, R. et al. (1999). The microscopic structure of bone in normal children and patients with osteogenesis imperfecta: A survey using backscattered electron imaging. *Calcified Tissue International* 64: 8–17.

Kamel, S.G., Kau, C.H., Wong, M.E. et al. (2009). The role of cone beam CT in the evaluation and management of a family with Gardner's syndrome. *Journal of Craniomaxillofacial Surgery* 37: 461–468.

Kan, W.Y., Seow, W.K., and Holcombe, T. (2010). Taurodontism in children with hypodontia and supernumerary teeth: A case control study. *Pediatric Dentistry* 32: 134–140.

Kapferer-Seebacher, I., Pepin, M., Werner, R. et al. (2016). Periodontal Ehlers-Danlos syndrome is caused by mutations in C1R and C1S, which encode subcomponents C1r and C1s of complement. *American Journal of Human Genetics* 99: 1005–1014.

Karacay, S., Saygun, I., Tunca, Y. et al. (2007). Clinical and intraoral findings of a patient with tricho-rhino-phalangeal syndrome type I. *Journal of the Indian Society of Pedodontics and Preventive Dentistry* 25: 43–45.

Karrer, S., Landthaler, M., and Schmalz, G. (2000). Ehlers-Danlos syndrome type VIII with severe periodontitis and apical root resorption after orthodontic treatment. *Acta Dermato-Venereologica* 80: 56–57.

Katou, F., Motegi, K., and Baba, S. (1989). Mandibular lesions in patients with adenomatosis coli. *Journal of Craniomaxillofacial Surgery* 17: 354–358.

Kawakami, M., and Takano-Yamamoto, T. (1997). Orthodontic treatment of a patient with hypophosphatemic vitamin D-resistant rickets. *ASDC Journal of Dentistry for Children* 64: 395–399.

Kelekis-Cholakis, A., Wiltshire, W.A., and Birek, C. (2002). Treatment and long-term follow-up of a patient with hereditary gingival fibromatosis: A case report. *Journal of the Canadian Dental Association* 68: 290–294.

Kikuiri, T., Mishima, H., Imura, H. et al. (2018). Patients with SATB2-associated syndrome exhibiting multiple odontomas. *American Journal of Medical Genetics Part A* 176: 2614–2622.

King, G.J., and Frias, J.L. (1979). A cephalometric study of the craniofacial skeleton in trichorhinophalangeal syndrome. *American Journal of Orthodontics* 75: 70–77.

Kjaer, I., Becktor, K.B., Lisson, J. et al. G. (2001). Face, palate, and craniofacial morphology in patients with a solitary median maxillary central incisor. *European Journal of Orthodontics* 23: 63–73.

Krusinskiene, V., Alvesalo, L., and Sidlauskas, A. (2005). The craniofacial complex in 47, XXX females. *European Journal of Orthodontics* 27: 396–401.

Kruszka, P., Addissie, Y.A., Tekendo-Ngongang, C. et al. (2020). Turner syndrome in diverse populations. *American Journal of Medical Genetics Part A* 182: 303–313.

Kucukyavuz, Z., Ozkaynak, O., Tuzuner, A.M. et al. (2006). Difficulties in anesthetic management of patients with micrognathia: Report of a patient with Stickler syndrome. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics* 102: e33–e36.

Lam, A.K., David, D.J., Townsend, G.C. et al. (2010). Van der Woude syndrome: Dentofacial features and implications for clinical practice. *Australian Dental Journal* 55: 51–58.

Lammi, L., Arte, S., Somer, M. et al. (2004). Mutations in AXIN2 cause familial tooth agenesis and predispose to colorectal cancer. *American Journal of Human Genetics* 74: 1043–1050.

Lepperdinger, U., Zschocke, J., and Kapferer-Seebacher, I. (2021). Oral manifestations of Ehlers-Danlos syndromes. *American Journal of Medical Genetics Part C: Seminars in Medical Genetics* 187(4): 520–526.

Lew, D., Dewitt, A., Hicks, R.J. et al. (1999). Osteomas of the condyle associated with Gardner's syndrome causing limited mandibular movement. *Journal of Oral & Maxillofacial Surgery* 57: 1004–1009.

Lichtenstein, J., Warson, R., Jorgenson, R. et al. (1972). The tricho-dento-osseous (TDO) syndrome. *American Journal of Human Genetics* 24: 569–582.

Liehr, T., Fleischer, N., and Al-Rikabi, A. (2021). Next-generation phenotyping in cat-eye syndrome based on computer-aided facial dysmorphology analysis of normal photographs. *Molecular Genetics & Genomic Medicine* 9: e1785.

Linch, D.C., and Acton, C.H. (1979). Ehlers-Danlos syndrome presenting with juvenile destructive periodontitis. *British Dental Journal* 147: 95–96.

Lukinmaa, P.L., Ranta, H., Ranta, K. et al. (1987a). Dental findings in osteogenesis imperfecta: I. Occurrence and expression of type I dentinogenesis imperfecta. *Journal of Craniofacial Genetics and Developmental Biology* 7: 115–125.

Lukinmaa, P.L., Ranta, H., Ranta, K. et al. (1987b). Dental findings in osteogenesis imperfecta: II. Dysplastic and other developmental defects. *Journal of Craniofacial Genetics and Developmental Biology* 7: 127–135.

Lumaka, A., Cosemans, N., Lulebo Mampasi, A. et al. (2017). Facial dysmorphism is influenced by ethnic background of the patient and of the evaluator. *Clinical Genetics* 92: 166–171.

Lund, A.M., Jensen, B.L., Nielsen, L.A. et al. (1998). Dental manifestations of osteogenesis imperfecta and abnormalities of collagen I metabolism. *Journal of Craniofacial Genetics and Developmental Biology* 18: 30–37.

Lux, C.J., Kugel, B., Komposch, G. et al. (2005). Orthodontic treatment in a patient with Papillon-Lefevre syndrome. *Journal of Periodontology* 76: 642–650.

Macfarlane, J.D., and Swart, J.G. (1989). Dental aspects of hypophosphatasia: A case report, family study, and literature review. *Oral Surgery, Oral Medicine, and Oral Pathology* 67: 521–526.

Malfait, F., Francomano, C., Byers, P. et al. (2017). The 2017 international classification of the Ehlers–Danlos syndromes. *American Journal of Medical Genetics Part C: Seminars in Medical Genetics*. 175(1): 8–26.

Malmgren, B., and Norgren, S. (2002). Dental aberrations in children and adolescents with osteogenesis imperfecta. *Acta Odontologica Scandinavica* 60: 65–71.

Matsuda, A., Suda, N., Motohashi, N. et al. (2006). Skeletal characteristics and treatment outcome of five patients with Robin sequence. *Angle Orthodontics* 76: 898–908.

McDonald, R.E., Avery, D.R., and Hartsfield, J.K., Jr. (2011). Acquired and developmental disturbances of the teeth and associated oral structures. In: J.A. Dean, D.R. Avery, & R.E. Mcdonald (eds.), *McDonald's and Avery's Dentistry for the Child and Adolescent*, 9th ed. St. Louis, MO: Mosby/Elsevier, pp. 85–125.

McLain, J.B., Proffit, W.R., and Davenport, R.H. (1983). Adjunctive orthodontic therapy in the treatment of juvenile periodontitis: Report of a case and review of the literature. *American Journal of Orthodontics* 83: 290–298.

Meskin, L.H., Gorlin, R.J., and Isaacson, R.J. (1964). Abnormal morphology of the soft palate. I. The prevalence of cleft uvula.

Cleft Palate Journal 35: 342–346.

Meskin, L.H., Gorlin, R.J., and Isaacson, R.J. (1965). Abnormal morphology of the soft palate. II. The genetics of cleft uvula. *Cleft Palate Journal* 45: 40–45.

Meskin, L.H., Gorlin, R.J., and Isaacson, R.J. (1966). Cleft uvula—a microform of cleft palate. *Acta Chirurgiae Plasticae* 8: 91–96.

Meyle, J., and Gonzales, J.R. (2001). Influences of systemic diseases on periodontitis in children and adolescents. *Periodontology 2000* 26: 92–112.

Midtbo, M., and Halse, A. (1994). Root length, crown height, and root morphology in Turner syndrome. *Acta Odontologica Scandinavica* 52: 303–314.

Momeni, P., Glockner, G., Schmidt, O. et al. (2000). Mutations in a new gene, encoding a zinc-finger protein, cause tricho-rhino-phalangeal syndrome type I. *Nature Genetics* 24: 71–74.

Morriss-Kay, G.M., and Wilkie, A.O. (2005). Growth of the normal skull vault and its alteration in craniosynostosis: insights from human genetics and experimental studies. *Journal of Anatomy* 207: 637–653.

Mulvihill, J.J. (1995). Craniofacial syndromes: No such thing as a single gene disease. *Nature Genetics* 9: 101–103.

Musich, D.R. (2006). Orthodontic intervention and patients with Down syndrome. *Angle Orthodontics* 76: 734–735.

Nagle, D.L., Karim, M.A., Woolf, E.A. et al. (1996). Identification and mutation analysis of the complete gene for Chediak-Higashi syndrome. *Nature Genetics* 14: 307–311.

Nandakumar, G., Morgan, J.A., Silverberg, D. et al. (2004). Familial polyposis coli: Clinical manifestations, evaluation, management and treatment. *Mount Sinai Journal of Medicine* 71: 384–391.

Nanni, L., Ming, J.E., Du, Y. et al. (2001). SHH mutation is associated with solitary median maxillary central incisor: A study

of 13 patients and review of the literature. *American Journal of Medical Genetics* 102: 1–10.

Nishisho, I., Nakamura, Y., Miyoshi, Y. et al. (1991). Mutations of chromosome 5q21 genes in FAP and colorectal cancer patients. *Science* 253: 665–669.

Norton, L.A., and Assael, L.A. (1997). Orthodontic and temporomandibular joint considerations in treatment of patients with Ehlers-Danlos syndrome. *American Journal of Orthodontics and Dentofacial Orthopedics* 111: 75–84.

O'Connell, A.C., and Marini, J.C. (1999). Evaluation of oral problems in an osteogenesis imperfecta population. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics* 87: 189–196.

Pantel, J.T., Hajjir, N., Danyel, M. et al. (2020). Efficiency of computer-aided facial phenotyping (DeepGestalt) in individuals with and without a genetic syndrome: Diagnostic accuracy study. *Journal of Medical Internet Research* 22: e19263.

Papapanou, P.N., Sanz, M., Buduneli, N. et al. (2018). Periodontitis: Consensus report of workgroup 2 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *Journal of Periodontology* 89: S173–S182.

Park, W.J., Bellus, G.A., and Jabs, E.W. (1995). Mutations in fibroblast growth factor receptors: Phenotypic consequences during eukaryotic development. *American Journal of Human Genetics* 57: 748–754.

Peña-Cardelles, J.F., Domínguez-Medina, D.A., Cano-Durán, J.A. et al. (2019). Oral manifestations of Ellis-Van Creveld syndrome. A rare case report. *Journal of Clinical and Experimental Dentistry* 11(3): e290–e295.

Petersen, K., and Wetzel, W.E. (1998). Recent findings in classification of osteogenesis imperfecta by means of existing dental symptoms. *ASDC Journal of Dentistry for Children* 65: 305–309.

Pierce, A.M., Sampson, W.J., Wilson, D.F. et al. (1996). Fifteen-year follow-up of a family with inherited craniofacial fibrous dysplasia. *Journal of Oral and Maxillofacial Surgery* 54: 780–788.

Prabhu, S.R., Daftary, D.K., and Dholakia, H.M. (1978). Chondroectodermal dysplasia (Ellis-van Creveld syndrome): Report of two cases. *Journal of Oral Surgery* 36: 631–637.

Proffit, W.R., and Frazier-Bowers, S.A. (2009). Mechanism and control of tooth eruption: Overview and clinical implications. *Orthodontics & Craniofacial Research* 12: 59–66.

Proffit, W.R., and Vig, K.W. (1981). Primary failure of eruption: A possible cause of posterior open-bite. *American Journal of Orthodontics* 80: 173–190.

Raghoebar, G.M., Boering, G., Jansen, H.W. et al. (1989). Secondary retention of permanent molars: A histologic study. *Journal of Oral Pathology and Medicine* 18: 427–431.

Reuland-Bosma, W., Reuland, M.C., Bronkhorst, E. et al. (2010). Patterns of tooth agenesis in patients with Down syndrome in relation to hypothyroidism and congenital heart disease: An aid for treatment planning. *American Journal of Orthodontics and Dentofacial Orthopedics* 137: 584.e1-9.

Rizos, M., and Spyropoulos, M.N. (2004) Van der Woude syndrome: A review. Cardinal signs, epidemiology, associated features, differential diagnosis, expressivity, genetic counselling and treatment. *European Journal of Orthodontics* 26: 17–24.

Roberts, W.E., and Hartsfield, J.K., Jr. (1997). Multidisciplinary management of congenital and acquired compensated malocclusions: Diagnosis, etiology and treatment planning. *Journal of the Indiana Dental Association* 76: 42–51.

Rogers, G.F., Lim, A.A., Mulliken, J.B. (2009). Effect of a syndromic diagnosis on mandibular size and sagittal position in Robin sequence. *Journal of Oral & Maxillofacial Surgery* 67: 2323–2331.

Sasaki, S., Kitaura, H., Goto, M. et al. (2021). Craniofacial characteristics and orthodontic treatment of Diamond Blackfan syndrome: Two case reports. *Cleft Palate-Craniofacial Journal* 60(1): 10556656211053774.

Satoh, K., Tsutsumi, K., Tosa, Y. et al. (2002). Le Fort III distraction osteogenesis of midface-retrusion in a case of Hajdu Cheny syndrome. *Journal of Craniofacial Surgery* 13: 298–302.

Schenkein, H.A. (1998). Inheritance as a determinant of susceptibility for periodontitis. *Journal of Dental Education* 62: 840–851.

Schulman, G.S., Redford-Badwal, D., Poole, A. et al. (2005). Taurodontism and learning disabilities in patients with Klinefelter syndrome. *Pediatric Dentistry* 27: 389–394.

Schwartz, S., and Tsipouras, P. (1984). Oral findings in osteogenesis imperfecta. *Oral Surgery, Oral Medicine, and Oral Pathology* 57: 161–167.

Shellhart, W.C., Casamassimo, P.S., Hagerman, R.J. et al. (1986). Oral findings in fragile X syndrome. *American Journal of Medical Genetics* 23: 179–187.

Silva, E.C., De Souza, P.E., Barreto, D.C. et al. (2002). An extreme case of cherubism. *British Journal of Oral and Maxillofacial Surgery* 40: 45–48.

Singleton, E.B., and Merten, D.F. (1973). An unusual syndrome of widened medullary cavities of the metacarpals and phalanges, aortic calcification and abnormal dentition. *Pediatric Radiology* 1: 2–7.

Smahi, A., Courtois, G., Vabres, P. et al. (2000). Genomic rearrangement in NEMO impairs NF-kappaB activation and is a cause of incontinentia pigmenti. The International Incontinentia Pigmenti (IP) Consortium. *Nature* 405: 466–472.

Smith, W.K., and Steinhauser, R.A. (1971). Vitamin D-resistant rickets with dental abnormalities. *Birth Defects Original Article*

Series 7: 274–275.

Stellzig-Eisenhauer, A., Decker, E., Meyer-Marcotty, P. et al. (2010). Primary failure of eruption (PFE)—clinical and molecular genetics analysis. *Journal of Orofacial Orthoptics* 71: 6–16.

Stewart, R.E., Hollister, D.W., and Rimoin, D.L. (1977). A new variant of Ehlers-Danlos syndrome: An autosomal dominant disorder of fragile skin, abnormal scarring, and generalized periodontitis. *Birth Defects Original Article Series* 13: 85–93.

Suda, N., Handa, S., Higashihori, N. et al. (2007). Orthodontic treatment of a patient with Stickler syndrome. *Angle Orthodontics* 77: 931–939.

Suda, N., Takada, J., and Ohyama, K. (2006). Orthodontic treatment in a patient with Van der Woude's syndrome. *American Journal of Orthodontics & Dentofacial Orthoptics* 129: 696–705.

Suri, L., Gagari, E., and Vastardis, H. (2004). Delayed tooth eruption: Pathogenesis, diagnosis, and treatment. A literature review. *American Journal of Orthodontics & Dentofacial Orthoptics* 126: 432–445.

Suri, S., Ross, R.B., and Tompson, B.D. (2006). Mandibular morphology and growth with and without hypodontia in subjects with Pierre Robin sequence. *American Journal of Orthodontics & Dentofacial Orthoptics* 130: 37–46.

Thomas, J.G., and Smith, H.W. (1981). Gardner's syndrome. Report of a case. *Oral Surgery, Oral Medicine, and Oral Pathology* 51: 213–214.

Timosca, G.C., Galesanu, R.M., Cotutiu, C. et al. (2000). Aggressive form of cherubism: Report of a case. *Journal of Oral & Maxillofacial Surgery* 58: 336–344.

Toutain, A., Dessay, B., Ronce, N., et al. (2002). Refinement of the NHS locus on chromosome Xp22.13 and analysis of five candidate genes. *European Journal of Human Genetics* 10: 516–520.

Utreja, A., and Evans, C.A. (2009). Marfan syndrome—an orthodontic perspective. *Angle Orthodontics* 79: 394–400.

Varela, M., and Ramos, C. (1996). Chondroectodermal dysplasia (Ellis-van Creveld syndrome): A case report. *European Journal of Orthodontics* 18: 313–318.

Varrela, J., Alvesalo, L., and Mayhall, J. (1990). Taurodontism in 45,X females. *Journal of Dental Research* 69: 494–495.

Vig, K.W. (1990). Orthodontic considerations applied to craniofacial dysmorphology. *Cleft Palate Journal* 27: 141–145.

Visinoni, A.F., Lisboa-Costa, T., Pagnan, N.A. et al. (2009). Ectodermal dysplasias: Clinical and molecular review. *American Journal of Medical Genetics A* 149A: 1980–2002.

Vlachos, A., Ball, S., Dahl, N. et al. (2008). Diagnosing and treating Diamond Blackfan anaemia: Results of an international clinical consensus conference. *British Journal of Haematology* 142: 859–876.

Westling, L., Mohlin, B., and Bresin, A. (1998). Craniofacial manifestations in the Marfan syndrome: Palatal dimensions and a comparative cephalometric analysis. *Journal of Craniofacial Genetics and Developmental Biology* 18: 211–218.

Wise, G.E., Frazier-Bowers, S., and D'Souza, R.N. (2002). Cellular, molecular, and genetic determinants of tooth eruption. *Critical Reviews in Oral and Biological Medicine* 13: 323–334.

Wright, J.T., Kula, K., Hall, K. et al. (1997). Analysis of the tricho-dento-osseous syndrome genotype and phenotype. *American Journal of Medical Genetics* 72: 197–204.

Yamashiro, T., Nakagawa, K., and Takada, K. (1998). Case report: Orthodontic treatment of dental problems in incontinentia pigmenti. *Angle Orthodontics* 68: 281–284.

Part II
The Growing Patient

5
Endocrinological Conditions and Orthodontic Treatment

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Summary

Several systemic conditions and specifically endocrinopathies may affect craniofacial or dental development, which may be expressed by altered clinical and radiographic characteristics of the affected individuals. Proper evaluation of clinical signs and symptoms is of high importance for the diagnostic procedure. Various abnormalities may be evident during examination in the dental environment. Decreased body height and delayed tooth eruption together with maxillary and mandibular hypoplasia may be signs of growth hormone deficiency, while increased body height, prominent mandible with interdental diastemas, and enlarged facial characteristics imply gigantism or acromegaly caused by excessive growth hormone production. Enlargement of the tongue and lips, poor periodontal health, delayed dental age, or teeth impaction together with reduced craniofacial dimensions can be observed in patients with hypothyroidism. In cases with mandibular osteoporosis, increased susceptibility to caries, periodontal disease, and accelerated dental eruption hyperthyroidism could be found. Disorders of parathyroid hormone secretion can cause dental tissue alterations, such as enamel hypoplasia, enamel opacities, hypodontia and eruption disturbances, or radiolucent lesions called “brown tumors,” especially in the mandible. Hyperpigmentation of the oral mucosa, the gingiva, or the tongue can be associated with primary adrenal insufficiency. Sclerotic lesions on radiographs coexisting with facial asymmetry and expanded skeletal tissue lead to the diagnosis of fibrous dysplasia. Patients with diabetes, a very common metabolic disorder, can suffer from severe periodontal disease. Exogenous hormonal administration due to medication can also influence the bones, the dentition, and orthodontic tooth movement and should be taken into consideration. The close cooperation of the dentist or orthodontist with the endocrinologist is essential to optimize multidisciplinary treatment in these patients.

Craniofacial growth and development are regulated by complex mechanisms under the influence of genes, hormones, nutrients, and environmental factors that give the craniofacial bone its final morphology, while any disturbances in this mechanism may result in a deviating growth pattern. Apart from the craniofacial skeleton, the development of the dentition, the growth of the facial soft tissue, and the function of muscles are regulated by many intrinsic and exogenous factors. Pathological conditions of general health may have implications in the orofacial region. Profound alterations are observed during a clinical examination or on radiographic images in patients presenting with various systemic diseases.

Knowledge of the physiological processes of the body and disease-free craniofacial, facial, oral, and dental development and architecture are essential for the proper and timely identification of any disturbance. Among pathological conditions, endocrinopathies have broad etiology, clinical manifestation, and laboratory findings, with different affected organs depending on the specific endocrinological disorder. This chapter aims to highlight endocrinological disorders and provide information regarding the general, craniofacial, and oral manifestations of these conditions that may affect dental and orthodontic treatment.

Growth hormone disorders

The pituitary gland produces several hormones such as growth hormone (GH), luteinizing hormone (LH), prolactin (PRL), adrenocorticotropic hormone (ACTH), and thyroid-stimulating hormone (TSH) (Adeel et al., 2020).

The most important hormone secreted by the pituitary gland is GH, which regulates the growth of several tissues in growing individuals. It is well understood that the pituitary gland has a critical role in the overall development of the body. GH is known to be released mostly during night sleep, with its main function being the promotion of insulin-like growth factor I (IGF-I).

Growth hormone deficiency

General characteristics

Disturbances in GH production can lead to GH deficiency (GHD), which can be either isolated (IGHD) or combined with other general medical conditions. Etiological factors for GHD may include pituitary gland abnormal function, syndromes such as Turner syndrome, and others. The clinical characteristics vary according to the etiological factor, the age of the child at onset of the disorder, and the severity of the deficiency. GHD has been found to cause impairment of growth of the long bones of the body, and abnormal development of the maxilla, the mandible, and the dentition in children.

Craniofacial and oral manifestations

GHD has a negative effect on the total length of the maxilla (Oliveira-Neto et al., 2011), causing midfacial hypoplasia, while severe deviations are found also in the total length and the mandibular body (Salas-Flores et al., 2010), resulting in Angle's Class II malocclusion (Torlińska-Walkowiak et al., 2021). The retrognathism of the mandible and maxilla is best evidenced by the values of the SNA° and SNB° angles (Preda et al., 2019). In the vertical plane, the posterior facial height (PFH) is smaller (Pirinen et al., 1994), while there is an open bite tendency with mandibular retrusion and convex profile (Salas-Flores et al., 2010). Regarding the anterior cranial base, its length was found to be decreased (Salas-Flores et al., 2010; Preda et al., 2019) and the cranial base angle (CL-SPhen) was smaller than in controls (Pirinen et al., 1994). In an attempt to create a classification of the affected structures, the total maxillary length was found to be the most reduced linear parameter followed by the posterior cranial base length, total mandibular length, total PFH, total anterior facial height (AFH), mandibular body length, and anterior cranial base length (Oliviera-Neto et al., 2011; Davidopoulou and Chatzigianni, 2017).

A relatively common clinical finding in children with GHD is a mean delay in dental age by about 1–2 years (Torlińska-Walkowiak et al., 2021). Studies in humans have also demonstrated that genetic polymorphisms in estrogen receptors and in GH receptors are associated with alterations in ameloblast function and

developmental defects of enamel (Arid et al., 2019). The presence of a single central incisor in children with GHD may be predictive of median line and pituitary gland disorders (Hamilton et al., 1998; Figure 5.1).

Orthodontic considerations

There is evidence that GH replacement therapy has a beneficial effect on the craniofacial complex (Partyka et al., 2018); facial convexity improves, mandibular length and lower facial height increase, while the arch width remains constant (Poole et al., 1982). Catch-up growth in height, skeletal age, AFH, PFH, and posterior cranial base length are evident with hormonal therapy (Cantu et al., 1997).

The effect of GH on dental development remains controversial. According to some studies, when GH replacement treatment is started early and lasts longer, the dental age is accelerated (Partyka et al., 2018). Nevertheless, in other studies GH did not markedly affect dental maturation (van Erum et al., 1998). The orthodontist should evaluate all possible deviations from the norm and the effect of GH replacement therapy on the craniofacial bones and the dentition before orthodontic treatment commences.

Growth hormone excess

General characteristics

Gigantism occurs when an increase in GH production commences before the fusion of the long bone epiphysis and is characterized by tall body height. Acromegaly occurs after adolescence, when GH hypersecretion occurs following the completion of skeletal maturity, leading to large extremities and characteristic facies. Elevated IGF-1 levels confirm the diagnosis (Bello and Garla, 2021).

Figure 5.1 (a, b) Child with growth gormone deficiency presenting a single central incisor due to median line and pituitary gland disorder.

With permission from 2nd Pediatric Dept., Aristotle University of Thessaloniki, AHEPA Hospital, Greece.

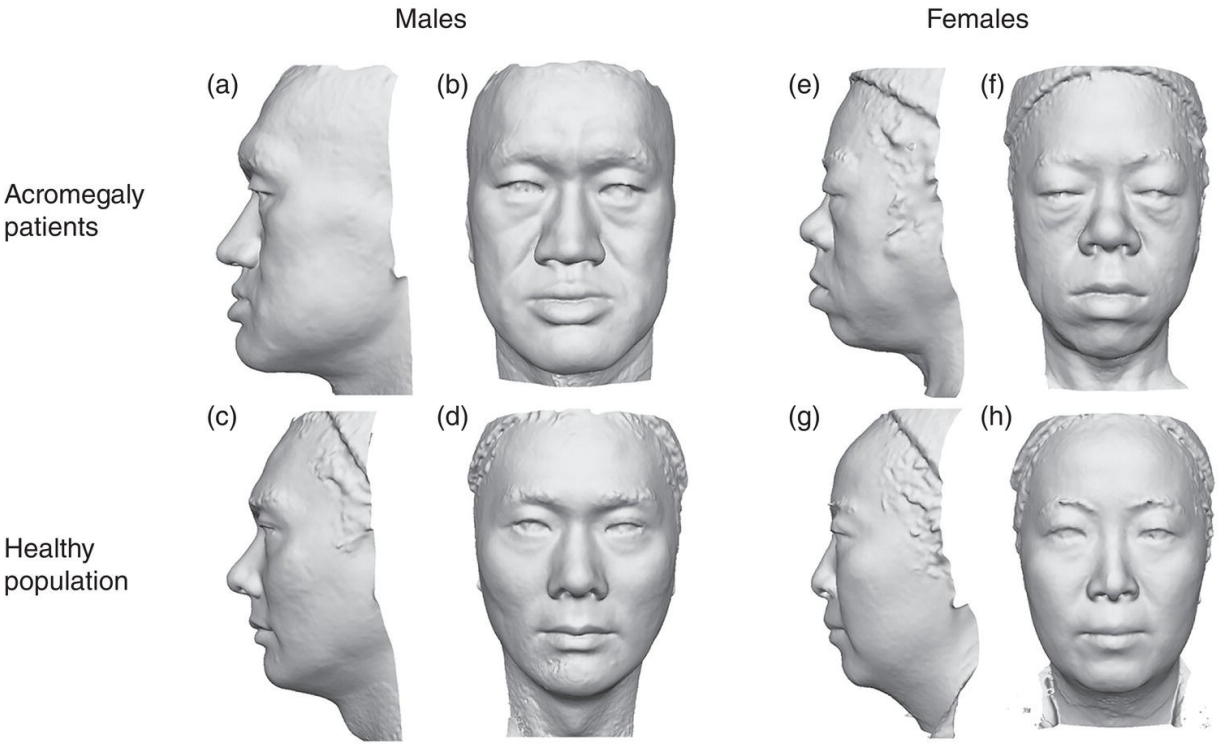

Figure 5.2 Three-dimensional (3D) facial analysis of (a–d) male and (e–h) female patients with acromegaly compared to healthy individuals.

Source: Guo et al. (2018) / Frontiers Media S.A. / CC BY 4.0.

Craniofacial and oral manifestations

The characteristic extraoral features include a prominent forehead and growth of the nose and ears (Kamal et al., 2020). In male acromegaly patients the nasal width, length, height, and depth were found to be increased and IGF-1 levels were linearly and positively correlated with nose width (Guo et al., 2018; Figure 5.2). Facial widths and facial heights were found to be much larger, along with an elongated clivus (Pirinen et al., 1994). Head dimensions and the cranial base angle were within normal values in patients with GH excess. A protrusion of the mandible is generally frequently observed and the gonion–gnathion distance is longer (Guo et al., 2018). When examined periorally, common findings in these patients are thicker upper lips and macroglossia with profound interdental spacing. Taurodontism can be seen on dental radiographs (Akintoye et al., 2003; Guo et al., 2018).

Orthodontic considerations

Patients with gigantism or acromegaly require detailed examination and thorough coordination between endocrinologists, orthodontists, and oral surgeons before the commencement of any treatment.

Thyroid disease

Thyroid hormones (THs) are critical regulators of metabolic processes, of growth, and of cell turnover in the body (Bochukova et al., 2012; Williams and Bassett, 2018). The mean prevalence of total thyroid dysfunction in Europe is 3.82% (Garmendia Madariaga et al., 2014). Abnormalities of the thyroid gland are expressed mainly as abnormal production of THs triiodothyronine-T3 and thyroxine-T4, causing either hypothyroidism or hyperthyroidism, which may have a negative effect on the orofacial tissues, such as the craniofacial, dental, and oral structures.

Hypothyroidism

General characteristics

Hypothyroidism refers to decreased production of THs from the thyroid gland, which leads to lower levels of those hormones in the blood. The mean prevalence of hypothyroidism in Europe was found to be 3.05% of the population (Garmendia Madariaga et al., 2014). The etiological factors may vary and be diverse, but clinical manifestations seem to be quite homogeneous. The most frequent disorder of autoimmune origin with clinical hypothyroidism is Hashimoto thyroiditis (HT). HT has the highest prevalence in the general population among hypothyroidism disorders and is characterized by reduced levels of thyroxine (fT4) and the metabolically active free triiodothyronine (fT3).

Frequently, myopathies are a severe symptom of hypothyroidism (Fariduddin and Bansal, 2021). Untreated hypothyroidism may cause general inflammation of the body's joints (Grozdinska et al., 2018).

Craniofacial and oral manifestations

Severe HT may cause subnormal growth of the maxilla and mandible and a decrease in facial dimensions. In an animal study on rats, the palatal, cranial, bizygomatic arch, and bigonial width measurements were significantly shorter in the HT groups compared to the control group. Cephalometric radiographs indicated that statistically significant differences were present in the HT groups for almost all linear and angular measurements (Gecgelen Cesur et al., 2016). A significantly elevated prevalence of temporomandibular disorder was found in patients with HT (Grozdinska et al., 2018; Figure 5.3).

Figure 5.3 Child with hypothyroidism. With permission from 2nd Pediatric Dept, Aristotle University of Thessaloniki, AHEPA Hospital, Greece.

Timing of tooth eruption, mineralization of tooth enamel, maxillary and mandibular bone, tongue morphology, and periodontal status are affected according to several studies (Chandna and Bathla, 2011; Dudhia and Dudhia, 2014, Vucic et al., 2017). It is generally accepted that decreased concentrations of THs could lead to delayed dental development in the child. Low levels of THs, not only during early childhood, but also during the mother's pregnancy in cases where maternal hormonal deviations are present, have been related to delayed tooth maturation and tooth development in the child (Vucic et al., 2017).

Orthodontic considerations

Severe HT has detrimental effects on tooth eruption, leading to impacted permanent teeth due to prolonged maintenance of primary teeth with a consequent malocclusion (Bedi and Brook, 1984; Gupta et al., 2014; Ferrazo et al., 2014). Oral effects of HT also include enlargement of the tongue and lips, poor periodontal health, and delayed wound healing (Pinto and Glick, 2002; Gupta et al., 2014; Gecgelen Cesur et al., 2016). Hypothyroidism has been associated with root resorption during orthodontic tooth movement.

Hyperthyroidism

General characteristics

Hyperthyroidism refers to overproduction of THs from the thyroid gland, which results in high bone turnover and accelerated bone metabolism. The mean prevalence of hyperthyroidism in Europe is 0.75% (Garmendia Madariaga et al., 2014). Clinical manifestations include tremor, anxiety, intolerance of heat, sinus tachycardia, increased susceptibility to heart failure, and others (Chandna and Bathla, 2011). Grave's disease is the most common disorder with clinical hyperthyroidism, together with pretibial swelling and exophthalmos.

Craniofacial and oral manifestations

Craniofacial and dental aspects of hyperthyroidism consist of maxillary or mandibular osteoporosis, increased susceptibility to caries, periodontal disease, accelerated dental eruption (Poumpros et al., 1994), and burning mouth syndrome (Pinto and Glick, 2002; Figure 5.4).

Orthodontic considerations

Bone metabolism has a significant impact on tissue reaction and consequently on tooth movement and retention period. Animal studies have resulted in differentiated tooth movement and bone resorption patterns in different bone metabolism groups (Verna and Melsen, 2003). In general, it is accepted that the orthodontic tooth movement rate may be higher in patients with hyperthyroidism.

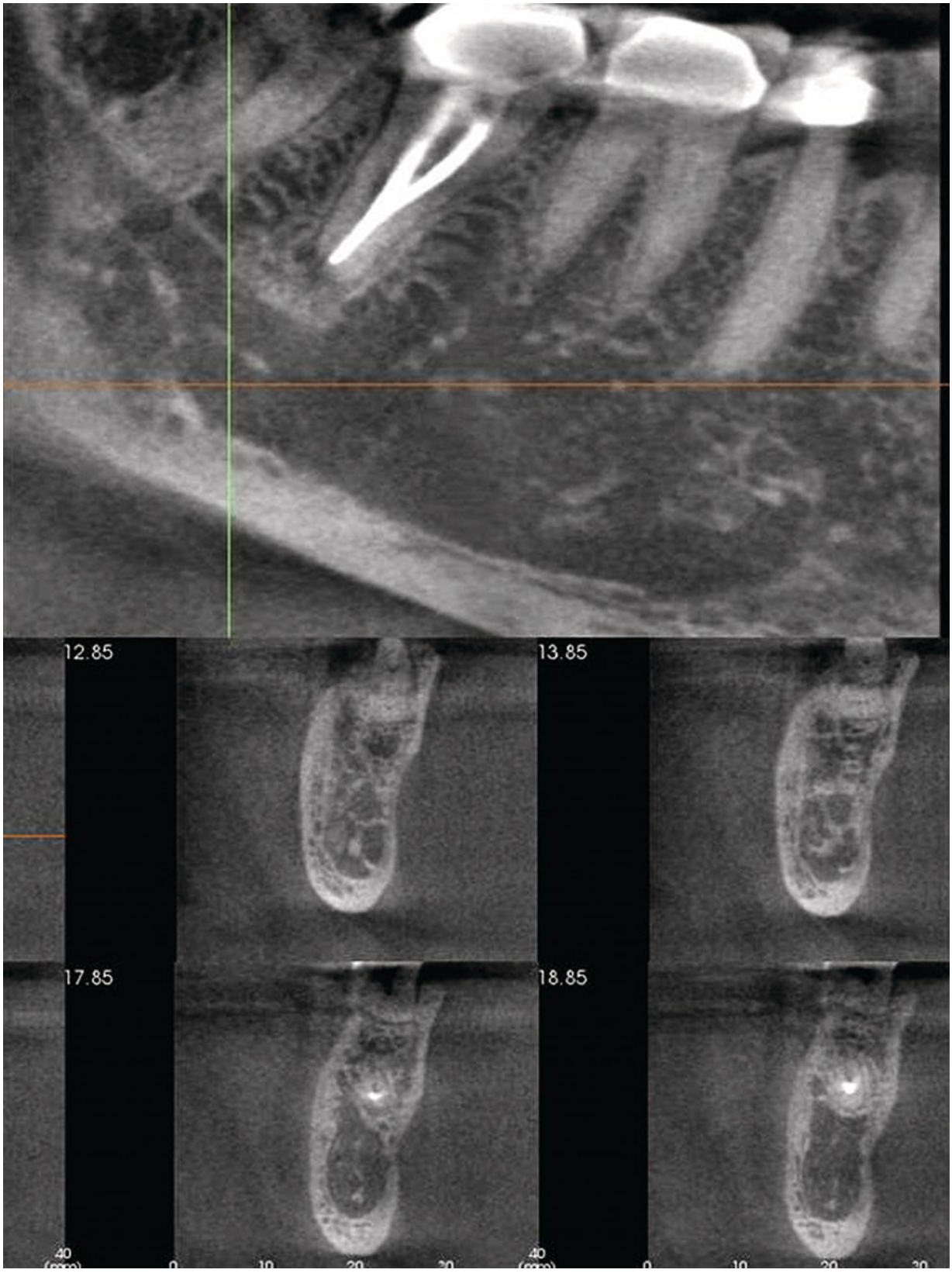
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Figure 5.4 Osteoporosis in a patient with hyperthyroidism.

Courtesy of Prof. Christos Angelopoulos.

Parathyroid gland disorders

The endocrine system is responsible for many physiological activities and maintaining homeostasis. Parathyroid hormone (PTH) is one of the most important hormones. It has a key role in calcium and phosphorus metabolism and hence has a great influence on bone and teeth mineralization (Žofková, 2016). Any disturbance of the parathyroid gland may cause either hyperproduction or hyposecretion of PTH. These two conditions distinguish oral and extraoral manifestations. The prevalence is 1 in 400 women and 1 in 1000 men and they usually affect middle-aged persons (Wu and Yeh, 2016).

Hyperparathyroidism

General characteristics

Hyperparathyroidism (HPT) is characterized by oversecretion of PTH. It will result in hypercalcemia due to increased mobilization of calcium from bone to body fluids. HPT is categorized into the following types:

- Primary HPT, caused by parathyroid adenoma, gland hyperplasia, or carcinoma.
- Secondary HPT, which is the result of another medical condition producing hypocalcemia, such as rickets, osteomalacia, vitamin D deficiency, intestinal malabsorption syndrome, chronic renal insufficiency, or long-term dialysis.
- Tertiary HPT, which arises from prolonged secondary HPT.
- A fourth type of HPT, because of an ectopic parathyroid gland, which occurs in patients with malignant diseases and adenomas.

Clinically, HPT shows great variation in signs and symptoms. Peptic ulcers, easy fatigue, a sense of weakness, depression, anxiety, and

myocardial, valvular, and vascular calcification and neuropathy may be present (Ibrahem, 2020; Palla et al., 2018).

Craniofacial and oral manifestations

In HPT, changes in bone metabolism form localized bone cystic lesions known as “brown tumors” (Nair et al., 2011; dos Santos et al., 2018). Radiographically these appear as osteolytic radiolucent lesions (Figure 5.5). In the maxillofacial region most lesions affect the mandible, while fewer cases have been reported in the maxilla (Palla et al., 2018). In cases of multiple brown tumors, a differential diagnosis may be necessary (Ibrahem, 2020). Other oral findings include facial asymmetry or swelling, pulp stones, alterations in dental eruption and tooth position, malocclusions, periodontal ligament widening, delay in dental development, expansion of cortical bone, root resorption, displacement of roots, calcification of the soft tissue, dental caries, and oral, dental or bone pain (Kakade et al., 2015; Palla et al., 2018).

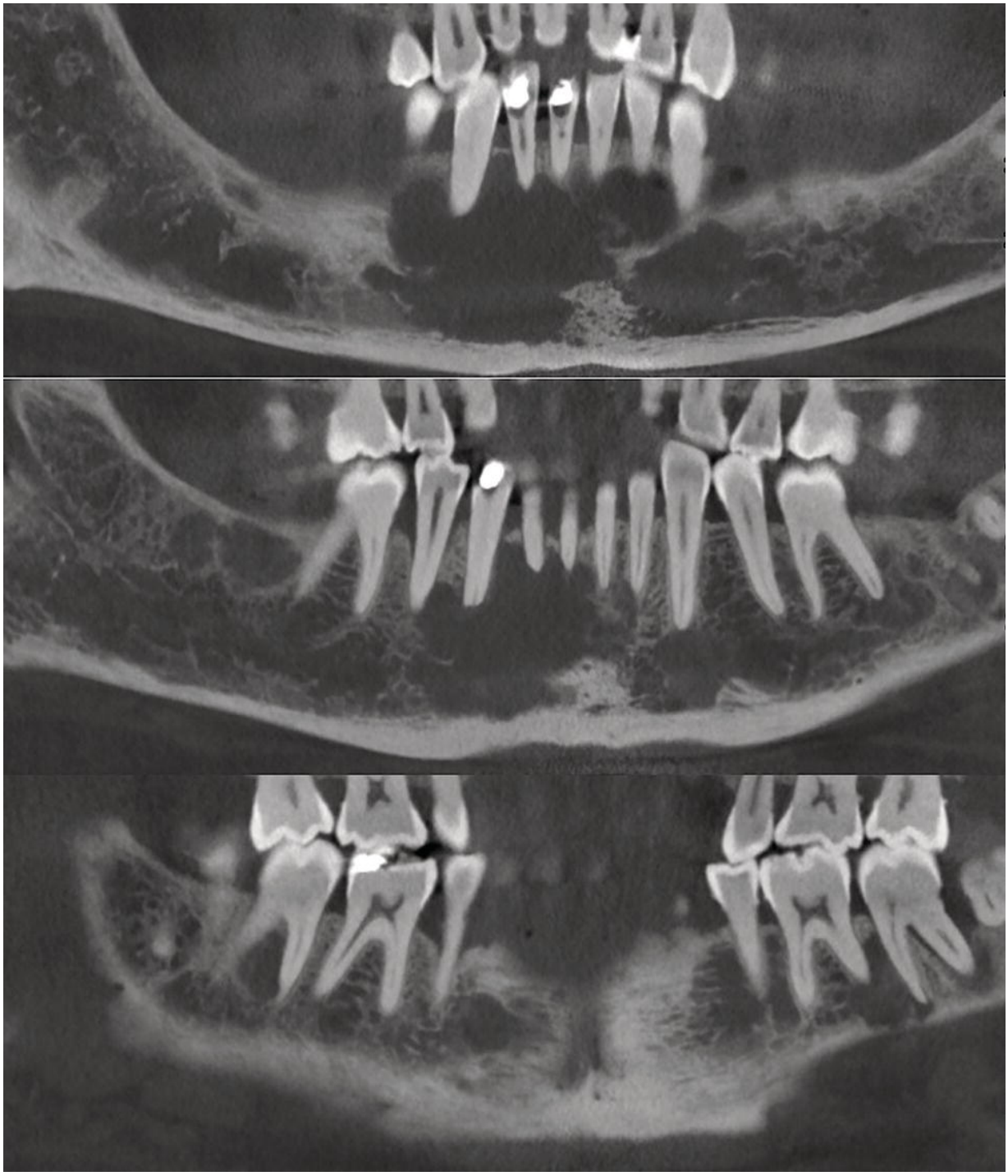

Figure 5.5 Cone beam computed tomographic slices presenting brown tumors in the mandible due to hyperparathyroidism.

Courtesy of Prof. Christos Angelopoulos.

Orthodontic considerations

The clinical management of these patients requires special attention. Management of brown tumors is often directed toward the normalization of PTH levels through management of the underlying cause of HPT. A surgical approach may be necessary in some cases. There is a higher risk of bone fracture, so precautions must be taken in surgical interventions. The increased incidence of spontaneous root resorption in such patients may complicate orthodontic tooth movement. Before providing endodontic treatment, differential diagnosis is important as, in some cases, these lesions appear as a radiolucency in the periapical region of teeth and can lead to misdiagnosis of a lesion of pulpal origin (Venkatesh and Nandini, 2009). During the management of this disease and before the start of the orthodontic intervention, a multidisciplinary team approach will be helpful.

Hypoparathyroidism

General characteristics

Hypoparathyroidism (hypoPT) is a systemic condition where the levels of PTH in the body fluids are significantly decreased, and low levels of plasma calcium and high levels of phosphate are also detected. The etiology may be of genetic or autoimmune origin or other causes.

Craniofacial and oral manifestations

Craniofacial abnormalities may be present when hypoPT coexists with other medical pathologies. In a systematic review aimed at examining dental disturbances in hypoPT, the prevalent findings were dental tissue alterations, such as enamel hypoplasia, enamel opacities, hypodontia, and eruption disturbances, especially delayed tooth eruption (Hejlesen et al., 2018).

Orthodontic considerations

As already mentioned, the dental alterations due to hypoPT may be identified as defects of mineralization, short and blunted roots, delayed eruptions, and clinically missing or impacted teeth. Patients

with multiple impacted permanent teeth and retained primary teeth have been reported (Reddy et al., 2018). The orthodontist should have knowledge of these systemic conditions to schedule treatment planning. For example, the identification of short dental roots on panoramic radiographs may be misleading for the orthodontist in terms of diagnosis of the etiology (Gallacher et al., 2018).

Primary adrenal insufficiency

General characteristics

Primary adrenal insufficiency (PAI) is caused by failure of the adrenal cortex to produce glucocorticoids. PAI most commonly arises from autoimmune adrenalitis, causing Addison disease (AD) and congenital adrenal hyperplasia (CAH) (Bancos et al., 2015).

Without proper pharmacological cover and additional steroid replacement, the patient may suffer a shock known as Addisonian, or adrenal, crisis. Symptoms of Addisonian crisis include weakness, hypotension, confusion, headache, nausea, and others (Addison's Self-help Group, www.addisonsdisease.org.uk).

Oral manifestations

Hyperpigmented spots can be found diffusely on the tongue, gingiva, buccal mucosa, and hard palate. However, numerous other conditions may be considered in the differential diagnosis (i.e. ethnic pigmentation, tobacco-related pigmentation, medication-related pigmentation, neurofibromatosis 1, McCune-Albright syndrome (MAS), Peutz-Jeghers syndrome, acromegaly, hyperthyroidism, or malignant lesions (Strakosch and Gordon, 1978; Sreeja et al., 2015).

Orthodontic considerations

Patients with PAI must take life-long corticosteroid replacement therapy. The daily dose of medication and monitoring of corticosteroid levels are regulated by the endocrinologist. Patients with PAI may require their usual glucocorticoid dose to be increased or supplemented at times of stress.

Dental procedures can be divided into three categories depending on the associated emotional and physical stress:

- Minor dental procedure, e.g. scale and polish, replacement of a filling, root canal treatment.
- Minor oral surgery, e.g. tooth extraction.
- Major dental surgical procedure, e.g. multiple tooth extraction.

Treatment steps include discussion on steroid cover and dose with the patient in advance, morning dental sessions (Miller et al., 2001), having available an Addison emergency hydrocortisone injection kit, relaxed and stress-free procedures, contact with the endocrinologist prior to treatment, and increase in dose or double dose of hydrocortisone in stressful conditions, such as tooth extraction, ideally one hour before the intervention (Henderson, 2014). A systematic review of the literature suggests that the administration of corticosteroids in oral surgery significantly decreases edema and pain (Dan et al., 2010). However, in other systematic research examining available interventions aiming to prevent general adrenal crisis, no evidence on methods that are certain to control the crisis was found (Shepherd et al., 2022).

Fibrous dysplasia

General characteristics

Fibrous dysplasia (FD) is an uncommon skeletal disorder resulting in deformity, fractures, pain, and functional impairment (Boyce, 2019). FD may occur in one bone (monostotic) or multiple bones (polyostotic) and in isolation or in combination with skin and endocrine characteristics, known as the McCune-Albright syndrome (MAS) (Boyce and Collins, 2020). FD/MAS results from postzygotic activating mutations in the *GNAS* gene (Weinstein et al., 2004).

FD in the body skeleton often presents radiographic radiolucent lesions, which result in fractures, limpness, and/or pain. FD lesions typically manifest during the first few years of life and expand during childhood and adolescence (Hart et al., 2007). The diagnosis of FD is

based on a combination of clinical, radiographic, pathological, and molecular information.

Craniofacial and oral manifestations

In the craniofacial area the patient with FD may have facial asymmetry (Figure 5.6a–c). FD lesions will often cross suture lines and involve adjacent bones, such as the sphenoid, temporal, frontal, occipital, and parietal bones. The progressive expansion of craniofacial lesions, expansion of bones, and displacement of structures may lead rarely to neurological complications and functional deficits, including vision loss, malocclusion, and obstruction of the nasal and otic canals, resulting in impairments (Frisch et al., 2015). FD may appear sclerotic on craniofacial radiographs (Boyce, 2019). The maxillary sinuses may be obliterated if FD affects the maxillary bones, appearing as a radiopacity on panoramic radiograph (Burke et al., 2017).

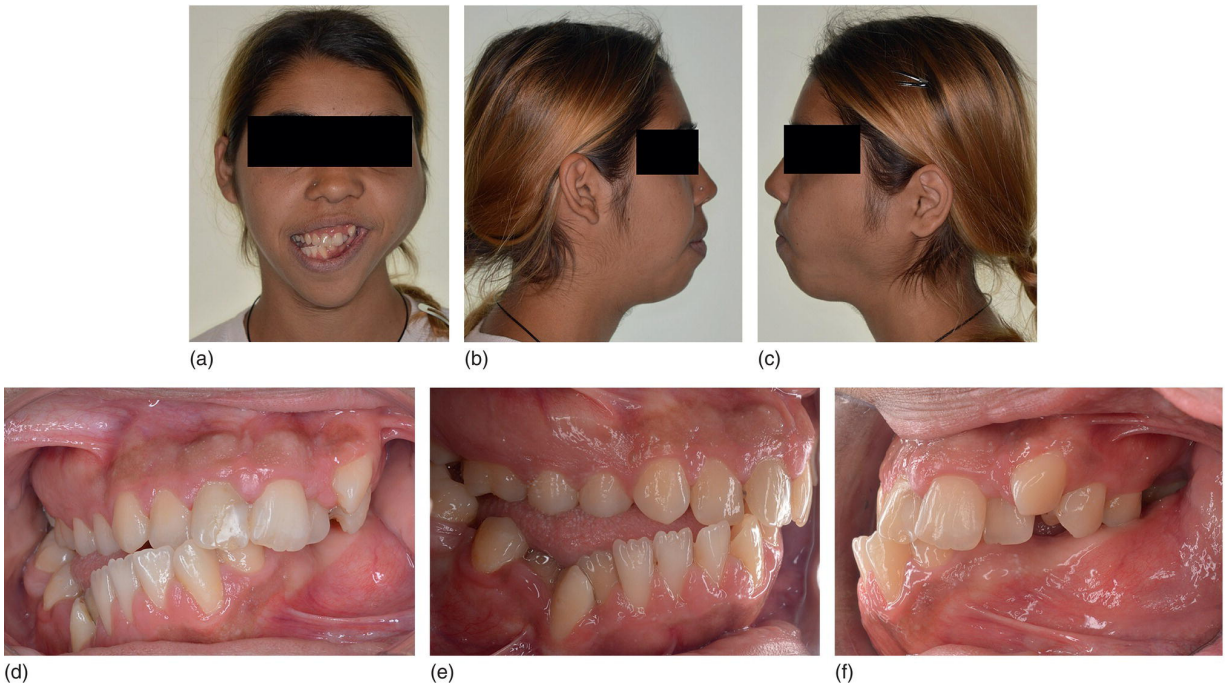

Figure 5.6 Patient with fibrous dysplasia presenting facial asymmetry and severe malocclusion: (a) extraoral frontal, (b) extraoral right, (c) extraoral left, (d) intraoral frontal, (e) intraoral right, and (f) intraoral left.

With permission from Dept. of Orthodontics, Aristotle University of Thessaloniki, Greece.

Teeth are pushed into malposition as the lesion advances and severe malocclusion is usually present (Burke et al., 2017; Figure 5.6d–f). Other described dental anomalies include dentin dysplasia, taurodontic pulp chambers, odontomas, and a high caries index (Akintoye et al., 2003). Finally, the metabolic dysfunction seen in MAS can have a potential effect on tooth development and the eruption sequence (Burke et al., 2017).

Orthodontic considerations

Craniofacial surgeries and orthodontic treatment should be planned by a team including oral and maxillofacial/craniofacial surgeons, plastic and reconstructive surgeons, otolaryngologists, neurosurgeons, pediatric dentists, orthodontists, speech therapists, and nursing specialists. The use of three-dimensional (3D) treatment

planning methods has helped to greatly improve outcomes in such complex patient populations.

Diabetes mellitus

General characteristics

Diabetes mellitus (DM) represents a group of metabolic diseases that are characterized by hyperglycemia due to a lack of insulin secretion, insulin resistance, or both. There are two types, type 1 and type 2 DM. Type 1 DM has its etiology in the inability of pancreatic beta-cells to produce insulin in response to glycemic input and is most common among children and young adults. Type 2 DM is caused by a combination of insulin resistance and inadequate insulin secretion from pancreatic beta-cells and usually occurs over the age of 40 years (Al-Maskari et al., 2011).

Oral manifestations

Oral complications include xerostomia, dental caries, root caries, periapical lesions, burning mouth syndrome, mucosal lesions (lichen planus or candida), altered taste, acetone breath, oral neuropathies, parotid enlargement, sialosis, and delayed wound healing (Patel et al., 2009; Al-Maskari et al., 2011; Mauri-Obradors et al., 2017; Almadih et al. 2018,). There is a strong correlation between diabetes and periodontal diseases. Patients with poorly controlled diabetes experience great periodontal attachment loss. A strong connection between periodontitis and type 2 DM is evident and treating these two diseases might help prevent each other's occurrence (Wu et al., 2020). The International Diabetes Federation recommends annual evaluation by a dental health specialist.

Orthodontic considerations

Orthodontic treatment is not a contraindication for patients with controlled DM (Patel et al., 2009). It is preferable to schedule appointments early in the morning. A periodontist should be involved, especially in adult patients, to control the periodontal status before and during orthodontic treatment. Orthodontists and

personnel should be trained to confront diabetic emergencies, such as hyper- or hypoglycemia (Patel et al., 2009; Alqahtani, 2019).

Orthodontics in patients with poorly controlled DM should be avoided as these patients are more likely to suffer from periodontal involvement (Almadih et al., 2018).

Diabetic-related microangiopathy can be expressed by toothache, tenderness to percussion, or potential loss of vitality (Bensch et al., 2003). In animal studies diabetic condition enhances osteoclast migration and activity, resulting in greater orthodontic tooth movement (Braga et al., 2011). For these reasons light orthodontic forces have been suggested for diabetic patients to avoid overloading of the teeth (Bensch et al., 2003; Patel et al., 2009). DM is also related to a greater incidence of peri-implantitis (Monje et al., 2017), which may have clinical importance in orthodontic treatment planning in patients with congenitally missing teeth. Close cooperation between the endocrinologist and the dentist/orthodontist is essential to optimizing the care of diabetic patients.

Sex-specific endocrine disorders

Male

General characteristics

Testosterone is an anabolic hormone produced by testicular Leydig cells and regulated by the hypothalamic–pituitary–gonadal axis. Testosterone regulates the maturation of muscles, bone, fat tissue, skin, and the male reproductive system. It is well established that testosterone concentration in men decreases with aging. Low testosterone levels have been associated with cardiovascular conditions, metabolic disease, reduced bone mineral density, and increased risk of fractures (Moran et al., 2015; Cittadini et al., 2022). The negative effects of testosterone deficiency in bone metabolism have been related to elevated proinflammatory cytokines and increased osteoclastic activity (Bellido et al., 1995; Kellesarian et al., 2017).

Craniofacial and oral manifestations

Animal studies on the long-term effects of orchidectomy and low testosterone on the craniofacial and dental development and maintenance of skeletal and oral health reported severe temporomandibular joint (TMJ) osteoarthritis, higher alveolar bone loss, and signs of severe periodontitis (Wang et al., 2016). Low testosterone serum levels and xerostomia associated with Sjögren syndrome have been described (Forsblad-d'Elia et al., 2009). However, the reported association between low testosterone levels in body fluids and the occurrence of chronic periodontitis (CP) is still questionable. A systematic review aimed to assess whether low testosterone levels in body fluids reflect CP. Within the limits of the evidence available, the relationship between low testosterone levels and CP remains debatable (Kellesarian et al., 2017).

Orthodontic considerations

Specific disturbance of sex hormones, if present, must be evaluated by the endocrinologist and dental specialist to construct an individualized treatment plan, depending on the clinical and hormonal characteristics of each patient.

Female

General characteristics

The most frequent endocrinological conditions in women include precocious puberty, pregnancy, menopause, and polycystic ovary syndrome (PCOS). Puberty in girls typically occurs between 8.5 and 13 years of age, when the activation of the hypothalamic–pituitary–gonadal axis starts, and the secondary sex characteristics develop. Precocious puberty (PP) is initiated with the appearance of physical and hormonal signs of pubertal development before the age of 8 years and in the long term has a high incidence of decreased body height due to premature epiphyseal fusion of the long bones. During pregnancy and menopause, hormonal and metabolic changes have a great impact on women's bone metabolism (Mukherjee and Almas, 2010). PCOS is one of the most frequently diagnosed endocrinopathies and its main symptoms are menstrual disorders,

hyperandrogenism, oligo/anovulation, and/or polycystic ovarian morphology, obesity, insulin resistance, and others (Sanchez-Garrido and Tena-Sempere, 2020).

Craniofacial and oral manifestations

Girls with PP exhibit earlier skeletal maturation, significant increases in posterior facial height, and a decrease in mandibular plane angle (Kang et al., 2020). There is a significantly higher prevalence of maxillary dental developmental abnormalities compared to the general population (Kim et al., 2020). Both maxillary teeth and the anterior pituitary gland, the latter of which secretes female hormones, are embryologically derived from the oral epithelium. Therefore, maxillary dental abnormalities may be embryologically associated with PP. A mesiodens has been found with a high prevalence in girls with PP and could be considered a strong predictor of the development of PP (Kim et al., 2020). In patients with idiopathic PP, dental age was significantly retarded compared to the chronological age, and skeletal age was significantly ahead of their chronological age (Roberts et al., 1985; Tabakcilar et al., 2021; Figure 5.7).

Increased estrogen levels during pregnancy are thought to promote gingivitis and susceptibility to periodontal disease is very common. Moreover, a positive association is evident between overweight/obesity and periodontitis (Foratori-Junior et al., 2022). Reports on the prevalence of TMD signs and symptoms in pregnant women are contradictory, with studies describing either higher or lower incidences of TMJ dysfunction during this period (Mayoral et al., 2013; Fichera et al., 2020).

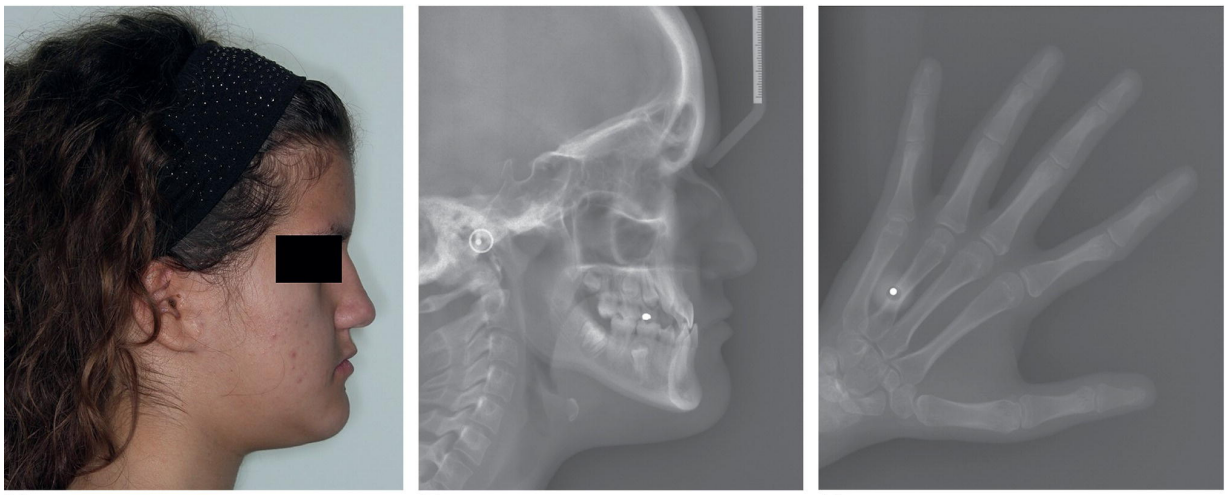

Figure 5.7 Female patient 9 years old with history of precocious puberty. (a) Extraoral lateral side showing hypoplastic maxilla. (b) Lateral cephalometric radiograph with characteristic craniofacial form according to the cephalometric analysis. (c) Hand–wrist radiograph showing completion of skeletal maturity.

With permission from Dept. of Orthodontics, Aristotle University of Thessaloniki, Greece.

During the menopause, low levels of estrogen predispose the TMJ to degeneration and increase alveolar bone loss, causing postmenopausal osteoporosis. Additionally, the salivary pH and flow rate in postmenopausal women showed a decrease, which in turn was related to periodontal problems and caries (Mishra et al., 2021).

Orthodontic considerations

In girls with PP, skeletal maturation ceases at an early stage and it is recommended that hand–wrist radiography and lateral cephalogram analysis should be performed for the prediction of growth (Kang et al., 2020), especially when skeletal problems are present and an orthodontic/orthopedic approach is needed. A systematic analysis of animal studies focusing on the metabolic changes occurring during pregnancy and lactation confirmed their impact on the rate of tooth movement (Omar and Kaklamanos, 2020). In animal studies, hormonal changes during the estrus cycle may also affect the rate of orthodontic tooth movement (Almidfa et al., 2021). When premenopausal and postmenopausal women received orthodontic

treatment the gingival crevicular fluid biomarkers showed no difference in their response to orthodontic activation (Smuthkochorn et al., 2017). Nonetheless, in animal studies ovariectomized animals had decreased orthodontic tooth movement. All these experimental outcomes and clinical signs and symptoms that may occur in various hormonal conditions in women must be taken into consideration.

Exogenous hormone administration

Several pharmaceutical intakes under systemic administration may be critical factors in the growth and structure of body tissues and organs. The interaction between altered bone metabolic conditions and orthodontic mechanical load at the histological level has been demonstrated. Various pharmaceutical substances could not only have an effect on general and dental health, but may also interfere with orthodontic treatment. This is reflected at a clinical level by a differentiated tooth movement rate according to the patient's metabolic state.

Evidence of the effect of medication in orthodontics is currently available mostly from animal studies. For example, the administration of TH and prostaglandin E2 seems to have a synergistic effect by decreasing root resorption and increasing the rate of orthodontic tooth movement in rats (Seifi et al., 2015).

Exogenous input of female sex hormones may decrease the rate of tooth movement in the long term and decrease orthodontically induced root resorption in animals (Kaklamanos et al., 2021a). In systematic reviews of animal studies, commonly prescribed medications showed variable effects on the rate of orthodontic tooth movement (Makrygiannakis et al., 2018) and the rate of orthodontic relapse during the retention period (Kaklamanos et al., 2021b).

The effect of growth hormone replacement therapy, as analyzed earlier, has a positive impact on the craniofacial complex and the dentition and has a synergistic role during orthodontic treatment.

Except for these factors, a great number of exogenously administered medications depending on the specific medical background of the patient may play a vital role in growth, metabolism, dentition, and orthodontic tooth movement and relapse (Krishnan et al., 2021). The

orthodontist should have basic knowledge of the underlying medical condition and of the replacement therapies, and understand the potential clinical implications and adverse effects that may occur.

Conclusions

The existence of endocrinological pathologies can influence the orthodontic treatment plan, since several craniofacial and oral disturbances may appear. Understanding the basic mechanisms underlying clinical manifestations of endocrinopathies is beneficial for the patient and offers an important advantage to the practitioner, who will be able to recognize these conditions. If a disorder of endocrinological etiology is suspected by the dental professional, seeking the advice of an endocrinologist is crucial for the ultimate diagnosis and treatment effectiveness. Enhancing and maintaining collaboration with the endocrinologist throughout the orthodontic diagnosis, treatment planning, treatment progress, and retention period ensures a good long-term result.

References

Adeel, K., Hafiz, M., and Mubassar, F. (2020). The implications of endocrinology in orthodontics – literature review. *Balkan Journal of Dental Medicine* 24: 8-13. doi: 10.2478/bjdm-2020-0002.

Akintoye, S.O., Lee, J.S., Feimster, T. et al. (2003). Dental characteristics of fibrous dysplasia and McCune-Albright syndrome. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics* 96(3): 275–282. doi: 10.1016/s1079-2104(03)00225-7.

Almadih, A., Al-Zayer, M., Dabel, S. et al. (2018). Orthodontic treatment consideration in diabetic patients. *Journal of Clinical Medicine Research* 10(2): 77–81. doi: 10.14740/jocmr3285w.

Al-Maskari, A.Y., Al-Maskari, M.Y., and Al-Sudairy, S. (2011). Oral manifestations and complications of diabetes mellitus: A review. *Sultan Qaboos University Medical Journal* 11(2): 179–186.

Almidfa, N., Athanasiou, A.E., Makrygiannakis, M.A. et al. (2021). Does the rate of orthodontic tooth movement change during the estrus cycle? A systematic review based on animal studies. *BMC Oral Health* 21(1): 526. doi: 10.1186/s12903-021-01875-8.

Alqahtani, H. (2019). Medically compromised patients in orthodontic practice: Review of evidence and recommendations. *International Orthodontics* 17(4): 776–788. doi: 10.1016/j.ortho.2019.08.015.

Arid, J., Oliveira, D.B., Evangelista, S.S. et al. (2019). Oestrogen receptor alpha, growth hormone receptor, and developmental defect of enamel. *International Journal of Paediatric Dentistry* 29(1): 29–35. doi: 10.1111/ipd.12434.

Bancos, I., Hahner, S., Tomlinson, J. et al. (2015). Diagnosis and management of adrenal insufficiency. *Lancet Diabetes and Endocrinology* 3(3): 216–226. doi: 10.1016/S2213-8587(14)70142-1.

Bedi, R., and Brook, A.H. (1984). Changes in general, craniofacial and dental development in juvenile hypothyroidism. *British Dental Journal* 157(2): 58–60. doi: 10.1038/sj.bdj.4805418.

Bellido, T., Jilka, R.L., Boyce, B.F. et al. (1995). Regulation of interleukin-6, osteoclastogenesis, and bone mass by androgens. The role of the androgen receptor. *Journal of Clinical Investigation* 95(6): 2886–2895.

Bello, M.O., and Garla, V.V. (2021). Gigantism and acromegaly. In: *StatPearls*. Treasure Island, FL: StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK538261.

Bensch, L., Braem, M., Van Acker, K. et al. (2003). Orthodontic treatment considerations in patients with diabetes mellitus. *American Journal of Orthodontics and Dentofacial Orthopedics* 123(1): 74–78. doi: 10.1067/mod.2003.53.

Bochukova, E., Schoenmakers, N., Agostini, M. et al. (2012). A mutation in the thyroid hormone receptor alpha gene. *New*

England Journal of Medicine 366(3): 243–249. doi: 10.1056/NEJMoa1110296.

Boyce, A.M. (2019). Fibrous dysplasia. In: K.R. Feingold, B. Anawalt, M.R. Blackman et al. (eds.). *Endotext*. South Dartmouth, MA: MDText.com. https://www.ncbi.nlm.nih.gov/books/NBK326740.

Boyce, A.M., and Collins, M.T. (2020). Fibrous dysplasia/McCune-Albright syndrome: A rare, mosaic disease of gαs activation. *Endocrine Reviews* 41(2): 345–370. doi: 10.1210/endrev/bnz011.

Braga, S.M., Taddei, S.R., Andrade, I., Jr., et al. (2011). Effect of diabetes on orthodontic tooth movement in a mouse model. *European Journal of Oral Sciences* 119(1): 7–14. doi: 10.1111/j.1600-0722.2010.00793.x.

Burke, A.B., Collins, M.T., and Boyce, A.M. (2017). Fibrous dysplasia of bone: Craniofacial and dental implications. *Oral Diseases* 23(6): 697–708. doi: 10.1111/odi.12563.

Cantu, G., Buschang, P.H., and Gonzalez, J.L. (1997). Differential growth and maturation in idiopathic growth-hormone-deficient children. *European Journal of Orthodontics* 19(2): 131–139. doi: 10.1093/ejo/19.2.131.

Chandna, S., and Bathla, M. (2011). Oral manifestations of thyroid disorders and its management. *Indian Journal of Endocrinology and Metabolism* 15(Suppl 2): S113–S116. doi: 10.4103/2230-8210.83343.

Cittadini, A., Isidori, A.M., and Salzano, A. (2022). Testosterone therapy and cardiovascular diseases. *Cardiovascular Research* 118(9): 2039–2057. doi: 10.1093/cvr/cvab241.

Dan, A.E., Thygesen, T.H., and Pinholt, E.M. (2010). Corticosteroid administration in oral and orthognathic surgery: A systematic review of the literature and meta-analysis. *Journal of Oral and Maxillofacial Surgery* 68(9): 2207–2220. doi: 10.1016/j.joms.2010.04.019.

Davidopoulou, S., and Chatzigianni, A. (2017). Craniofacial morphology and dental maturity in children with reduced somatic growth of different aetiology and the effect of growth hormone treatment. *Progress in Orthodontics* 18(1): 10. doi: 10.1186/s40510-017-0164-2.

dos Santos, B., Koth, V.S., Figueiredo, M.A. et al. (2018). Brown tumor of the jaws as a manifestation of tertiary hyperparathyroidism: A literature review and case report. *Special Care in Dentistry* 38(3): 163–171. doi: 10.1111/scd.12284.

Dudhia, S.B., and Dudhia, B.B. (2014). Undetected hypothyroidism: A rare dental diagnosis. *Journal of Oral and Maxillofacial Pathology* 18(2): 315–319. doi: 10.4103/0973-029X.140922.

Fariduddin, M.M., and Bansal, N. (2021). Hypothyroid myopathy. In: *StatPearls*. Treasure Island, FL: StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK519513.

Ferrazzo, K.L., Payeras, M.R., Ferrazzo, V.A. et al. (2014). Craniofacial and dental manifestations of triple X syndrome associated with congenital hypothyroidism: A case report. *Special Care in Dentistry* 34(3): 156–159. doi: 10.1111/scd.12050.

Fichera, G., Polizzi, A., Scapellato, S. et al. (2020). Craniomandibular disorders in pregnant women: An epidemiological survey. *Journal of Functional Morphology and Kinesiology* 5(2): 36. doi: 10.3390/jfmk5020036.

Foratori-Junior, G.A., Pereira, P.R., Gasparoto, I.A. et al. (2022). Is overweight associated with periodontitis in pregnant women? Systematic review and meta-analysis. *Japanese Dental Science Review* 58: 41–51. doi: 10.1016/j.jdsr.2022.01.001.

Forsblad-d'Elia, H., Carlsten, H., Labrie, F. et al. (2009). Low serum levels of sex steroids are associated with disease characteristics in primary Sjogren's syndrome; supplementation with dehydroepiandrosterone restores the concentrations. *Journal of Clinical Endocrinology & Metabolism* 94(6): 2044–2051.

Frisch, C.D., Carlson, M.L., Kahue, C.N. et al. (2015). Fibrous dysplasia of the temporal bone: A review of 66 cases. *Laryngoscope* 125(6): 1438–1443. doi: 10.1002/lary.25078.

Gallacher, A.A., Pemberton, M.N., and Waring, D.T. (2018). The dental manifestations and orthodontic implications of hypoparathyroidism in childhood. *Journal of Orthodontics* 45(1): 46–50. doi: 10.1080/14653125.2017.1406685.

Garmendia Madariaga, A., Santos Palacios, S., Guillén-Grima, F. et al. (2014). The incidence and prevalence of thyroid dysfunction in Europe: A meta-analysis. *Journal of Clinical Endocrinology and Metabolism* 99(3): 923–931. doi: 10.1210/jc.2013-2409.

Gecgelen Cesur, M., Cesur, G., Ogrenim, M. et al. (2016). Do prenatal and postnatal hypothyroidism affect the craniofacial structure? *An experimental study. Angle Orthodontist* 86(5): 854–861. doi: 10.2319/080315-521.1.

Grozdinska, A., Hofmann, E., Schmid, M. et al. (2018). Prevalence of temporomandibular disorders in patients with Hashimoto thyroiditis. *Journal of Orofacial Orthopedics* 79(4): 277–288. doi: 10.1007/s00056-018-0140-6.

Guo, X., Meng, T., Huang, J. et al. (2018). 3D facial analysis in acromegaly: Gender-specific features and clinical correlations. *Frontiers in Endocrinology* 9: 722. doi: 10.3389/fendo.2018.00722.

Gupta, R., Goel, K., Solanki, J. et al. (2014). Oral manifestations of hypothyroidism: A case report. *Journal of Clinical and Diagnostic Research* 8(5): ZD20–ZD22. doi: 10.7860/JCDR/2014/8905.4379.

Hamilton, J., Blaser, S., and Daneman, D. (1998). MR imaging in idiopathic growth hormone deficiency. *American Journal of Neuroradiology* 19(9): 1609–1615.

Hart, E.S., Kelly, M.H., Brillante, B. et al. (2007). Onset, progression, and plateau of skeletal lesions in fibrous dysplasia and the

relationship to functional outcome. *Journal of Bone and Mineral Research* 22(9): 1468–1474. doi: 10.1359/jbmr.070511.

Hejlesen, J., Underbjerg, L., Gjørup, H. et al. (2018). Dental findings in patients with non-surgical hypoparathyroidism and pseudohypoparathyroidism: A systematic review. *Frontiers in Physiology* 9: 701. doi: 10.3389/fphys.2018.00701.

Henderson, S. (2014). What steroid supplementation is required for a patient with primary adrenal insufficiency undergoing a dental procedure? *Dental Update* 41(4): 342–344. doi: 10.12968/denu.2014.41.4.342.

Ibrahem, H.M. (2020). Gnathic bones and hyperparathyroidism: A review on the metabolic bony changes affecting the mandible and maxilla in case of hyperparathyroidism. *Advances in Medicine* 2020: 6836123. doi: 10.1155/2020/6836123.

Kakade, S.P., Gogri, A.A., Umarji, H.R. et al. (2015). Oral manifestations of secondary hyperparathyroidism: A case report. *Contemporary Clinical Dentistry* 6(4): 552–558. doi: 10.4103/0976-237X.169840.

Kaklamanos, E.G., Makrygiannakis, M.A., and Athanasiou, A.E. (2021a). Does exogenous female sex hormone administration affect the rate of tooth movement and root resorption? A systematic review of animal studies. *PloS One* 16(9): e0257778. doi: 10.1371/journal.pone.0257778.

Kaklamanos, E.G., Makrygiannakis, M.A., and Athanasiou, A.E. (2021b). Could medications and biologic factors affect post-orthodontic tooth movement changes? A systematic review of animal studies. *Orthodontics & Craniofacial Research* 24(1): 39–51. doi: 10.1111/ocr.12411.

Kamal, A.T., Mahmood, H.T., and Fida, M. (2020). The Implications of endocrinology in orthodontics—literature review. *Balkan Journal of Dental Medicine* 24(1): 8–13.

Kang, S.T., Choi, S.H., Kim, K.H. et al. (2020). Evaluation of cephalometric characteristics and skeletal maturation of the

cervical vertebrae and hand-wrist in girls with central precocious puberty. *Korean Journal of Orthodontics* 50(3): 181–187. doi: 10.4041/kjod.2020.50.3.181.

Kellesarian, S.V., Malmstrom, H., Abduljabbar, T. et al. (2017). Low testosterone levels in body fluids are associated with chronic periodontitis. *American Journal of Men's Health* 11(2): 443–453. doi: 10.1177/1557988316667692.

Kim, Y., Lee, N.K., Kim, J.H. et al. (2020). Association of maxillary dental developmental abnormality with precocious puberty: A case-control study. *Maxillofacial Plastic and Reconstructive Surgery* 42(1): 30. doi: 10.1186/s40902-020-00274-3.

Krishnan, V., Zahrowski, J,J., and Davidovitch, Z. (2021) The effect of drugs, hormones, and diet on orthodontic tooth movement. In: V. Krishnan, A.M. Kuijpers-Jagtman, and Z. Davidovitch (eds.), *Biological Mechanisms of Tooth Movement*, 3rd ed. Hoboken, NJ: Wiley Blackwell, pp. 199–215.

Makrygiannakis, M.A., Kaklamanos, E.G., and Athanasiou, A.E. (2018). Does common prescription medication affect the rate of orthodontic tooth movement? A systematic review. *European Journal of Orthodontics* 40(6): 649–659. doi: 10.1093/ejo/cjy001.

Mauri-Obradors, E., Estrugo-Devesa, A., Jané-Salas, E. et al. (2017). Oral manifestations of diabetes mellitus. A systematic review. *Medicina Oral, Patologia Oral y Cirugia Bucal* 22(5): e586–e594. doi: 10.4317/medoral.21655.

Mayoral, V.A., Espinosa, I.A., and Montiel, A.J. (2013). Association between signs and symptoms of temporomandibular disorders and pregnancy (case control study). *Acta Odontologica Latinoamericana* 26(1): 3–7.

Miller, C.S., Little, J.W., and Falace, D. A. (2001). Supplemental corticosteroids for dental patients with adrenal insufficiency: Reconsideration of the problem. *Journal of the American Dental Association* 132(11): 1570–1597. doi: 10.14219/jada.archive.2001.0092.

Mishra, R., Haider, K., Rizwan, R. et al. (2021). Assessment of effect of menopause on saliva and oral health status. *Journal of Pharmacy & Bioallied Sciences* 13(Suppl 2): S1535–S1537. doi: 10.4103/jpbs.jpbs_276_21.

Monje, A., Catena, A., and Borgnakke, W.S. (2017). Association between diabetes mellitus/hyperglycaemia and peri-implant diseases: Systematic review and meta-analysis. *Journal of Clinical Periodontology* 44(6): 636–648. doi: 10.1111/jcpe.12724.

Moran, J.M., Martin, R.R., Pedrera-Canal, M. et al. (2015). Low testosterone levels are associated with poor peripheral bone mineral density and quantitative bone ultrasound at phalanges and calcaneus in healthy elderly men. *Biological Research for Nursing* 17(2): 169–174. doi: 10.1177/1099800414532710.

Mukherjee, P.M., and Almas, K. (2010). Orthodontic considerations for gingival health during pregnancy: A review. *International Journal of Dental Hygiene* 8(1): 3–9. doi: 10.1111/j.1601-5037.2009.00383.x.

Nair, P.P., Gharote, H.P., Thomas, S. et al. (2011). Brown tumour of the jaw. *BMJ Case Reports* 2011: bcr0720114465. doi: 10.1136/bcr.07.2011.4465.

Oliveira-Neto, L.A., Melo, M., Franco, A.A. et al. (2011). Cephalometric features in isolated growth hormone deficiency. *Angle Orthodontist* 81(4): 578–583. doi: 10.2319/102210-618.1.

Omar, M., and Kaklamanos, E.G. (2020). Does the rate of orthodontic tooth movement change during pregnancy and lactation? A systematic review of the evidence from animal studies. *BMC Oral Health* 20(1): 237. doi: 10.1186/s12903-020-01223-2.

Palla, B., Burian, E., Fliefel, R et al. (2018). Systematic review of oral manifestations related to hyperparathyroidism. *Clinical Oral Investigations* 22(1): 1–27. doi: 10.1007/s00784-017-2124-0.

Partyka, M., Chałas, R., Dunin-Wilczyńska, I. et al. (2018). Influence of growth hormone therapy on selected dental and skeletal system

parameters. *Annals of Agricultural and Environmental Medicine* 25(1): 60–65. doi: 10.5604/12321966.1233573.

Patel, A., Burden, D.J., and Sandler, J. (2009). Medical disorders and orthodontics. *Journal of Orthodontics* 36(Suppl), 1–21. doi: 10.1179/14653120723346.

Pinto, A., and Glick, M. (2002). Management of patients with thyroid disease: Oral health considerations. *Journal of the American Dental Association* 133(7): 849–858. doi: 10.14219/jada.archive.2002.0299.

Pirinen, S., Majurin, A., Lenko, H.L. et al. (1994). Craniofacial features in patients with deficient and excessive growth hormone. *Journal of Craniofacial Genetics and Developmental Biology* 14(3): 144–152.

Poole, A.E., Greene, I.M., and Buschang, P.H. (1982). The effect of growth hormone therapy on longitudinal growth of the oral facial structures in children. *Progress in Clinical and Biological Research* 101: 499–516.

Poumpros, E., Loberg, E., and Engström, C. (1994). Thyroid function and root resorption. *Angle Orthodontist* 64(5): 389–394. doi: 10.1043/0003-3219(1994)064<0389:TFARR>2.0.CO;2.

Preda, S.A., Albulescu, D.M., Mitroi, M.R. et al. (2019). Craniofacial morphology aspects in children with isolated growth hormone deficiency – a cephalometric study. *Romanian Journal of Morphology and Embryology/Revue roumaine de morphologie et embryologie* 60(2): 653–658.

Reddy, G.S., Chalapathi, K.V., Reddy, D.S. et al. (2018). Multiple impacted permanent teeth, an indicator for early detection of hypoparathyroidism: A rare case report. *Journal of Family Medicine and Primary Care* 7(5): 1096–1099. doi: 10.4103/jfmpc.jfmpc_352_1.

Roberts, M.W., Li, S.H., Comite, F. et al. (1985). Dental development in precocious puberty. *Journal of Dental Research* 64(8): 1084–1086. doi: 10.1177/00220345850640081301.

Salas-Flores, R., González-Pérez, B., Barajas-Campos, R.L. et al. (2010). Changes on craniofacial structures in children with growth-hormone-deficiency. *Revista medica del Instituto Mexicano del Seguro Social* 48(6): 591–595.

Sanchez-Garrido, M.A., and Tena-Sempere, M. (2020). Metabolic dysfunction in polycystic ovary syndrome: Pathogenic role of androgen excess and potential therapeutic strategies. *Molecular Metabolism* 35: 100937. doi: 10.1016/j.molmet.2020.01.001.

Seifi, M., Hamedi, R., and Khavandegar, Z. (2015). The effect of thyroid hormone, prostaglandin E2, and calcium gluconate on orthodontic tooth movement and root resorption in rats. *Journal of Dentistry (Shiraz, Iran)* 16(1 Suppl): 35–42.

Shepherd, L.M., Schmidtke, K.A., Hazlehurst, J.M. et al. (2022). Interventions for the prevention of adrenal crisis in adults with primary adrenal insufficiency: A systematic review. *European Journal of Endocrinology* 187(1): S1–S20. doi: 10.1530/EJE-21-1248.

Smuthkochorn, S., Palomo, J.M., Hans, M.G. et al. (2017). Gingival crevicular fluid bone turnover biomarkers: How postmenopausal women respond to orthodontic activation. *American Journal of Orthodontics and Dentofacial Orthopedics* 152(1): 33–37. doi: 10.1016/j.ajodo.2016.11.027.

Sreeja, C., Ramakrishnan, K., Vijayalakshmi, D. et al. (2015). Oral pigmentation: A review. *Journal of Pharmacy & Bioallied Sciences 7*(Suppl 2): S403–S408. doi: 10.4103/0975-7406.163471.

Strakosch, C.R., and Gordon, R.D. (1978). Early diagnosis of Addison's disease; pigmentation as sole symptom. *Australian and New Zealand Journal of Medicine* 8(2): 189–190. doi: 10.1111/j.1445-5994.1978.tb04510.x.

Tabakcilar, D., Bundak, R., and Gencay, K. (2021). Dental age in precocious and delayed puberty periods. *European Journal of Dentistry* 15(3): 539–545. doi: 10.1055/s-0041-1726156.

Torlińska-Walkowiak, N., Majewska, K.A., Kędzia, A. et al. (2021). Clinical implications of growth hormone deficiency for oral health in children: A systematic review. *Journal of Clinical Medicine* 10(16): 3733. doi: 10.3390/jcm10163733.

van Erum, R., Mulier, G., Carels, C. et al. (1998). Craniofacial growth and dental maturation in short children born small for gestational age: Effect of growth hormone treatment. Own observations and review of the literature. *Hormone Research* 50(3): 141–146. doi: 10.1159/000023262.

Venkatesh, K.V., and Nandini, V.V. (2009). Periapical radiolucency not requiring endodontic therapy: An unusual case. *Indian Journal of Dental Research* 20(1): 126–128. doi: 10.4103/0970-9290.49057.

Verna, C., and Melsen, B. (2003). Tissue reaction to orthodontic tooth movement in different bone turnover conditions. *Orthodontics & Craniofacial Research* 6(3): 155–163.

Vucic, S., Korevaar, T., Dhamo, B. et al. (2017). Thyroid function during early life and dental development. *Journal of Dental Research* 96(9): 1020–1026. doi: 10.1177/0022034517708551.

Wang, Q., Kessler, M.J., Kensler, T.B. et al. (2016). The mandibles of castrated male rhesus macaques (Macaca mulatta): The effects of orchidectomy on bone and teeth. *American Journal of Physical Anthropology* 159(1): 31–51. doi: 10.1002/ajpa.22833.

Weinstein, L.S., Liu, J., Sakamoto, A. et al. (2004). Minireview: GNAS: Normal and abnormal functions. *Endocrinology* 145(12): 5459–5464. doi: 10.1210/en.2004-0865.

Williams, G.R., and Bassett, J. (2018). Thyroid diseases and bone health. *Journal of Endocrinological Investigation* 41(1): 99–109. doi: 10.1007/s40618-017-0753-4.

Wu, C.Z., Yuan, Y.H., Liu, H.H. et al. (2020). Epidemiologic relationship between periodontitis and type 2 diabetes mellitus. *BMC Oral Health* 20(1): 204. doi: 10.1186/s12903-020-01180-w.

Wu, J.X., and Yeh, M.W. (2016). Asymptomatic primary hyperparathyroidism: Diagnostic pitfalls and surgical intervention. *Surgical Oncology Clinics of North America* 25(1): 77–90. doi: 10.1016/j.soc.2015.08.004.

Žofková, I. (2016). Hypercalcemia. Pathophysiological aspects. *Physiological Research* 65(1): 1–10. doi: 10.33549/physiolres.933059.

6
Nutrition in Orthodontic Practice

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Summary

Maintenance of good oral health and optimal orthodontic outcomes greatly depend on adequate nutrition. The nutritional status influences the development of the oral cavity and its structures. Both deficiencies and toxicities may cause malformations and other oral diseases. After tooth eruption, nutritional factors influence the teeth topically and significantly affect the prevention and development of dental caries. Good nutrition can maximize, while poor nutrition can undermine, the appropriate biological response of the periodontal ligament and alveolar bone to orthodontic forces. This chapter reviews the relevance of nutrition to orthodontic care and how the orthodontist can assist in facilitating good nutrition for good oral health. It will provide practical advice for delivering patient education designed to promote positive dietary behavior change. This includes simple, quick, and routine diet risk assessment tools used during an orthodontist's office visit. This chapter will also provide advice on assessing nutritional risk, and provide simple dietary recommendations and guidance for patients. Furthermore, it discusses when to refer patients to specialists such as registered dietitians, if a more complex nutritional issue or disease is uncovered. The key to effective diet education in the orthodontic office is a logical, ordered approach, which includes patient education, data collection, evaluation, proper diagnosis, providing nutrition guidance, follow-up, re-evaluation, and a personalized care plan. A basic understanding of nutrition as well as good guidance and communication skills will help orthodontic practitioners to improve their orthodontic outcomes in addition to helping improve the quality of care of their patients.

The importance of diet and nutrition in oral health

Nutrition, oral health, and general health are bidirectionally linked to one another. In the 2021 report on *Oral Health in America*, the Surgeon General of the United States emphasized the need for "all healthcare providers to play an active role in promoting healthy lifestyles by incorporating nutrition counseling into their practices" (Stanski and

Palmer, 2015; Satcher and Nottingham, 2017; National Institutes of Health, 2021). A recent report on oral health in America emphasized the importance of oral health for disease prevention (National Institute of Health, 2021). Other major organizations such as the American Dental Association, American Dental Hygienists Association, and Academy of Pediatric Dentistry have followed this and issued nutrition guidelines for dental practice. The Academy of Nutrition and Dietetics has issued a position statement supporting the importance of nutrition and diet in oral health. Furthermore, the American Dental Education Association (ADEA), a prominent organization in dental education, recently issued a report recommending that dental students exhibit the ability to provide intervention, motivation, and nutrition as essential health promotion and disease prevention strategies (Surgeon General, 2000; Touger-Decker et al., 2007; Johnson et al., 2016; Satcher and Nottingham, 2017; Gondivkar et al., 2019).

This is particularly important for dental professionals, as oral health plays an important role in nutrition and vice versa. The health of the oral cavity can facilitate or impede the desire and ability to eat. Conversely, diet and nutrition play important roles in oral health promotion and caries prevention as well as overall health, disease prevention, and overall quality of life. Dietary habits can affect oral health disease progression, for instance eating fewer snacks can reduce the risk of dental caries, and uncontrolled diabetes can increase the risk of periodontal disease (Stöhr et al., 2021; EFSA Panel on Nutrition, 2022). Overall, health and oral health are inseparable.

Many orthodontists report regularly engaging in dietary discussions with their patients (Huang et al., 2006; Schmitz et al., 2016). This is because the orthodontist is well positioned to help in screening for dietary issues and providing meaningful dietary advice. Nutrition and diet are relevant topics for discussion between practitioner and patient, as good nutrition maximizes orthodontic outcomes. Orthodontists usually see patients during childhood or early adolescence. This allows for early detection of and intervention for dietary problems and promotion of healthy eating habits early in the life cycle. When nutrition issues relate directly to dental or orthodontic problems, the orthodontist can assist in promoting behavior change for good oral health. Considering the importance of nutrition and diet in overall health and, more specifically, oral health, it is important to define the difference between diet and nutrition.

Diet versus nutrition

The words “nutrition” and “diet” are often used interchangeably, but when thinking about nutrition as it relates to oral health it is important to differentiate between the two. *Nutrition* is the science of how the body uses food/nutrients to meet its requirements for growth, development, repair, and maintenance, whereas *diet* is the pattern of individual food intake, eating habits, food choices, and quantities. Diet can be influenced by ethnicity, tradition, religion, lifestyle, peers, personal attitudes (likes and dislikes), and health conditions. Diet and nutrition can affect general health and may change due to chronic disease or other health conditions (Palmer and Boyd, 2016).

As important as it is to know the difference between nutrition and diet, it is also important to understand who the experts in the field of nutrition and dietetics are. In the United States, a nutritionist is anyone who completes any degree in nutrition and can refer to him/herself as a nutritionist. This could involve varying levels of education and training, which will determine the type of credentials such as certified nutrition specialist (CNS) or certified/clinical nutritionist (CN; Public Health Degrees, 2023). Registered dietitian nutritionists (RDNs), however, are food and nutrition experts who have met the following criteria to earn the RDN credential:

- Completed a minimum of a bachelor’s degree at an accredited university/college or approved by the Accreditation Council for Education in Nutrition and Dietetics (ACEND) of the Academy of Nutrition and Dietetics.
- Completed an ACEND-accredited supervised practice program. The practice program will run from 6 to 12 months in length across all different specialties.
- Passed a national examination administered by the Commission on Dietetic Registration (CDR).
- Completed continuing professional educational requirements to maintain registration.

The easiest way to remember this is that every registered dietitian is a nutritionist, but *not* every nutritionist is a registered dietitian.

What is an adequate diet?

An adequate diet is a diet that meets all the known nutritional requirements for health, growth, and development. However, nutrition is not a one-size-fits-all approach. Nutritional needs and dietary habits are specific to age, sex, weight, exercise level, and medical history. The specific nutritional needs of individuals are represented in dietary reference intakes (DRIs), which offer four different reference values: recommended dietary allowance (RDA), estimated average requirement (EAR), adequate intake (AI), and tolerable upper limit (UL), depending on the knowledge available at the time. Most countries have similar standards, however as the standards are listed in physiologically needed amounts (e.g. grams, milligrams, micrograms/day etc.), they are not user-friendly to the average consumer (Yates et al., 1998; Philips et al., 2020; Figure 6.1).

As knowledge about human nutritional needs evolves over time, so does the appetite for a more palatable and user-friendly version of the DRIs.

The dietary guidelines are the cornerstone of federal nutrition policy and nutrition education activities, providing food-based recommendations to promote health, help prevent diet-related disease, and meet nutrient needs. The US Department of Agriculture and Health and Human Services jointly publish dietary guidelines every five years (Philips, 2021). The body of scientific evidence on diet and health informing the dietary guidelines is representative of the US population: it includes people who are healthy; people at risk for diet-related chronic conditions and diseases, such as cardiovascular disease, type 2 diabetes, and obesity; and people who are living with one or more diet-related chronic illnesses (Philips, 2021). *The Dietary Guidelines for Americans, 2020–2025* is the first set of guidelines that provide guidance for healthy dietary patterns by life stage, from birth through older adulthood. For the first time, there are chapters devoted to each life stage, including chapters on infants and toddlers and women who are pregnant or lactating. This edition of the dietary guidelines emphasizes the importance of choosing nutrient-dense foods and beverages in place of less healthy choices at every life stage, and that it is never too early or too late to improve food and beverage choices to build a healthy dietary pattern. Its call to action is “Make Every Bite Count with the Dietary Guidelines for Americans” (Philips, 2021; Table 6.1 and Figure 6.2). The four overarching guidelines to help accomplish these goals are:

- Follow a healthy dietary pattern at every life stage.
- Customize and enjoy nutrient-dense food and beverage choices to reflect personal preferences, cultural traditions, and budgetary considerations.

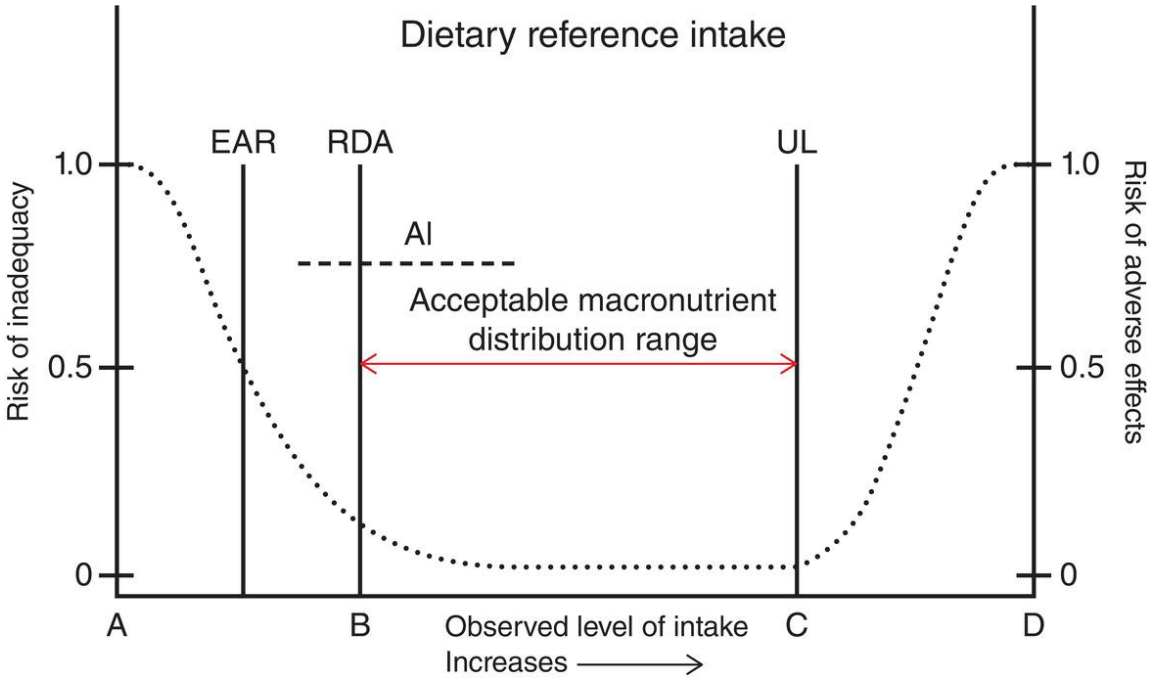

Figure 6.1 Dietary reference intakes. A–D are reference points. AI, average intake; EAR, estimated average requirement; RDA, recommended dietary allowance; UL, upper limit.

Source: Reproduced with permission from Phillips et al. (2020) / Oxford University Press.

- Focus on meeting food group needs with nutrient-dense foods and beverages and stay within calorie limits.
- Limit foods and beverages higher in added sugars, saturated fat, and sodium, and limit alcoholic beverages.

Dietary habits

Role of diet in chronic diseases

Diet and nutrition can play an important role in the *prevention* and *treatment* of certain chronic diseases. There is a well-documented correlation between diet/nutrition, systemic health, and oral health.

While it is not within the scope of practice for orthodontists to provide nutrition counseling to manage chronic diseases, it is important for orthodontists to be knowledgeable on the prevention, pathophysiology, and treatment of these systemic and oral diseases.

Diabetes

Diabetes mellitus encompasses a group of disorders characterized by high levels of blood glucose (hyperglycemia; Gondivkar et al., 2019). Diabetes has several classifications:

- ***Type 1 diabetes*** is due to autoimmune beta-cell destruction, usually leading to absolute insulin deficiency.
- ***Type 2 diabetes*** is due to a progressive loss of adequate beta-cell insulin secretion, frequently against a background of insulin resistance.
- ***Gestational diabetes mellitus*** is diabetes diagnosed in the second or third trimester of pregnancy that was not overt diabetes prior to gestation (American Diabetes Association, 2021).

Diabetes is diagnosed at a glycated hemoglobin (HbA1c) equal to or more than 6.5%. The global diabetes prevalence in 2019 is estimated to be 9.3% (463 million people), rising to 10.2% (578 million) by 2030 and 10.9% (700 million) by 2045 (Saeedi et al., 2019). The goal for those with diabetes is to always maintain close to normal blood glucose levels and reduce spikes in blood glucose primarily through diet, exercise, and in severe cases medication.

Uncontrolled diabetes can lead to retinopathy, nephropathy, neuropathy, and periodontal disease. The reverse is also true: periodontitis may affect blood glucose control, and people who have diabetes may be more susceptible to bacterial infection, leading to gum disease. Nearly 1 in 5 people with severe gum disease had type 2 diabetes and did not know it (Teeuw et al., 2019). The connection between periodontal disease and diabetes is so closely linked that oral health providers must treat periodontal disease while managing diabetes and vice versa.

Heart disease

Although the connection is not as conclusive, there is also a lot of research that shows a connection between periodontal disease and heart disease. According to the World Health Organization, cardiovascular

disease is the leading cause of death globally. It is estimated that 17.9 million people died from cardiovascular disease in 2019, representing 32% of all global deaths (World Health Organization, 2021). Cardiovascular disease is a group of disorders of the heart and blood vessels. However, most cardiovascular diseases can be prevented by modifying lifestyle choices like tobacco cessation, losing excess weight, increasing physical activity, moderate alcohol use, and implementing a healthy diet (Leishman et al., 2010). If these lifestyle choices are not addressed, increased systemic inflammation in the body can ultimately enter the bloodstream and lead to inflamed gingivae and vice versa (Leishman et al., 2010). Even though a direct correlation cannot be proved, it is imperative that treatment of cardiovascular disease includes treatment of oral diseases.

Table 6.1 Dietary guidelines for Americans, 2020–2025.

Source: US Department of Agriculture and US Department of Health and Human Services (2020). Dietary Guidelines for Americans, 2020–2025, 9th ed. Available at DietaryGuidelines.gov.

Categories	Key Recommendations	Practical recommendations for improving diet quality
Fruit	1.5–2.5 cups/day	Add fresh fruit to cereal, granola, oatmeal, waffles, pancakes, toast, or yogurt Eat fruit for snacks Eat fruit for dessert with frozen yogurt or whipped topping Fresh, canned, frozen, and dried fruits all count, but choose those without added sugar or heavy syrup
Vegetables	2.5–3.5 cups/day	Eat fresh vegetables with a dip or hummus for snacking Add vegetables to pasta dishes, casseroles, pizza, stir fries, and sandwiches Start meals with a small salad Fresh, canned, or frozen vegetables all count, but choose those without added salt or butter or creamy sauces
Dairy	2.5–3 cups/day	Use low-fat or fat-free milk on your cereal Snack on low-fat or fat-free yogurt or cheese Add low-fat or fat-free cheese to sandwiches or salad
Starches and grains	5–10 oz (140–280 g)/day fiber. Varies depending on age and sex, but generally:	Choose wholegrain bread products, wholegrain pasta, brown rice, barley, and bulgar for meals Choose wholegrain crackers,

Categories	Key Recommendations	Practical recommendations for improving diet quality
	Women: 25 g Men: 38 g	plain popcorn, or oatmeal cookies for snacks
Fat	Adults: Total fat should comprise 20–35% of the total calories with most coming from monounsaturated fats and polyunsaturated fats Adolescents: Total fat should comprise 25–35% of the total calories with most coming from monounsaturated fats and polyunsaturated fats Saturated fats should be limited to less than 10% of total calories Limit trans fat to as low as possible	Vegetable oils, fatty fish, avocados, nuts, and nut butters are all good sources of mono- and polyunsaturated fats Serve salmon for dinner or add it as a protein to a salad Add avocado to sandwiches and salads, or eat it as a snack with lemon Cook with vegetable oil instead of lard or butter Snack on nuts or make a nut butter sandwich Limit red meat, lard, and full-fat dairy including milk, yogurt, cheese, sour cream, butter, cream, and ice cream Limit fried fast food, commercially prepared bakery goods (pies, donuts, cookies, crackers), and shortenings
Protein	4–7 oz equivalent/day	Lean flesh proteins include lean cuts of beef (tenderloin, flank steak, roast beef, or London broil); lean cuts of pork (tenderloin or fresh ham); lean cuts of veal and lamb (roast or chop); chicken and turkey meat with skin removed; fish and shellfish, tuna canned in water; sardines, and low-fat luncheon meat Lean vegetarian proteins

Categories	Key Recommendations	Practical recommendations for improving diet quality
		include tofu, beans, low-fat cheese or cottage cheese, egg whites, and egg substitute
Added sugars	Less than 10% of total calories to come from added sugar Women and children: <6 teaspoons (24 g)/day Men: <9 teaspoons (36 g)/day	Limit drinking of sugar-sweetened beverages including regular soda, sweetened coffee or tea, energy drinks, sports drinks, or imitation fruit drinks Limit sugar-containing foods between meals Limit sucking on hard candies, breath mints, or cough drops Avoid constantly sipping on sugar-sweetened beverages including regular soda, sweetened coffee or tea, energy drinks, sports drinks, or imitation fruit drinks
Physical activity	Adults: 30 minutes of moderate-intensity physical activity 5 days a week to reduce the risk of chronic disease and 60 minutes to prevent gradual weight gain into adulthood Adolescents: 60 minutes of physical activity most days of the week	Take the stairs, park further from the store in a parking lot, limit time in front of the television and computer, join a sports team or a gym, or walk outside
Minerals	Limit sodium to 2300 mg/day	Limit processed foods such as frozen meals or partially prepared boxed meal starters Choose low-sodium or no-salt-added canned foods or rinse regular canned foods

Categories	Key Recommendations	Practical recommendations for improving diet quality
		Avoid adding extra salt during cooking or at the table

Obesity

One of the fastest-growing chronic conditions is obesity both in adults and in children (Flegal et al., 2012). Overweight and obesity are defined by abnormal or excessive fat accumulation that may impair health. Body mass index (BMI) is calculated by a person's weight in kilograms divided by the square of their height in meters (kg/m^2). BMI is the most widely accepted tool for defining obesity; however, there have been concerns over the accuracy of this calculation (Stanford et al., 2019). Worldwide obesity has tripled since 1975 (Wright and Aronne, 2012). In 2016, 1.9 billion adults (39%) were overweight and 650 million (13%) were obese, as well as over 340 million children and adolescents (5–19 years old) being overweight or obese. While environmental (access to healthy food, health insurance) and genetic risk factors are not easily modifiable, obesity can be managed through diet and exercise. Just like cardiovascular disease, there is no direct correlation between obesity and oral health; however, diets consisting of high-calorie, non-nutrient-dense foods (fermentable carbohydrates) and inactivity can increase a patient's risk for obesity, dental caries, and periodontal disease.

Management of chronic diseases depends on the individual, his or her comorbidities, and the onset of the diagnosis, and includes modifying risk factors like diet and physical activity. Diet can be modified based on chronic conditions or the current stage of the life cycle. If lifestyle modification proves to be ineffective, more invasive interventions are required. This is where medication prescriptions are introduced as part of the treatment plan. It should be noted that many medications, including common over-the-counter ones such as antihistamines, can cause decreased salivary flow or xerostomia. As important as it is for dental professionals to understand the connections between diet/nutrition, oral health, and overall health, when nutrition issues are beyond the orthodontic scope of practice, referral can be made to a physician or a registered dietitian.

Age-specific concerns influencing diet

Research helps health professionals give general dietary recommendations for the public. However, there is no one size that fits all. Every patient will require personalized diet and nutrition advice based on their age, activity level, and chronic conditions among other factors. Each stage of life is distinct and has unique needs that impact health and disease risk.

Children

On average, 19.4% (14.4 million) American children are defined as obese. Childhood obesity has more than tripled in the past 30 years. It is widely understood that obese children are more likely to become obese adults and are more likely to have risk factors for adult-onset chronic diseases such as cardiovascular disease and type 2 diabetes (Estrada et al., 2014). Obese children are also more likely to have low self-esteem, which may contribute to poor socialization and poor academic performance (Wu et al., 2016; Gong et al., 2022).

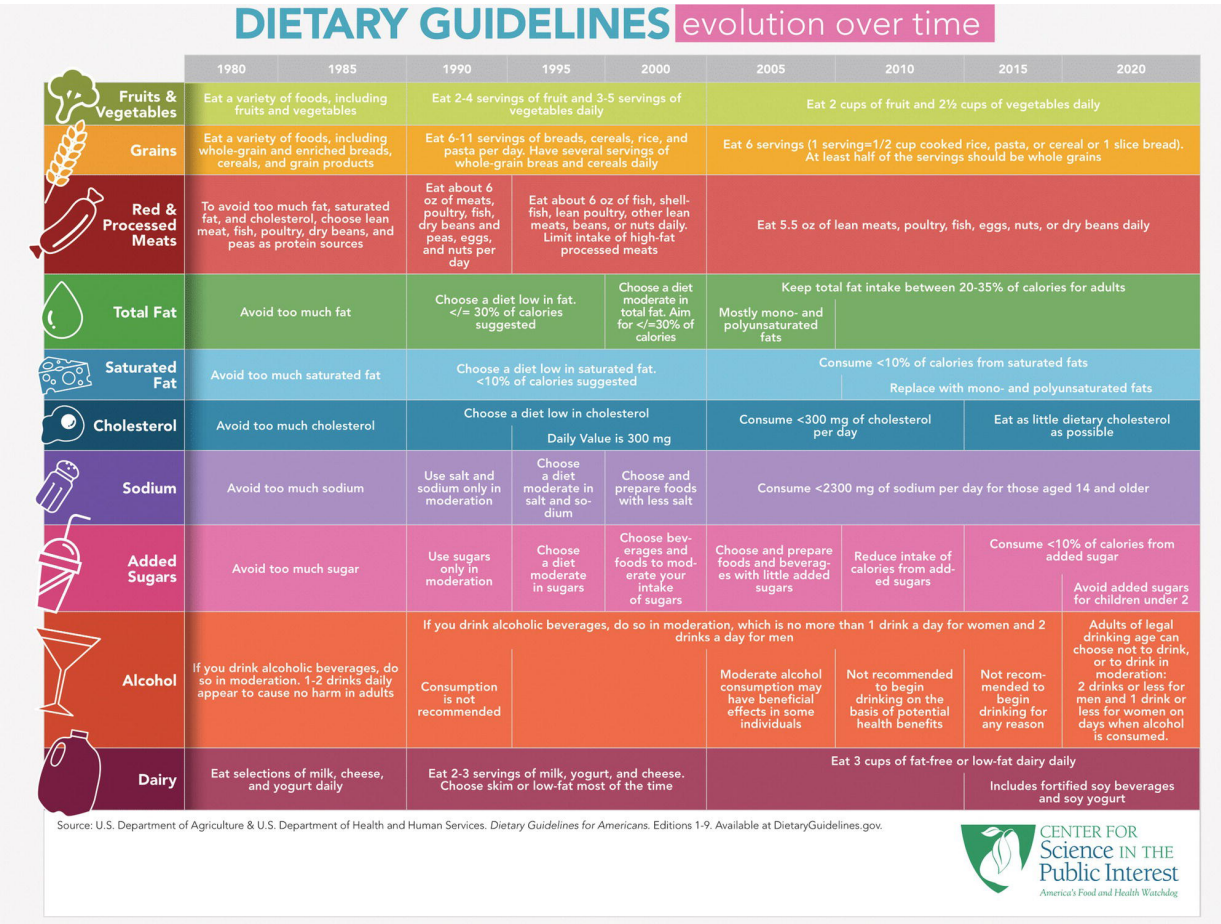

Figure 6.2 American dietary guidelines: evolution over time.

The method of presenting the dietary guidelines to the general population has evolved over time, from the 1940s and the Basic Seven to the Food Pyramid in 1992 and MyPyramid in 2005 (Figures 6.3–6.5). The most current adaptation, known as MyPlate, was created with the 2010 dietary guidelines and not only provides general dietary guidelines for health, but also offers specific recommendations based on age, sex, weight, and exercise level (Figure 6.6). This can be a useful tool for both orthodontists and patients alike. While these nutritional recommendations and guidelines apply to the general population, it is important to understand that there are recommendations for those with specific chronic conditions.

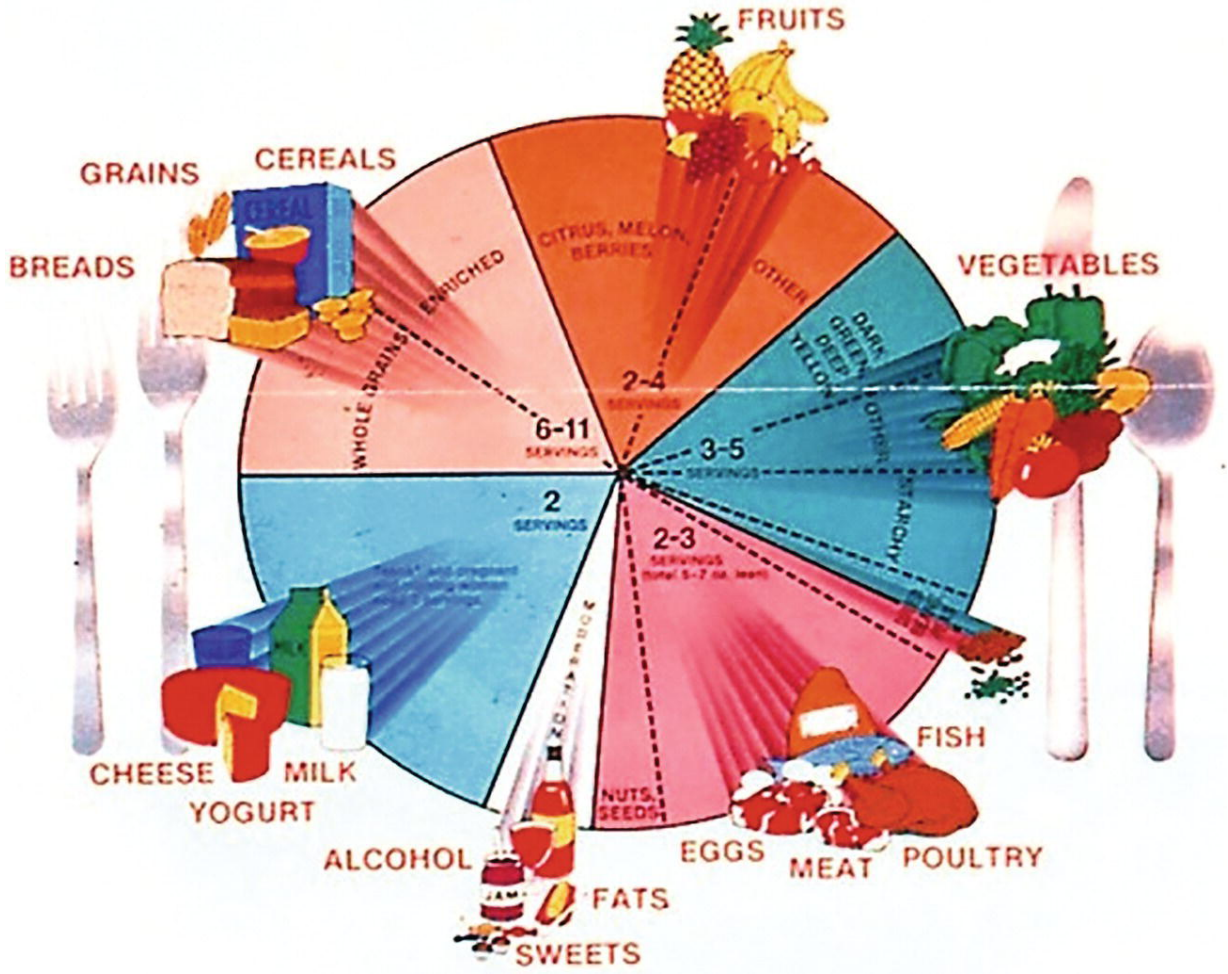

Figure 6.3 Food wheel: A pattern of daily food choices.

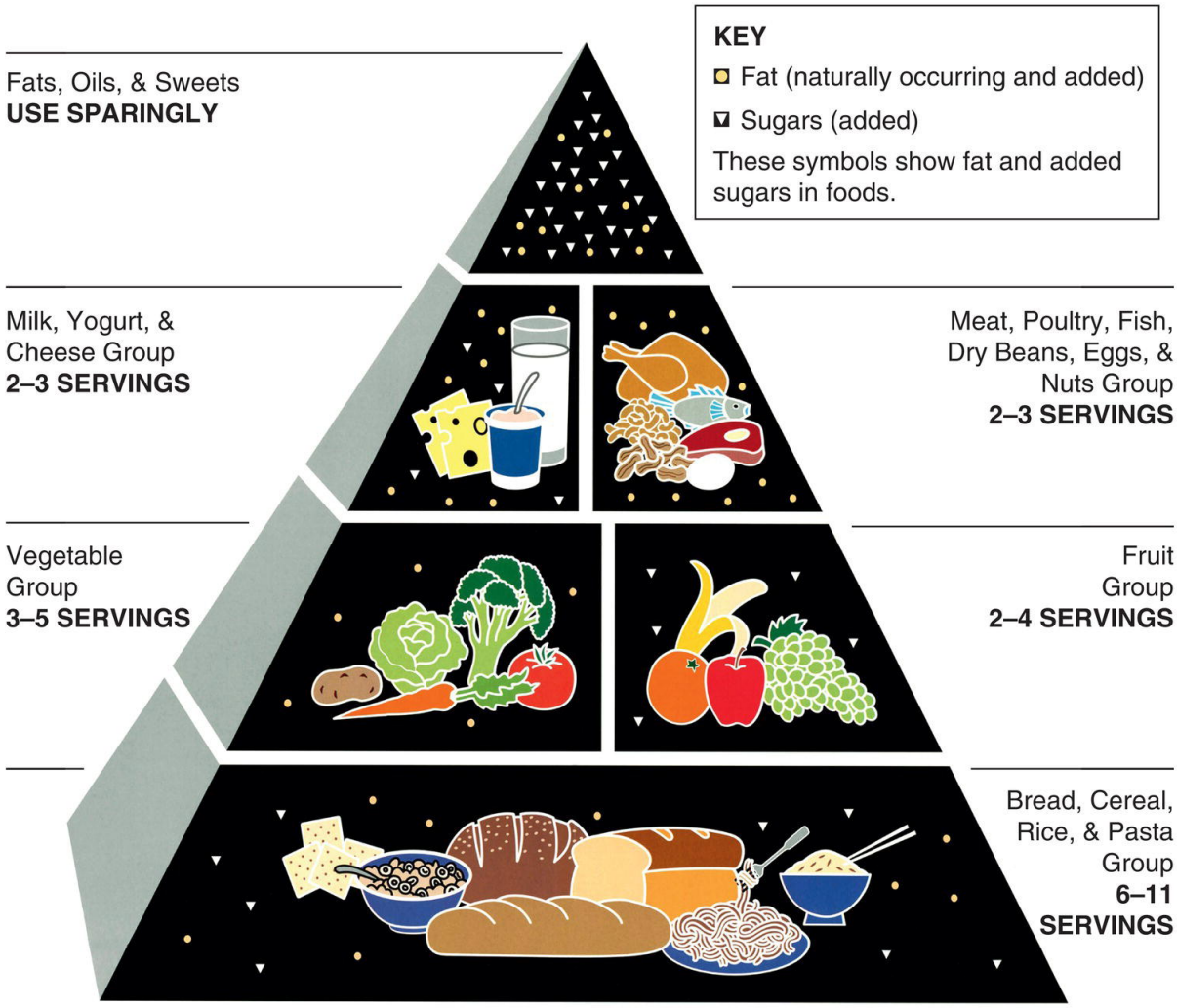

Figure 6.4 The food guide pyramid.

Source: US Department of Agriculture / US Department of Health and Human Services / Public Domain.

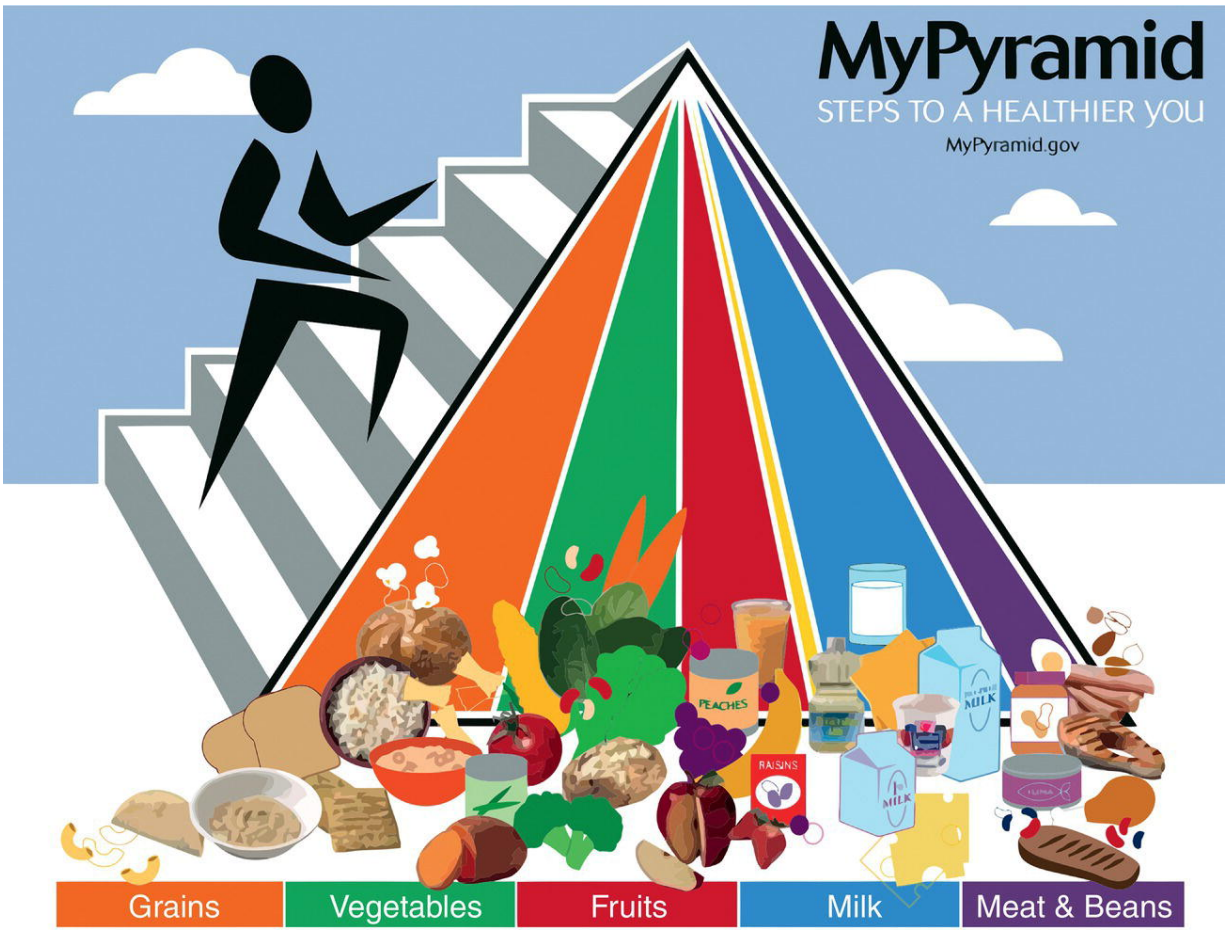

Figure 6.5 My Pyramid: Steps to a healthier you.

Source: MyPyramid.gov / US Department of Agriculture / Public Domain.

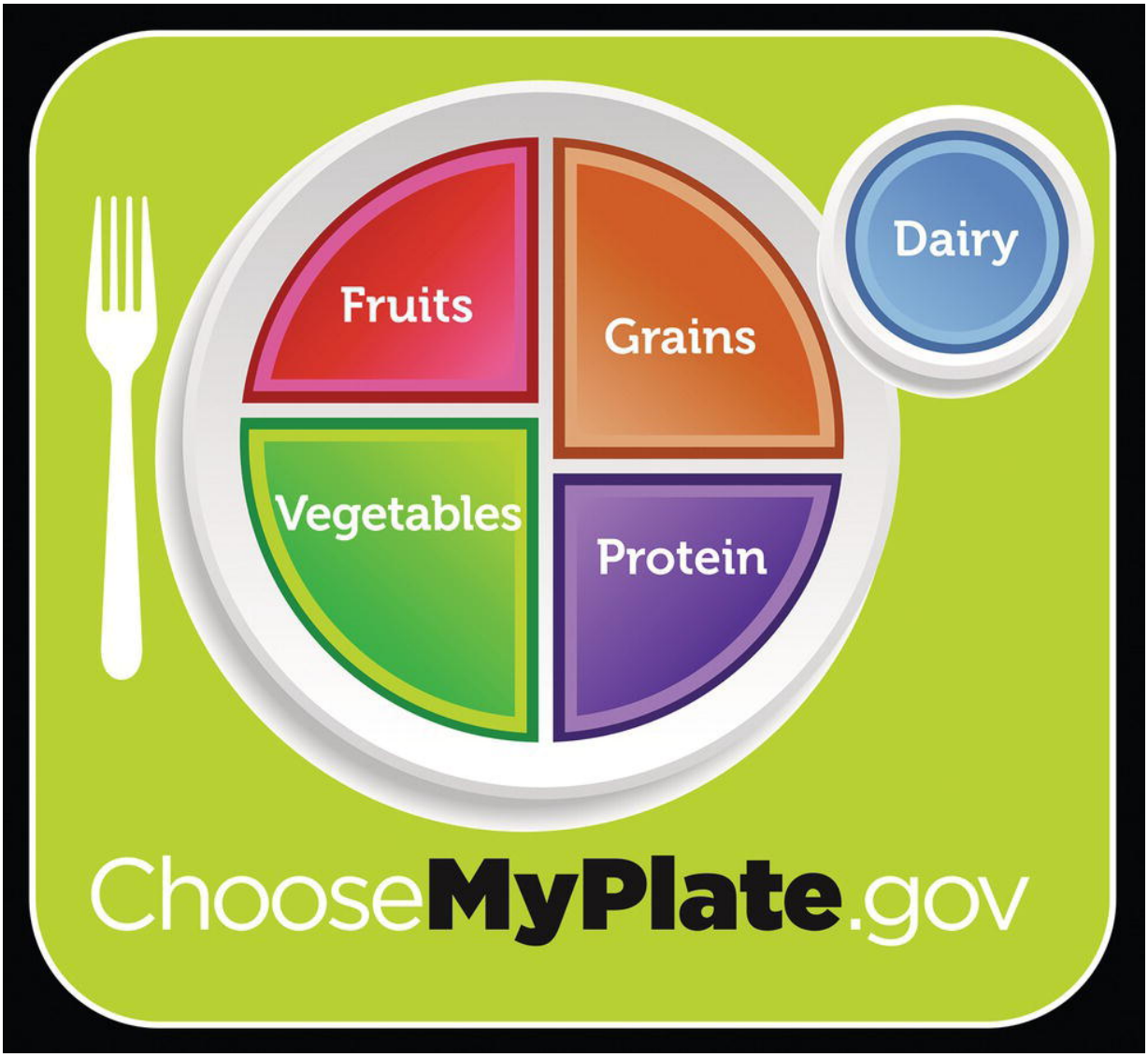

Figure 6.6 ChooseMyPlate.

Source: ChooseMyPlate.org / US Department of Agriculture / Public Domain.

The etiology of obesity is multifactorial and includes genetic and lifestyle components such as diet and physical activity. Other factors contributing to childhood obesity are the home/school environments, the larger community, and the societal environment. However, there is a current consensus among the scientific community that diet and nutrition play a significant role in the prevention and treatment of childhood obesity. Worsening dietary habits such as eating larger portions, snacking frequently, overconsumption of processed food, and consuming sugar-laden beverages are postulated to contribute to childhood obesity. These dietary patterns are also associated with increased risk of dental caries

and therefore can and should be addressed in the orthodontic office. The entire healthcare team must be willing to address nutrition issues to improve the general and oral health of our youth in the current childhood obesity epidemic.

Teens/Adolescents

Adolescence encompasses major changes in physical, emotional, psychosocial, and cognitive development. Many studies show a high prevalence of weight-control behaviors among adolescents, especially girls. One study, Eating Among Teens (Project EAT, https://www.sph.umn.edu/research/projects/project-eat), found that 45% of adolescent girls were trying to lose weight. Oftentimes, they choose unhealthful weight-loss techniques such as use of diet pills, laxatives, diuretics, or vomiting. Project EAT found that 12% of girls report these extreme weight-loss behaviors. Evidence of such behaviors could indicate more serious psychological conditions such as bulimia or anorexia nervosa. Signs of eating disorders frequently appear first in the oral cavity. Manifestations of eating disorders in the oral cavity include tooth sensitivity, inflamed gums, and tooth erosion (Hasan et al., 2020; Lin et al., 2021). When evidence of these behaviors is found, patients should be referred for medical evaluation. Many hospitals now have eating disorder clinics that provide important multidisciplinary approach to care.

In adolescent boys, major physical growth continues and calorie requirements increase significantly. Appetite usually increases dramatically, resulting in consumption of large amounts of food. Although more common among girls, dieting and extreme weight-loss behaviors also occur among adolescent boys. Project EAT reports that 21% of boys were currently trying to lose weight, while 5% reported using extreme behaviors to achieve weight loss. Males make up 25% of people with anorexia. Boys and men are likely underdiagnosed with eating disorders because clinical assessment tools emphasize a desire to lose weight as opposed to building muscle. Delayed diagnosed puts this population at higher risk of dying compared to their female counterparts.

The patient's stage of life is an important nutritional consideration during orthodontic treatment. Orthodontic patients are often treated during the adolescent growth spurt. This growth period is a time of increased nutritional requirements, making dietary choices even more important (Bhutta et al., 2017; Ibrahim et al., 2017). The role of the

orthodontist is crucial to help these patients to make healthy dietary food choices and learn healthy eating habits early.

Typical eating patterns

Among both male and female adolescents, dietary patterns are generally poor. Starting in adolescence, more food is consumed away from the home and teens begin to make their own food choices. Food may be used to establish an independent identity separate from the family unit. As adolescents begin to exert their independence from family life, peer influence becomes more significant and may influence food choices. Characteristic patterns include:

- Irregular meals.
- Meal skipping.
- Frequent snacking.
- Vending machine use.
- Fast food purchases.
- Meals on the go.
- High sugar-sweetened, carbonated, and/or caffeinated beverage intake.
- Mindless eating.
- Eating late at night.

These patterns do not align with generally healthful eating recommendations for adolescents and significantly affect oral health. For example, poor calcium intake is common in girls, precisely during this most important period of bone density accretion. Frequent use of sugar-sweetened beverages and frequent snacking can be associated with increased caries risk in teens. It is important to understand the factors that influence teens' eating behaviors to be able to be effective in helping them make dietary improvements. Orthodontic discharge instructions should always include healthy age appropriate dietary recommendations.

Adults

The demography of orthodontics is changing rapidly. According to the American Association of Orthodontists (AAO), 27% of US and Canadian

orthodontic patients are adults. This percentage means that there are 1,441,000 orthodontic patients who are 18 and older.

Adult patients can come with their own challenges. Typically, adult patients have a lengthier medical history. Many adults have chronic diseases that may influence treatment. Practitioners should understand these diseases and their impact on the oral cavity and orthodontic treatment, and refer patients for further care if it appears that these health conditions are not well controlled. For example, type 2 diabetes mellitus is common and often results from adult obesity. If a patient's diabetes is not well controlled, they may have episodes of hypoglycemia in the dental office and may even require medical attention. Quickly absorbed sugar such as fruit juice should be kept on hand for the hypoglycemia that can occur if a patient has not eaten before their appointment. Those with poorly controlled diabetes may carry hard candies with them to use to overcome hypoglycemia, but if these are used too frequently, dental caries could result. Many adults also take one or more medications with side effects like xerostomia, which increases the risk of root caries and recurrent caries around existing dental restorations.

Nutrition and oral health

Importance of nutrition during development and for maintenance of oral tissues

Nutritional status can affect orthodontic treatment. Healthy bone and tissues are required for periodontal ligament and bone to respond positively to orthodontic tooth movement (Bhutta et al., 2017; Ibrahim et al., 2017). Growth and development of all tissues and structures, including those of the oral cavity, directly depend on adequate nutrition. Tooth development begins *in utero* and continues until the third decade of life, when the third molars emerge into the oral cavity and all teeth complete root formation. Following their emergence into the oral cavity, the dental crowns become exposed to the oral environment. At the time of emergence the dental roots are incomplete, and while the eruptive movement continues the tissues surrounding the teeth model and remodel as part of overall growth, activity that continues into adult life. In both children and adults, nutrition plays a pivotal role in determining the nature of tissue growth and remodeling, and the individual response to physical and chemical challenges. Thus, all age groups are dependent

on consistently good nutrition (Romito, 2003). Good nutrition includes adequate caloric needs for age, sex, and activity level and ensuring the patient is daily consuming foods from each food group at every meal.

Oral development (including tooth mineralization) begins *in utero* and prenatal nutrition of the mother is the first important factor that affects the ultimate oral development of the child. Maternal deficiencies of folic acid, riboflavin, and zinc during pregnancy can lead to severe craniofacial abnormalities such as cleft lip and palate in the child. General malnutrition and specific nutrient deficiencies (as well as nutrient toxicities) during tooth development can adversely affect tooth size, formation, and eruption pattern. Due to the rapid cellular turnover (3–7 days) of the oral cavity, a wide variety of nutritional toxicities/deficiency are first observed as clinical manifestations in the oral cavity. For example, protein deficiency during early childhood can affect tooth size and eruption sequence (Zameer et al., 2016). Vitamin C deficiency may alter collagen formation and bone development (Padayatty and Levine, 2016). In developing countries where malnutrition is rampant, such nutrition-related defects are commonly observed. In developed countries, however, overt malnutrition and specific nutrient deficiencies are less common. However, issues related to nutrient toxicity do occur. A few years ago, the accidental overfortification of milk with vitamin D by a commercial dairy resulted in malformation defects in erupted dentition in a young child (Yeh et al., 2017). Thus, orthodontists should be aware of the importance of nutrition during oral growth and development, and should counsel pregnant women, children, and teens about the importance of optimal nutrition for health. They should caution against the random use of nutritional supplements other than multivitamins or calcium/vitamin D supplements unless they are prescribed by a physician. A list of common vitamin and mineral deficiencies, toxicities, and food sources is provided in Table 6.2.

Role of diet in dental caries

The orthodontist, like other dental professionals, is in an ideal position to educate patients about diet and dental caries because of the role diet plays in the formation of cavities. Orthodontists play an even more pivotal role, since orthodontic appliances increase the available surfaces for plaque accumulation, resulting in more areas for caries. Furthermore, patients visit the orthodontist more frequently than their general dentist.

The caries process

Dental caries results from the demineralization of tooth enamel and dentin by organic acids formed by bacterial metabolism of dietary sugars, specifically fermentable carbohydrates. The only cariogenic foods are those that are composed of one or more of the simple sugars. For the general public, the term *sugar* that is associated with dental caries is often synonymous with the disaccharide sucrose, or table sugar. However, all monosaccharides (glucose, fructose, galactose) and disaccharides (sucrose, maltose, lactose) have cariogenic potential. These include sugars added during manufacturing (formerly sucrose, now primarily high-fructose corn syrup) as well as table sugar added in cooking and naturally occurring sugar found in fruit, juice, honey, and molasses (Moynihan and Petersen, 2004).

An alarming dietary trend in recent years is the increased consumption of sugars in the diet of younger adults and children. Dentists need to be aware of these trends, including common and hidden sources of sugars. This will allow them to give better-informed dietary counseling to their patients and suggest healthier alternatives (Bailey et al., 2018). In the realm of dental health, the term *fermentable carbohydrates* is often used to refer to those carbohydrates that can be metabolized by oral bacteria to produce acid and, as a result, increase caries risk (Kandelman, 1997). These are primarily mono- and disaccharides, but starches can also be cariogenic when held in the mouth long enough for salivary amylase to hydrolyze them to simple sugars. It is important to remember that the total amount of sugars consumed does not seem to be the most important factor in the cariogenic potential of the diet. Dietary patterns that include frequent snacking/sipping on foods or beverages that contain simple sugars are more conducive to caries development than infrequent snacking (Moynihan and Petersen, 2004).

When making recommendations to patients, sometimes offering simple modifications can increase compliance. It is therefore important to communicate that protein, fats, and food fibers are *not* cariogenic. The development of dental caries is influenced primarily by the total amount of *time* fermentable carbohydrates (simple sugars: mono- and disaccharides) are in contact with dental plaque. Thus, the following dietary habits can increase the risk of caries development:

- The frequency of consumption.
- The form of sugar (indicating retention of sugar in the mouth).

- The timing of consumption (at or between meals).

Protective role of diet/nutrition against dental caries

Fluoride is commonly accepted to be the most effective way to protect against dental caries. Topical fluoride increases the resistance of enamel to demineralization by organic acids following sugar consumption. Frequent exposure to fluoride helps protect enamel against the detrimental effects of acid, but it does not eliminate the risk of developing caries. Overly frequent consumption of cariogenic sugars can overwhelm the benefits of fluoride. The primary source of fluoride is fluoridated community drinking water. Fluoride is also found in tea, but is not present in appreciable amounts in most other foods. Most bottled waters are ***not*** good sources of fluoride. The most reliable sources are fluoridated drinking water and fluoridated dentifrice. Topical fluoride is also a good source of fluoride and can be protective against caries, for example using fluoridated toothpaste or mouth rinse.

Table 6.2 Common vitamin and mineral deficiencies, toxicities, and food sources.

Sources: Adapted from Palmer and Boyd (2016) and NIH Fact Sheets for Health Professionals.

Nutrient	Deficiency	Toxicity	Food source
Vitamin A	Mild: Inadequate differentiation of cells leading to impaired healing and tissue regeneration; desquamation of oral mucosa; early keratinization of mucosa (keratosis); increased risk of candidiasis, gingival hypertrophy, and inflammation; leukoplakia, decreased taste sensitivity, xerostomia, disturbed or arrested enamel development leading to poor or absent calcification and hypoplasia in mature teeth Severe: may lead to irregular tubular dentin formation and increased caries risk	Impairs cell differentiation and epithelialization resulting in delayed and impaired healing of oral tissues (mimicking signs and symptoms of deficiency)	Sweet potatoes, spinach, pumpkin, carrots, dairy products like cheese and milk, cantaloupe, mangos, red peppers
B2 Riboflavin	Angular cheilosis, atrophy of filiform papillae, enlarged fungiform papillae, shiny red		Yogurt, milk, chicken, beef, mushrooms, cheese, chicken, eggs, quinoa,

Nutrient	Deficiency	Toxicity	Food source
	lips, magenta tongue, sore tongue		fortified breakfast cereal
B3 Niacin	Angular cheilosis, mucositis, stomatitis, oral pain, ulceration, denuded tongue, glossitis, glossodynia (tongue: tips are red, swollen, beefy, dorsum is smooth and dry), ulcerative gingivitis		Chicken, turkey, salmon, tuna, beef, brown and white rice, peanuts, potato, fortified breakfast cereal
Folic acid	Angular cheilosis, mucositis, stomatitis, sore or burning mouth, increased risk of candidiasis, inflamed gingiva, glossitis (tongue: red, swollen tip or borders, slick bald pale dorsum), apthous-type ulcers		Spinach, asparagus, brussel sprouts, white rice, avocado, fortified breakfast cereal
B6 Pyridoxine	Angular cheilosis, sore burning mouth, glossitis, glossodynia		Chickpeas, tuna, salmon, chicken, turkey, banana, potato, fortified breakfast cereal
B12 Cynocobalamin	Angular cheilosis, sore burning mouth, mucositis/stomatits, hemorrhagic gingiva, halitosis, epithelial dysplasia of oral mucosa, oral		Clams, tuna, salmon, beef, yogurt, milk, cheese, nutritional yeast, fortified breakfast cereal

Nutrient	Deficiency	Toxicity	Food source
	paresthesia (numbness, tingling), detachment of periodontal fibers, loss or distortion of taste, glossitis, glossodynia (tongue: beefy red, smooth, glossy), delayed wound healing, xerostomia, bone loss, apthous-type ulcers		
Vitamin C	Mild: exaggerated tissue response to and increased risk of infection, blood vessel fragility, increased periodontal signs and symptoms, delayed wound healing Severe: (scurvy) red swollen gingiva, gingival friability and bleeding on provocation, interdental papillary infusions, petechia, sore burning mouth, increased risk of candidiasis, subperiosteal hemorrhages, periodontal destruction,	Chronic overdosing can increase metabolism of vitamin C as an adaptation; rebound scurvy may occur after dose normalization	Red and green peppers, orange and orange juice, grapefruit and grapefruit juice, kiwi, strawberries, brussel sprouts, broccoli, tomato and tomato juice, cantaloupe, cabbage, spinach, green peas

Nutrient	Deficiency	Toxicity	Food source
	increased tooth mobility and exfoliation, soft tissue ulceration, teeth are malformed with normal enamel but inadequate dentin that can easily fracture		
Vitamin D	Abnormal bone regeneration, osteoporosis, osteomalacia, incomplete calcification of teeth and alveolar bone, rickets	Pulp calcification, enamel hypoplasia	Egg yolk, cheddar cheese, salmon, trout, mushrooms, fortified products like milk or orange juice Nonfood source: sunlight
Vitamin K	Increased risk of bleeding and candidiasis	Interfere with certain medications (Coumadin)	Green leafy vegetables like collard greens, spinach and kale, broccoli, soybeans, pumpkin, pine nuts, blueberries
Calcium	Incomplete calcification of teeth, rickets, osteomalacia, excessive bone resorption and bone fragility, osteoporosis, increased tendency to hemorrhage, and increased tooth mobility and premature loss		Dairy products like yogurt, milk, and cheeses, tofu, salmon, beans, kale, broccoli, fortified breakfast cereals, orange juice

Nutrient	Deficiency	Toxicity	Food source
Copper	Decreased trabeculae of alveolar bone, decreased tissue vascularity, increased tissue fragility		Oysters, potatoes, mushrooms, cashews, crab, sunflower seeds, dark chocolate, tofu
Fluoride	Decreased resistance to dental caries, builds enamel	Fluorosis leading to enamel hypoplasia: mild = mottled enamel (white spots)/high caries resistance; milder signs of toxicity are esthetically un-pleasant but increase caries resistance; moderate = unsightly brown stain/high caries resistance: severe = hypoplasia of enamel, with decreased caries resistance; more severe toxicity results in interference with amelogenesis	Only trace amounts are naturally present in food. Check local water sources for fluoridation

Nutrient	Deficiency	Toxicity	Food source
		and decreased caries resistance	
Iron	Angular cheilosis, pallor of lips and oral mucosa, sore, burning tongue, atrophy/denudation of filiform papillae, glossitis, increased risk of candidiasis		Beef, seafood, white beans, chocolate, lentils, spinach, tofu, chickpea, tomatoes, potato, fortified breakfast cereal
Magnesium	Alveolar bone fragility, gingival hypertrophy		Seeds (pumpkin/chia), nuts (almond/cashew), beans, peanut butter, potato, brown rice, fortified breakfast cereal
Phosphorus	Incomplete calcification of teeth, increased susceptibility to caries if present during tooth development, increased susceptibility to periodontal disease via effects on alveolar bone		Dairy products like yogurt, milk, and cheese, beef, salmon, chicken, lentils, potatoes, rice
Zinc	Loss or distortion of taste and smell acuity, loss of tongue sensation, delayed wound healing, impaired		Oysters, crab, lobster, beef, chicken, beans, yogurt, nuts, fortified breakfast cereal

Nutrient	Deficiency	Toxicity	Food source
	keratinization of epithelial cells, epithelial thickening, atrophic oral mucosa, increased susceptibility to periodontal disease and candidiasis, xerostomia, increased susceptibility to caries if present during tooth formation		

Another protective measure against caries is saliva. Saliva plays a major role in preventing dental caries by promoting enamel remineralization, cleansing the mouth, and helping neutralize acids. The act of chewing facilitates salivary flow. Many medications, including common over-the-counter medications, can cause decreased salivary flow or cause xerostomia (Marcott et al., 2020). Xerostomia increases the caries risk associated with the diet, due to the loss of the acid-mitigating effects. Thus, hydration to maintain salivary flow is vital for caries prevention (Moynihan and Petersen, 2004).

Foods high in calcium and phosphorus (dairy products: cheese, milk, and hight protein foods such as nuts and grains etc.) can also be protective against the formation of caries, by reducing bacterial adhesion to teeth, inhibiting biofilm formation, and enhancing enamel remineralization while reducing demineralization. Studies have shown that cheese, when provided after a cariogenic challenge such as a cookie, immediately facilitates plaque return to neutral (Tanaka et al., 2012). Although the etiological mechanism is not clear, it has been postulated that the salivary-stimulating effect of chewing these foods, the remineralizing effect of the calcium from the cheese, or the plaque-coating effect of the fat from the cheese or nuts may be contributing factors. Chewing gum (artificially sweetened) has the same beneficial effect. Gum containing xylitol has a heightened effect as the xylitol itself is cariostatic (Cocco et al., 2017). Unfortunately, sugar-free chewing gum and nuts may not be

appropriate suggestions for orthodontic patients treated with fixed appliances. Protein alternatives for orthodontic patients include soft cheese, yogurt, and milk. Patients should be advised to focus on “good” fats such as those found in plants, for example olive oil, avocado, and coconut oil (Box 6.1).

Role of nutrition in periodontal disease

Periodontitis is an inflammatory disease of the supportive tissues of the teeth caused by groups of specific microorganisms, resulting in progressive destruction of the periodontal ligament and alveolar bone with increased probing depth formation, recession, or both. If untreated, it leads to the progressive loss of the alveolar bone and loss of teeth. Periodontal health is influenced by many factors such as oral hygiene, genetic and epigenetic factors, systemic health, and nutrition. Many studies have observed that a balanced diet has an essential role in maintaining periodontal health. Tissue regeneration and healing are affected by good balanced nutrition, specifically adequate intake of vitamins and minerals such as calcium, iron, zinc, vitamin C, and vitamin D, among others. Deficiencies in vitamins and minerals can have detrimental impacts on the progression of periodontal disease (Najeeb et al., 2016; Feu, 2020). Moreover, bone formation and periodontal regeneration are also influenced by numerous vitamins, minerals, and trace elements. Sugars contribute to dental caries and periodontal disease because bacteria ferment them and produce acid, leading to demineralization of the tooth structure (Edgar, 1993).

Box 6.1 The intraoral effects of proteins and fats in the diet.

Proteins:

- Neutralize/buffer acid production,
- Help to avoid fermentable carbohydrates sticking to teeth.
- Digested late in the digestive process and typically to an alkaline product.

Fats:

- Help to avoid fermentable carbohydrates sticking to teeth.
- Increase oral clearance.
- Low concentrations of linolenic and oleic acid can inhibit growth of oral bacteria.
- Digested late in the digestive process.

Occasionally patients with periodontal disease may seek orthodontic treatment. For these patients the treatment plan should be individualized based on the degree of periodontal disease and bone loss present in order to achieve favorable orthodontic outcomes.

Importance of diet during orthodontic treatment

In addition to a healthy diet and nutrition that is adequate for proper development and maintenance of the oral cavity, diet and nutrition also play a role in facilitating the tissue reactions to orthodontic force systems applied to the periodontal ligament and alveolar bone, necessary for tooth movement. During orthodontic treatment, applied force systems mechanically induce inflammation to encourage the bone modeling and remodeling processes, eventually leading to tooth movement. This biological response, as well as the bone modeling/remodeling processes, require adequate nutrition. Orthodontic treatments with fixed appliances

typically can last between 1 and 3 years, in which short-term dietary changes to easy-to-consume foods typically outweigh nutritional value. However, long-term dietary changes to easy-to-chew, less nutrient-dense foods can increase risk for vitamin and mineral deficiencies that can ultimately affect orthodontic treatment by influencing the proper biological response to applied forces and undermine orthodontic outcomes. Nutrient deficiencies can occur secondary to dietary changes, decreased overall intake, or decrease utilization of ingested food (decreased mastication). These nutrient deficiencies can present as symptoms in the mouth that could ultimately affect dietary intake, and can also affect orthodontic treatment.

Many nutrients are important for bone health, including calcium, phosphorus, magnesium, copper, zinc, iron, fluoride, and vitamins D, A, C, and K (Ilich and Kerstetter, 2000). The role of nutrition in general bone modeling/remodeling and bone health is well documented in the literature and can be extrapolated to the bone modeling that occurs during orthodontic tooth movement. Most adult peak bone mass is acquired through bone modeling during childhood and adolescence. Nutritional deficits during this critical period in life may set the stage for poor bone development as well as lack of tooth integrity later in life, leading to osteoporosis or osteopenia. Nutritional deficiencies during more intensive bone modeling – as occurs during orthodontic force application – can greatly influence final outcomes.

Most studies looking at the effect of nutrient deficiencies/toxicities and orthodontics are done in animal studies. ***Vitamin C*** influences tooth movement and is important for collagen synthesis and osteoid formation; a deficiency during orthodontic treatment reduces tooth movement because of its effect on tissue healing (Paria et al., 2020), as well as the vitamin being very important for postorthodontic retention treatment (Bose et al., 2021). Deficiency of vitamin C often leads to relapse (Bose et al., 2021). ***Vitamin D*** plays a role in absorption of calcium and phosphorus, essential minerals for skeletal and dental growth. Due to the beneficial effect of Vitamin D on bone, a deficiency can be assumed to inhibit tooth movement (Paria et al., 2020). ***Calcium*** must be absorbed in sufficient quantities to build bone structure during growth and maintain it in maturity. Although an adequate intake is important for bone health, excessive amounts of calcium (generally >2500 mg/day) may interfere with the absorption of other nutrients, such as iron (Katsimbri, 2019). See Table 6.2 for good sources of these vitamins and minerals.

Another principal dietary concern during orthodontic treatment arises from the physical presence of the appliances. Brackets and banding increase surface area and exposure time for debris and demineralization on hard and soft oral tissues, as well as gingival irritation. Food gets trapped on surfaces (facial side of the tooth) that typically are cavity free. Therefore, eating for general caries prevention becomes an even greater priority. To minimize fixed appliance breakage, a gentler diet is also recommended (see Box 6.2).

Box 6.2 Dietary recommendations to minimize appliance breakage.

Foods to avoid

- Avoid crunchy foods such as nuts, popcorn, and hard pretzels.
- Avoid sticky foods such as taffy, caramels, tootsie rolls, starburst, skittles, and dried fruit.
- Avoid chewy foods such as gum or chewy fruit snacks.
- Avoid chewing on frozen treats like ice cubes, ice-cream bars, and fruit bars.
- Avoid hard foods such as hard candies or lollipops.

Foods to be cautious of

- Use caution when biting into tough meats, hard cheeses, or crusty breads like bagels, croutons, and hard pizza crust. Cut them into small bites and chew them with your back teeth.
- Use caution when eating hard fresh fruits or vegetables like apples, pears, peaches, carrots, and corn on the cob. Cut them into small pieces and chew them with your back teeth.

Orthodontic guide to performing nutrition risk assessments

Nutrition screening

While adequate nutrition and appropriate dietary choices are essential for effective orthodontic treatment, it is understood that nutrition and dietary discussions are rarely the sole topic during orthodontic visits. It is one of many topics that are covered in the visit. A rapid, simple, and effective diet risk assessment of a patient's nutritional status can help orthodontists prioritize patients and their needs. While being very different from full nutritional assessments that are performed by registered dietitians or nutritionists, a diet risk assessment in an orthodontic setting can be a straightforward screening tool used to *assess the general diet quality, caries risk, and the risk of orthodontic appliance breakage*.

There are many tools used by dental professionals to assess a patient's caries risk that include nutrition-related questions like frequency of eating and consumption of fluoridated water. The four best-known ones are the Caries Management by Risk Assessment (CAMBRA), Cariogram, American Dental Association (ADA), and American Academy of Pediatric Dentistry (AAPD) caries risk assessments (Featherstone et al., 2021). While these tools are widely used in the dental world, they do not encompass the entire nutritional status or risk of each patient. This results in dietary discussions in orthodontic offices being less involved than those in dietitians' or nutritionists' offices.

There are also many dietary assessment tools that are quick, inexpensive, and easy to use that orthodontists or other dental professionals can introduce into their office to better assess nutritional status. One of the most practical nutrition screening tools is a 24-hour dietary recall. This is a structured interview intended to capture detailed information about all food, beverages, and dietary supplements consumed in the past 24 hours (National Cancer Institute, 2022). Unlike closed-ended questions that can be leading and may not highlight dietary habits, a 24-hour dietary recall can provide more detailed information like how the food was prepared, how much was consumed, and how frequently a certain product was consumed throughout the day. Completing 24-hour dietary recalls is easy to perform, but it takes significant training and practice to understand reporter bias and avoid leading questions (like "What did

you eat for breakfast?"), and they can only capture a short intake period (National Cancer Institute, 2022).

In addition to subjective data provided by the individual or guardian, other objective data that can have an impact on nutritional status include chronic/underlying medical conditions, restrictive diets, and inability to chew and swallow. These risk factors can be obtained from a medical history or a clinical examination. Chronic diseases like cardiovascular disease, diabetes, and/or Crohn's disease can influence dietary intake, risk for infection, and absorption. After conducting a diet risk assessment, orthodontic practitioners can use the information from the assessment to provide simple dietary recommendations and guidance to patients.

Nutrition assessment

Nutrition risk assessment includes assembling an overall picture of the patient's dietary status based on subjective data (as collected from the diet assessment tools) and objective data (as collected from the clinical evaluation; Palmer and Boyd, 2016). It is a critical step for the orthodontist to assess if the nutritional risk falls within their scope of practice. Simple suggestions to improve food group intake or reduce the cariogenic potential of the diet are well within the realm of practice of the orthodontist. Patients may be surprised to be discussing nutrition and diet during an orthodontic visit. This is a good opportunity for practitioners to explain the importance of dietary choices during orthodontic treatment.

However, findings that indicate that there is a significant nutrition problem are usually beyond an orthodontist's scope of practice and indicate that a referral should be made. For example, if evidence is found of nutritional deficiencies or an underlying medical condition such as bulimia nervosa or diabetes mellitus, such conditions cannot be dealt with in the orthodontic setting. When trying to integrate nutrition counseling provided in the dental office along with performance, the biggest driving force for any healthcare initiative is insurance coverage. Despite very few states allowing for Medicaid reimbursement, dental insurance does not reimburse widely for nutrition counseling for the control and prevention of oral disease. Until insurance companies see the impact that diet has on oral health, dental professionals, understandably, may continue not to take the time out of their already

short appointment to address something that is financially not lucrative. The flow chart for nutrition assessment is provided in Figure 6.7.

Nutrition recommendations

If orthodontists assess that the nutritional needs of their patient fall into their scope of practice, the next step includes nutrition recommendations. While the focus of these recommendations is oral health, any recommendations should also be nutritionally sound. Incorrect recommendations are almost as harmful as no recommendations at all. For example, eating small frequent meals throughout the day may increase one's risk for cavities, but is important for an insulin-dependent diabetic to avoid hypoglycemia; the dilution of juice may decrease the total amount of sugar in your patient's diet, but does not necessarily decrease their risk for cavities. Once the recommendations have been discussed with the patient, the orthodontist should work with the patient to determine appropriate improvements in the form of goals. Goals should be small and should be set by patients and practitioners collaboratively. This ensures that patients are taking an active role in their treatment, increasing the likelihood of the patient achieving their goal.

Goals are important for moving the patient in the right direction. They should be customized to each patient and most pressing dietary habit modification. It is unrealistic to expect patients to make major or multiple changes immediately. The goals you set with your patients should be SMART goals. These are goals that are:

- **Specific** – set out exactly what your patient wants to achieve: instead of saying "I will eat more vegetables," say "Half my plate will be vegetables."
- **Measurable** – set a measurable outcome: "Half my plate will be vegetables at lunch and dinner."
- **Attainable** – make the goals patient directed to ensure they are achievable: "Half my plate will be vegetables at lunch and dinner, including the salad available at my local supermarket."
- **Realistic** – focus on what is a realistic change for your patient under the current circumstances: "Half my plate will be vegetables at lunch and dinner at least four days a week."

- **Timely** – include a time frame that will be used to follow up whether the goal has been met: “Half my plate will be vegetables at lunch and dinner for 3 weeks.”

Follow-up and reassessment

An important step in setting nutritional goals is the follow-up. Without follow-up there is no other way of assessing if the goals were achieved. Orthodontic appointments may happen frequently or every few months, but the orthodontist should document goals in the patient’s health records and follow up on how far the goal has been completed at each subsequent visit. Revisiting the SMART goals that were set at the previous appointment usually starts by asking patients if they believe they have made any progress with the dietary changes discussed during the last visit. Any successes should be celebrated, but if a patient shares that they were not able to meet their goals, it is best to try to understand from the patient what the barriers that prevented this change being met. Subjective and objective data can be collected once more to gain a more concrete understanding of any progress. Depending on the patient’s progress, the practitioner can provide reinforcement on dietary choices, or they can discuss barriers that prevent dietary changes from occurring. As a final step, the orthodontist should provide an updated plan for the patient based on the shared goal setting and a method to overcome the barriers to changes in health behavior.

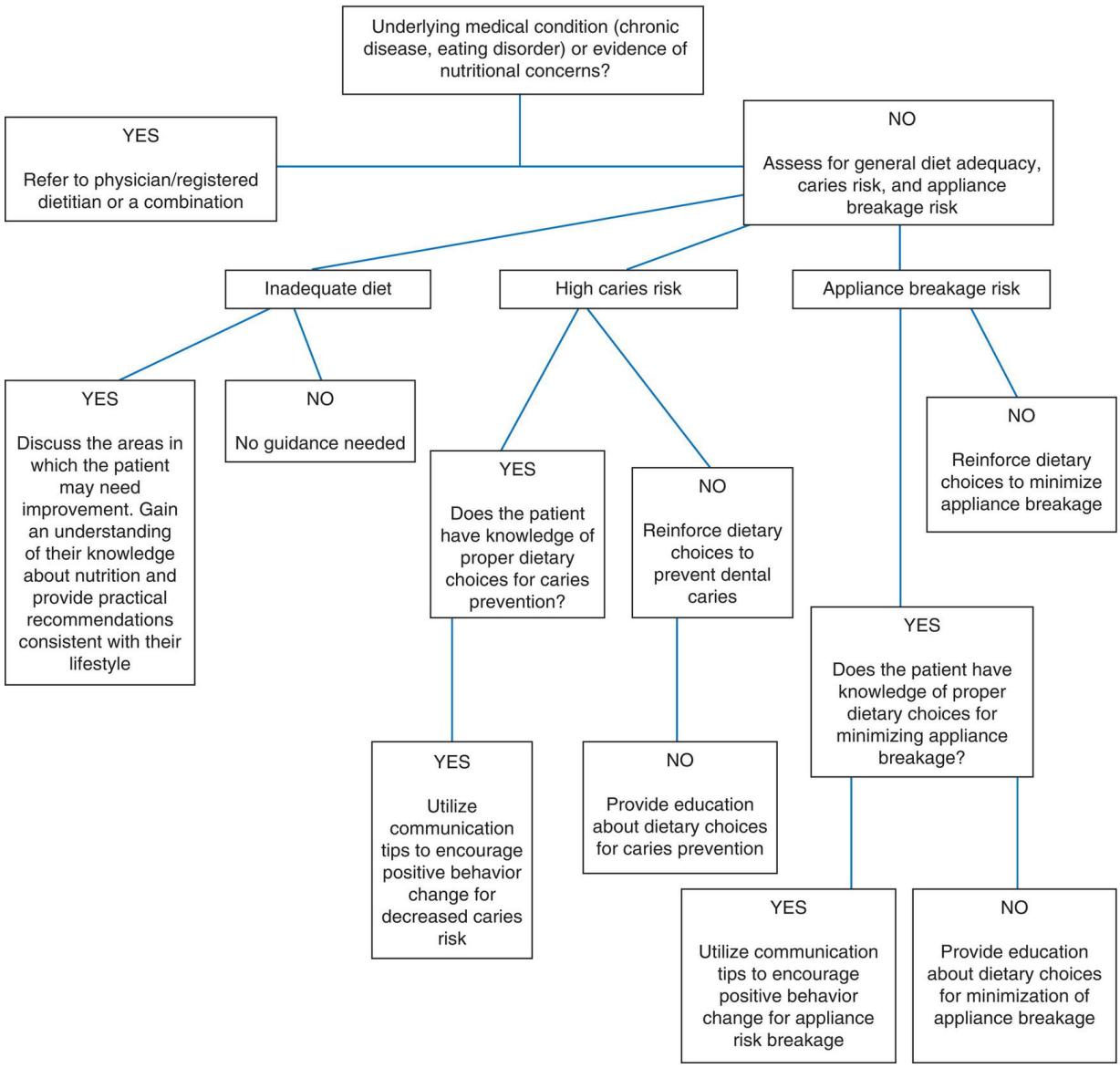

Figure 6.7 Flowchart for nutritional assessment.

Conclusion

Nutrition is an important factor to consider for all dental professionals, including orthodontists. Adequate nutrition allows for proper growth and development and a proper healing response to the orthodontic forces. Additionally, dietary patterns greatly influence dental caries risk and development of many chronic diseases, for example type 2 diabetes mellitus, both of which affect the health of the oral cavity. Life stage is another important consideration during orthodontic treatment. Children, adolescents, and adults come with different characteristic

eating patterns that may present challenges in the orthodontic setting. However, orthodontists must remember that every patient is an individual. Quick and simple dietary assessments can be used to evaluate individual eating patterns that may affect overall diet adequacy, caries risk, or appliance breakage risk – areas relevant to orthodontic outcomes. Then individual recommendations can be made to patients, utilizing effective communication strategies. Dental professionals also need to understand when to refer to dietitians, as well as understand the difference between a nutritionist and a registered dietitian, provide a list of additional resources on nutrition and oral health, dietary recommendations, and dietary supplements, and facilitate patient behavior change.

References

American Diabetes Association (2021). 2. Classification and diagnosis of diabetes: *Standards of Medical Care in Diabetes–2021*. *Diabetes Care* 44(Suppl 1): S15–S33. doi: 10.2337/dc21-S002.

Bailey, R.L., Fulgoni, V.L., Cowan, A.E. et al. (2018). Sources of added sugars in young children, adolescents, and adults with low and high intakes of added sugars. *Nutrients* 10(1): 102. doi: 10.3390/nu10010102.

Bhutta, Z.A., Berkley, J.A., Bandsma, R. et al. (2017). Severe childhood malnutrition. *Nature Reviews Disease Primers* 3: 17067. doi: 10.1038/nrdp.2017.67.

Bose, M., Bagga, D.K., and Agrawal, P. (2021). Managing nutrition but not damaging the orthodontic attachments: A consideration. *Annals of the Romanian Society for Cell Biology* 25(4): 586–590.

Cocco, F., Carta, G., Cagetti, M.G. et al. (2017). The caries preventive effect of 1-year use of low-dose xylitol chewing gum. A randomized placebo-controlled clinical trial in high-caries-risk adults. *Clinical Oral Investigations* 21(9): 2733–2740. doi: 10.1007/s00784-017-2075-5.

Edgar, W.M. (1993). Extrinsic and intrinsic sugars: A review of recent UK recommendations on diet and caries. *Caries Research* 27(Suppl 1): 64–67. doi: 10.1159/000261605.

EFSA Panel on Nutrition, Novel Foods and Food Allergens (NDA), Turck, D., Bohn, T. et al. (2022). Tolerable upper intake level for dietary sugars. *EFSA Journal* 20(2): e07074. doi: 10.2903/j.efsa.2022.7074.

Estrada, E., Eneli, I., Hampl, S. et al. (2014). Children's Hospital Association consensus statements for comorbidities of childhood obesity. *Childhood Obesity* 10(4): 304–317. doi: 10.1089/chi.2013.0120.

Featherstone, J., Crystal, Y.O., Alston, P. et al. (2021). A comparison of four caries risk assessment methods. *Frontiers in Oral Health* 2: 656558. doi: 10.3389/froh.2021.656558.

Feu, D. (2020). Orthodontic treatment of periodontal patients: Challenges and solutions, from planning to retention. *Dental Press Journal of Orthodontics* 25(6): 79–116. doi: 10.1590/2177-6709.25.6.079-116.sar.

Flegal, K.M., Carroll, M.D., Kit, B.K. et al. (2012). Prevalence of obesity and trends in the distribution of body mass index among US adults, 1999–2010. *JAMA* 307(5): 491–497. doi: 10.1001/jama.2012.39.

Gondivkar, S.M., Gadbail, A.R., Gondivkar, R.S. et al. (2019). Nutrition and oral health. *Disease-a-Month* 65(6): 147–154. doi: 10.1016/j.disamonth.2018.09.009.

Gong, W.J., Fong, D., Wang, M.P. et al. (2022). Late-onset or chronic overweight/obesity predicts low self-esteem in early adolescence: A longitudinal cohort study. *BMC Public Health* 22(1): 31. doi: 10.1186/s12889-021-12381-5.

Hasan, S., Ahmed, S., Panigrahi, R. et al. (2020). Oral cavity and eating disorders: An insight to holistic health. *Journal of Family Medicine and Primary Care* 9(8): 3890–3897. doi: 10.4103/jfmpc.jfmpc_608_20.

Huang, J.S., Becerra, K., Walker, E. et al. (2006). Childhood overweight and orthodontists: Results of a survey. *Journal of Public Health Dentistry* 66(4): 292–294. doi: 10.1111/j.1752-7325.2006.tb04087.x.

Ibrahim, M.K., Zambruni, M., Melby, C.L. et al. (2017). Impact of childhood malnutrition on host defense and infection. *Clinical*

Microbiology Reviews 30(4): 919–971. doi: 10.1128/CMR.00119-16.

Ilich, J.Z., and Kerstetter, J.E. (2000). Nutrition in bone health revisited: A story beyond calcium. *Journal of the American College of Nutrition* 19(6): 715–737. doi: 10.1080/07315724.2000.10718070.

Johnson, D.L., Gurenlian, J.R., & Freudenthal, J.J. (2016). A study of nutrition in entry-level dental hygiene education programs. *Journal of Dental Education* 80(1): 73–82.

Kandelman, D. (1997). Sugar, alternative sweeteners and meal frequency in relation to caries prevention: New perspectives. *British Journal of Nutrition* 77(Suppl 1): S121–S128. doi: 10.1079/bjn19970109.

Katsimbri, P. (2017). The biology of normal bone remodelling. *European Journal of Cancer Care* 26(6). doi: 10.1111/ecc.12740.

Leishman, S.J., Do, H.L., and Ford, P.J. (2010). Cardiovascular disease and the role of oral bacteria. *Journal of Oral Microbiology* 2. doi: 10.3402/jom.v2i0.5781.

Lin, J.A., Woods, E.R., and Bern, E.M. (2021). Common and emergent oral and gastrointestinal manifestations of eating disorders. *Gastroenterology & Hepatology* 17(4): 157–167.

Marcott, S., Dewan, K., Kwan, M. et al. (2020). Where dysphagia begins: Polypharmacy and xerostomia. *Federal Practitioner* 37(5): 234–241.

Moynihan, P., and Petersen, P.E. (2004). Diet, nutrition and the prevention of dental diseases. *Public Health Nutrition* 7(1A): 201–226. doi: 10.1079/phn2003589.

Najeeb, S., Zafar, M.S., Khurshid, Z. et al. (2016). The role of nutrition in periodontal health: An update. *Nutrients* 8(9): 530. doi: 10.3390/nu8090530.

National Cancer Institute (2022). 24-hour dietary recall (24HR) at a glance. https://dietassessmentprimer.cancer.gov/profiles/recall.

National Institutes of Health (2021). *Oral health in America: Advances and challenges*. Bethesda, MD: US Department of Health and Human Services, National Institute of Dental and Craniofacial Research.

Padayatty, S.J., and Levine, M. (2016). Vitamin C: The known and the unknown and Goldilocks. *Oral Diseases* 22(6): 463–493. doi:

10.1111/odi.12446.

Palmer, C., and Boyd, L.D. (2016). *Diet and Nutrition in Oral Health*, 3rd ed. New York: Pearson.

Paria, P., Patel, R., and Mehta, F. (2020). Role of nutrition and hormone in orthodontics. *Journal of Emerging Technologies and Innovative Research* 10(7): 2321–2325.

Phillips, J.A. (2021). Dietary guidelines for Americans, 2020–2025. *Workplace Health & Safety* 69(8): 395.

Phillips, S.M., Paddon-Jones, D., and Layman, D.K. (2020). Optimizing adult protein intake during catabolic health conditions. *Advances in Nutrition* 11(4): S1058–S1069. doi: 10.1093/advances/nmaa047.

Public Health Degrees (2023). Dietitian vs. nutritionist: Degree and careers comparison. https://www.publichealthdegrees.org/careers/become-registered-dietitian/dietitian-vs-nutritionist.

Romito, L.M. (2003). Introduction to nutrition and oral health. *Dental Clinics of North America* 47(2): 187–207. doi: 10.1016/s0011-8532(02)00096-4.

Saeedi, P., Petersohn, I., Salpea, P. et al. (2019). Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Research and Clinical Practice* 157: 107843. doi: 10.1016/j.diabres.2019.107843.

Satcher, D., and Nottingham, J.H. (2017). Revisiting oral health in America: A report of the Surgeon General. *American Journal of Public Health* 107(S1): S32–S33. doi: 10.2105/AJPH.2017.303687.

Schmitz, K.E., Liles, S., Hyman, A.N. et al. (2016). Youth receiving orthodontic care are not immune to poor diet and overweight: A call for dental providers to participate in prevention efforts. *Pediatric Dimensions* 1(3): 59–64. doi: 10.15761/PD.1000113.

Stanford, F.C., Lee, M., and Hur, C. (2019). Race, ethnicity, sex, and obesity: Is it time to personalize the scale? *Mayo Clinic Proceedings* 94(2): 362–363. doi: 10.1016/j.mayocp.2018.10.014.

Stanski, R., and Palmer, C.A. (2015). Oral health and nutrition as gatekeepers to overall health: We are all in this together. *European Journal of General Dentistry* 4(3): 99–105.

Stöhr, J., Barbaresko, J., Neuenschwander, M. et al. (2021). Bidirectional association between periodontal disease and diabetes mellitus: A systematic review and meta-analysis of cohort studies. *Scientific Reports* 11(1): 1–9.

Surgeon General (2000). Oral health in America: A report of the Surgeon General. *Journal of the California Dental Association* 28(9): 685–695.

Tanaka, K., Miyake, Y., Sasaki, S. et al. (2012). Dairy products and calcium intake during pregnancy and dental caries in children. *Nutrition Journal* 11: 33. doi: 10.1186/1475-2891-11-33.

Teeuw, W.J., Kosho, M.X., Poland, D.C. et al. (2017). Periodontitis as a possible early sign of diabetes mellitus. *BMJ Open Diabetes Research & Care 5*(1): e000326. doi: 10.1136/bmjdrc-2016-000326.

Touger-Decker, R., Mobley, C.C., and American Dietetic Association (2003). Position of the American Dietetic Association: Oral health and nutrition. *Journal of the American Dietetic Association* 103(5): 615–625. doi: 10.1053/jada.2003.50130.

World Health Organization (2021). Cardiovascular disease. https://www.who.int/en/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds).

Wright, S.M., and Aronne, L.J. (2012). Causes of obesity. *Abdominal Imaging* 37(5): 730–732. doi: 10.1007/s00261-012-9862-x.

Wu, X., Kirk, S.F., Ohinmaa, A. et al. (2016). Health behaviours, body weight and self-esteem among grade five students in Canada. *SpringerPlus* 5(1): 1099. doi: 10.1186/s40064-016-2744-x.

Yates, A.A., Schlicker, S.A., and Suitor, C.W. (1998). Dietary reference intakes: The new basis for recommendations for calcium and related nutrients, B vitamins, and choline. *Journal of the American Dietetic Association* 98(6): 699–706. doi: 10.1016/S0002-8223(98)00160-6.

Yeh, E.B., Barbano, D.M., and Drake, M. (2017). Vitamin fortification of fluid milk. *Journal of Food Science* 82(4): 856–864. doi:

10.1111/1750-3841.13648.

Zameer, M., Basheer, S.N., Anwar, N.G. et al. (2016). A study on nutritional status and tooth crown size among 6-9-year-old children: An observational cross-sectional study. *Journal of Forensic Dental Sciences* 8(3): 135–138. doi: 10.4103/0975-1475.195122.

7

Cleft Lip and Palate: Role of the Orthodontist in the Interdisciplinary Management Team

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Summary

The treatment of patients with cleft lip and palate (CLP) is a challenge. The principal role of the interdisciplinary CLP team is to provide integrated care for children with clefts, and to assure quality and continuity of patient care and longitudinal follow-up. The orthodontist has proven to be an essential partner in the cleft palate team, not only responsible for the orthodontic and facial orthopedic treatment, but, more importantly, also the guardian of the child's maxillofacial growth. By nature, orthodontists have a long-term treatment perspective in mind, which will assist the team in its consideration of treatment techniques, sequence, and timing, in relation to the effect on maxillofacial growth. Moreover, standardized records collected by the orthodontist provide a valuable basis for center audits, studies on treatment outcome, and intercenter comparisons. Finally, in recent times orthodontists seem to be quite often the motor behind large-scale intercenter randomized control trials in the field of CLP.

Cleft lip with or without cleft palate (CL ± P), and isolated cleft palate (CP) are serious birth defects that affect approximately 1 in every 600 newborn babies worldwide. Assuming that 15,000 children are born per hour worldwide, it means that approximately every 2.5 minutes a child is born with some form of an orofacial cleft somewhere in the world (World Health Organization, 2002).

It has been recognized for a long time that prevalence varies for the type of cleft, sex, population, and geographical location. Birth prevalence is not known for some parts of the world and the methods of ascertainment vary. In 2011, the International Perinatal Database of Typical Orofacial Clefts (IPDTOC), which was established in 2003, published the first results of a global study on the prevalence of cleft lip with and without cleft palate. The data covered at least one complete year during the period 2000–2005 from 54 registries in 30 countries all over the world. Data on a total of 7704 cases of CL ± P, including live births, stillbirths, terminations of pregnancy, and unknown pregnancy outcome, were available, resulting from a total of more than 7.5 million births. The overall estimate of the

prevalence of CL ± P turned out to be 9.92 per 10,000 (95% confidence interval [CI] 9.70 to 10.14); that of cleft lip was 3.28 per 10,000 (95% CI 3.15 to 3.41), and that of cleft lip and palate (CLP) 6.64 per 10,000 (95% CI 6.46 to 6.82). Just over three-quarters of the cases were isolated, 16% multi-malformed, and 7% occurred as part of recognized syndromes (IPDTOC Working Group, 2011). Overall, it is indicated that orofacial clefts occur in 1 in 700 live births (Mossey et al., 2009), and in low- and middle-income countries 1 in every 730 children is born with CL ± P (Kadir et al., 2017), although the latter study is hampered by deficient country data.

The healthcare burden of children with clefts and their families is high. Presently, the treatment history often starts with prenatal counseling of the expecting parents as soon as a CLP deformity of the fetus has been detected by ultrasound. Treatment continues from birth until maturity involving, among other actions, feeding counseling and clinical nursing, several surgeries to close the defect, genetic screening, speech and hearing assessments and management of middle ear infections, orthodontic and facial orthopedic management, speech interventions, psychological counseling, and dental and prosthodontic care.

There has been consensus since the early 1950s that children with clefts need comprehensive, coordinated care by an interdisciplinary team. The team should function as an organization with a general policy for the treatment, and each member of the team should understand and facilitate the different aspects of treatment. The team provides cleft care and usually includes specialists from the following disciplines: pediatrics and obstetrics, plastic and reconstructive surgery, orthodontics, genetics, social work and/or nursing, ear nose and throat (ENT), speech/language pathology, maxillofacial surgery, (prosthetic) dentistry, and psychology. Consultation with other medical and dental professionals should also be available, if needed.

The aim of the interdisciplinary treatment approach is to create the conditions that allow the affected child to grow up with an esthetically pleasing face, good hearing and speech, properly functioning and esthetically acceptable dentition, and, last but not

least, harmonious social-psychological development (Kuijpers-Jagtman, 2006).

Interdisciplinary team care

The principal role of the interdisciplinary CLP team is to provide patient- and family-centered, efficient, and effective, integrated care for children born with orofacial clefts in close collaboration with the patient and the parents, and to assure quality and continuity of patient care and longitudinal follow-up. Why do we need interdisciplinary teams instead of multidisciplinary teams? The distinction does seem to be quite arbitrary, but it is not so.

In multidisciplinary teams, specialists work together in a more or less loose connection, treating the various problems of the patient, but not within the framework of a mutually agreed treatment plan. Comparing interdisciplinary and multidisciplinary teams, Day (1981: 769) states: "A multidisciplinary approach can occur as a series of isolated evaluations by several disciplines and does not imply the merger of evaluative insights or the shared development of a treatment plan, which are the hallmarks of an interdisciplinary team." An interdisciplinary team, on the other hand, is one in which professionals from different disciplines are involved in conducting a joint evaluation and developing a treatment plan in which expertise is pooled and decision making is collective (Day, 1981; Strauss, 1999). It seems obvious that we should aim for the latter team format when treating children with orofacial clefts. Joint team consultations, where the patients are examined and discussed by all team members at the same time, are the backbone of well-functioning teams. The patient and the family are the leading figures in the team deliberations. These sessions might be confusing or even overwhelming for the patient and the family. This situation, however, can be prevented by structuring the consultations according to a strict protocol that the patient and the family after a while recognize as a routine, and by having the clinical nurse or social worker around all the time to reassure the family. The team coordinator or one of the other designated team specialists then serves at the end to summarize the session for the patient and the family, and to meet any other needs they might have.

The team coordinator and the team leader do not have to be the same person. The role of the team coordinator is to facilitate and coordinate the treatment plan, and to communicate it with the patient and the family (Strauss, 1999). The team leader oversees coordination of the activities of the team and the clinic; he or she monitors the functioning and decision-making process of the interdisciplinary team and represents the team in contacts with hospital management, health authorities, insurance companies, and patient support organizations. The medical or dental discipline of the team leader is less important than the ability to show leadership in getting the group to function as a team, and resolving slumbering conflicts between disciplines about boundaries and responsibilities.

Members of the cleft lip and palate team and their roles

Each patient seen by the team requires comprehensive, interactive treatment planning to achieve maximum habilitation, with efficient use of parent and patient time and resources. There is broad consensus on this premise and what a team should look like (Frederick et al., 2022). The American Cleft Palate-Craniofacial Association has described the team organization and the roles of the team members in a position paper on “Parameters for evaluation and treatment of patients with cleft lip/palate or other craniofacial anomalies” in 1993; the fifth (revised) edition dates from 2018. This is a useful document that is available to download from the website of the Association at https://acpacares.org. Recently, a Clinical Practice Guideline (CPG) on the treatment of patients with cleft lip, alveolus, and palate was developed in the Netherlands (Mink van der Molen et al., 2021). The objective was to optimize cleft care based on scientific evidence – if available – and to reduce practice variation between cleft teams, which makes the team approach more understandable for parents, patients, and healthcare professionals.

In what follows, the role of the team members is described according to the chronology in which they get involved in the treatment of a child with an orofacial cleft (Figure 7.1). Not all CLP teams have the same composition. National agreements, for example on regional distribution of cleft care around the country or on which

medical/dental discipline performs which operation, local spearheads, and scientific interests, may influence the composition of the team.

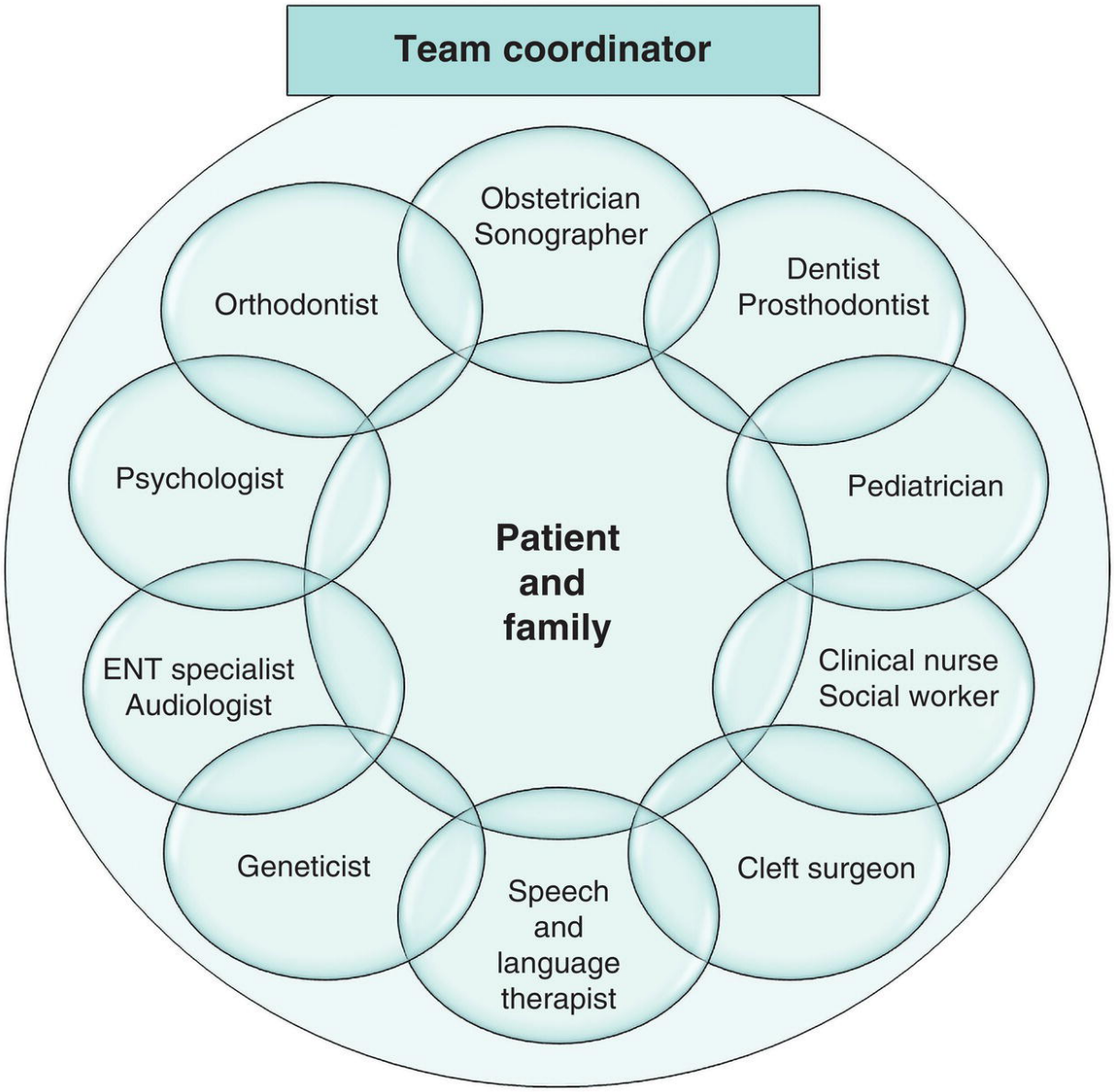


Figure 7.1 Participating specialists in the interdisciplinary team in a patient- and family-centered care setting.

Obstetrics

The first report on prenatal detection of a CLP deformity in two fetuses by transabdominal ultrasound was published by Christ and

Meininger (1981). Currently, almost all pregnant women receive routine ultrasound screening during their pregnancy. This examination usually involves two-dimensional (2D) ultrasound and is performed in a primary care setting. The problem is that transabdominal 2D ultrasound screening for orofacial clefts in a low-risk population has relatively low detection rates, ranging from 9% to 100% for CL ± P, from 0% to 22% for CP only, and from 0% to 73% for all types of clefts (Maarse et al., 2010). The favorable result of this finding is that it is associated with few false-positive diagnoses. If there is suspicion of a fetal anomaly, the woman should be referred for more advanced three-dimensional (3D) ultrasound imaging, which has, in high-risk women, much higher detection rates of 100% for cleft lip, and 86–90% for CLP. However, CP only is hardly detected on 2D ultrasound, and 3D ultrasound is also unable to arrive at a reliable diagnosis for CP only, as detection rates vary widely from 0% to 89% (Maarse et al., 2010).

Today, in our center, more than 60% of the expecting parents have received a prenatal diagnosis of their child and have been counseled accordingly. Detection of the facial cleft *in utero* by ultrasound has resulted in an established routine between the referring obstetrician and the CLP team for informing the parents of the deformity and the sequential steps necessary for its correction. The way of communicating the diagnosis, "breaking the news," and the quality of the information received at the time of diagnosis can considerably affect the long-term well-being of expecting parents, as well as their attitudes toward the diagnosis, further antenatal testing, and even pregnancy termination (Stock et., 2019a). Due to unsatisfactory information and a perceived lack of empathy from health professionals, respondents reported feeling upset, offended, and/or anxious following the diagnosis (Stock et al., 2019b). Expecting parents need to be aware that a negative ultrasound result does not necessarily mean that their unborn child is without an orofacial cleft (Maarse et al., 2010).

Pediatrics

The pediatrician is an essential part of the CLP team, providing initial diagnosis and referral, close monitoring of the day-to-day

medical issues including immunizations, management of growth (particularly for infants who have difficulty with feeding and weight gain), treatment of acute ear infections, assessment of development, and family support (Kasten et al., 2008). More importantly, CL ± P may occur in association with other congenital malformations. In a Swedish study, 21% of the infants with clefts had associated malformations that required follow-up treatment. A systematic review regarding associated developmental defects that included 13 studies with postnatal data revealed that the prevalence of associated anomalies was lowest in babies with a cleft lip (7.6–41.4%; Maarse et al, 2012). A more extensive cleft seems to be associated with a higher risk for associated malformations (for CLP 21.1–61.2%). However, girls with CP only, which has a different embryological origin, showed the highest percentage of associated anomalies (22.2–78.3%; Maarse et al., 2012).

Clinical nursing and/or social work

The clinical nurse or social worker is the vital link between the CLP team and the parents and child. He or she guides them through the treatment process from birth until maturity, or sometimes even earlier if playing a role in the prenatal counseling. Because many children have difficulties nursing from a breast or bottle, the clinical nurse is there to assist the parents directly after birth regarding feeding issues, and to provide psychological support for the parents to deal with acceptance of their child with a deformity. The clinical nurse assumes the role of “case manager,” organizing and coordinating services throughout the clinical pathway followed by the patient, serving as a walking encyclopedia for questions from the family and the patient. In our experience, the availability of advice and counseling by phone or through a protected online environment is very helpful, but sometimes home visits are necessary.

The clinical nurse or social worker will organize, if needed, contacts with social and vocational rehabilitation services, insurance companies, schoolteachers, and governmental support systems (Frederick et al., 2022).

Surgery

Anatomical defects of the lip, oral cavity, nose, pharynx, and upper airway need surgical reconstruction to restore function, facial esthetics, speech, and hearing (Frederick et al., 2022). Children with a complete unilateral or bilateral cleft undergo at least three surgical interventions: cleft lip repair, hard and soft palate repair, and alveolar bone grafting. Additional secondary surgery may be needed for velopharyngeal incompetence, skeletal discrepancies, lip revision, and nasal deformities. Table 7.1 gives an overview of one center's treatment plan and timing of interventions. It should be realized that large variation exists between centers, as there is no approved "superior" schedule. It depends on national agreements and from which discipline the surgeon who is performing these operations originates. Possibilities are maxillofacial surgery, and/or plastic and reconstructive surgery, and/or otorhinolaryngology.

The experience and skills of the surgeon seem to be a major issue in achieving a good treatment outcome. Results from the EUROCLEFT study suggest that decentralized care and low-volume surgeons are associated with low-quality treatment results (Shaw et al., 1992a, 1992b). These findings induced the Clinical Standards Advisory Group (CSAG) study in the UK in 1998 that confirmed the poor outcomes of cleft care in the country (Bearn et al., 2001). Eventually, the UK government took the decision to reduce the number of cleft centers from 57 to 16 that function as managed clinical networks (Sandy et al., 2020). A follow-up study, performed in 2013 and known as the CCUK (Cleft Care United Kingdom) study, showed that centralization of cleft care was indeed associated with better outcomes for facial and dento-alveolar variables (Al-Ghatam et al., 2015). This finding emphasizes the great importance of centralized care for children with clefts.

Orthodontics

The orthodontist has an active role in the interdisciplinary care of children with orofacial clefts, from birth until they become adults. Longitudinal evaluation, including standardized follow-up documentation, and record taking to provide a general overview of

treatment outcomes are in the hands of the orthodontist. Five distinct stages of orthodontic mechanotherapy can be distinguished. A detailed description of these stages is provided later in the chapter.

Genetics

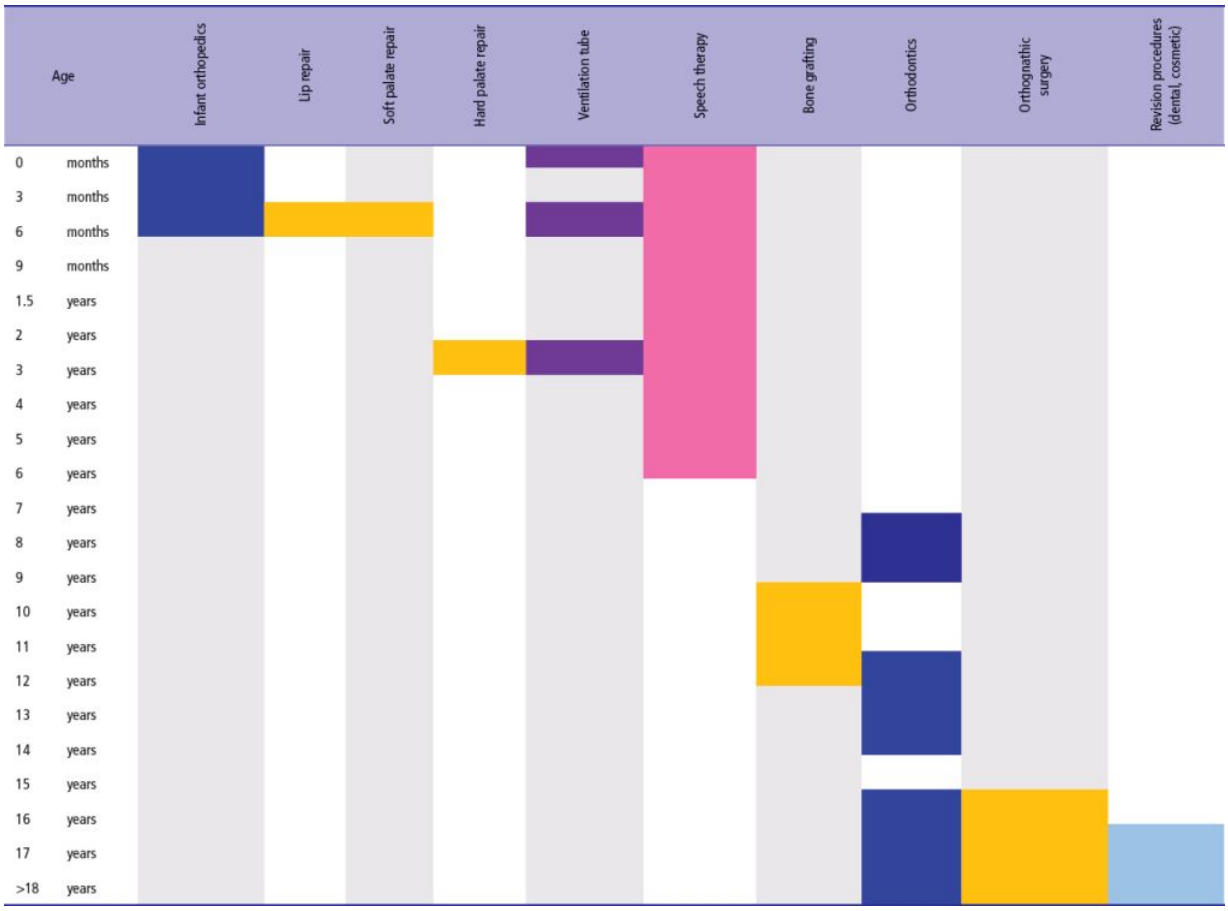
Genetics is becoming increasingly important in the search for the etiology of orofacial clefts, and therefore the role of the clinical geneticist in the CLP team increases as well. All parents expecting a child who has been diagnosed prenatally as having a cleft with associated anomalies should be counseled antenatally by the clinical geneticist. About 3–6 months after birth, all children with clefts are examined by the clinical geneticist, preferably before their first operation (Mink van der Molen et al., 2021). This timing is important, as not all associated congenital malformations may manifest at birth. However, when growth problems or developmental delay with associated abnormalities become manifest, and a syndrome diagnosis or chromosomal abnormality is suspected, earlier genetic examination is recommended (Mink van der Molen et al., 2021). Parents are also counseled about the risk of having another child with a cleft. Over the years we have learned that adults with CLP who were treated by the team return with questions about their own risk of having a child with a cleft.

ENT and audiology

The ENT specialist and audiologist are responsible for the audiological and otological management of children with clefts. The association of the presence of a CP with middle ear effusion is widely recognized (Hubbard et al., 1985; Gani et al., 2012). CP may lead to disruption of the tensor veli palatini muscle, which plays a role in the function of the Eustachian tube. Dysfunction of the Eustachian tube increases the risk of serous otitis media and more than 90% of patients with CP have middle ear effusions. Placement of ventilating tubes (grommets) is frequently utilized. Increasing evidence suggests the benefits of grommets for speech and language development in CLP children with otitis media with effusion (Kuo et al., 2014). Some children require multiple sets of tubes, and there is increased risk of persistent hearing loss. The ENT specialist is responsible for

prescribing hearing aids when necessary, and may also address issues of tonsillar and adenoidal hypertrophy, sinusitis, nasal abnormalities, and nasal obstruction (Kasten et al., 2008).

Table 7.1 Overview of a center's treatments and timing of interventions from birth to adulthood. Colors indicate the different specialists. A large variation between centers exists as there is no approved "superior" schedule.



Speech-language pathology

A speech-language pathologist, specialized in CP speech, is indispensable in a CLP team. Children with CLP are at a higher risk for speech disorders, and to a lesser degree for language disorders. The speech disorders in children with orofacial clefts concern articulation, phonation, and resonance disorders, primarily hypernasality. The speech-language pathologist treats communication disorders and contributes the necessary information

to the team when surgical interventions are considered to improve speech. Careful planning of orthodontic treatment in relation to speech therapy is also needed, as certain developmental stages of the dentition and some orthodontic appliances interfere with speech therapy. The speech-language pathologist is heavily involved in the care of children with clefts during the first nine years of life. After that age, most speech problems have already been solved. In some teams the speech therapist also serves as a lactation consultant or feeding expert; in others this is the role of the clinical nurse.

Dental care

Caries is often a problem in children with CL ± P. They have more decayed, missing, or filled teeth/surfaces than noncleft controls, in both the deciduous and the permanent dentition (Abirami et al., 2022). The pediatric dentist of the team plays an important role in implementing caries prevention strategies for the child with an orofacial cleft. Routine dental care should be provided by the family dentist, in close contact with the CLP team. As many children with orofacial clefts have a suboptimal oral hygiene, an oral/dental hygienist could assist the dentist and the orthodontist in maintaining good oral hygiene through the years of orthodontic treatment. The prosthodontist is responsible for replacement of missing teeth, and embellishment of abnormally shaped teeth, as an adjunct to the orthodontic and surgical treatment plan. Therefore, the prosthodontist always works in close collaboration with the orthodontist and, eventually, the surgeon.

Psychology

Last, but not least, the psychologist is mentioned as an important team member. When a child with a cleft is born, at first the parents experience psychological distress and the event will have an impact on the family (Stock et al., 2020; Sagar and Sahu, 2022). For some children psychosocial support is never needed, while others have numerous psychological and social problems. Living with a facial disfigurement is not easy, as the deformity is always visible and may be hampered by speech and hearing difficulties. This may have a severe impact on the well-being of the child. Moreover, teasing and

social rejection at school and by peers can grow into a severe problem that needs to be addressed professionally. Fostering psychosocial adjustment, positive self-esteem, and healthy social skills are objectives that should be met by the team treatment (Sagar and Sahu, 2022).

Orthodontic management

The orthodontist is actively involved in the life of a child born with a cleft, from birth until maturity. Shortly after birth, the child with a cleft is seen by the CLP team, more in particular by the pediatrician, clinical geneticist, plastic surgeon, and orthodontist, and, if available, also by the social worker or clinical nurse of the team. From then on, each patient is treated according to the overall comprehensive treatment plan that has been established by the team.

The orthodontic procedures focus on monitoring craniofacial growth and development, and on correcting jaw relationships and dental occlusion, in order to achieve optimal function and appearance (Kuijpers-Jagtman, 2006; Santiago and Grayson, 2009; American Cleft Palate-Craniofacial Association, 2018; Kharbanda, 2022). The orthodontic and dentofacial orthopedic treatment of a child with a complete unilateral or bilateral cleft takes many years, and the challenge for the orthodontist is to avoid continuous active orthodontic intervention from birth to the age of permanent dentition. Children become bored of endless treatment and may develop serious compliance problems. Therefore, it is wise to distinguish well-defined treatment courses and try to keep some "orthodontics-free" time in between. For the description of the orthodontic management of patients with CLP in this chapter, three periods of orthodontic management are distinguished: from birth to 7 years of age, from 8 to 15 years, and from 16 years of age into adulthood.

From birth to 7 years of age

At the first visit to the team a clinical examination is performed, while concomitant medical conditions of the child are also taken in consideration (Worley et al., 2018). Together with the parents, an

initial holistic treatment plan is made. The short-term goals are supporting the family to overcome psychological or social distress, solving eventual feeding difficulties, and reconstructive surgery of the lip and/or the palate, while infant orthopedics can precede the surgical closure of the lip.

Baseline documentation is then created, consisting of frontal, right, and left lateral facial views, a close-up of the lips, and a worm's-eye view (a view of the patient's face from below). It is quite difficult to make standardized pictures of young toddlers. It is easier to photograph them lying down, at least until the age of 6 months when they begin to sit up by themselves. A palatal intraoral view could be obtained in the operating room. The Institute of Medical Illustrators of the UK has developed an excellent illustrated guideline for photography of patients with clefts, which can be downloaded from its website (lnstitute of Medical Illustrators, 2021).

3D stereophotogrammetry images have the advantage that they produce a 3D image of the deformity, which allows for sophisticated quantitative analysis of the face in three dimensions and does not require ionizing radiation (Brons et al., 2019b; Kuijpers et al., 2022). However, in our experience such images are difficult to obtain before the age of 3 months, despite the very short capture time, as head balance has not developed before that time and the parents need to hold the child's head, which may disturb the facial soft tissues. Furthermore, it is impossible to ask a baby to keep a neutral facial expression (Brons et al., 2019a).

A baseline maxillary dental cast of the unoperated cleft condition has been proven to be very helpful for later ascertainment of the exact diagnosis for research purposes. Due to the risk of respiratory obstructions resulting in cyanotic events or worse, maxillary impressions should only be taken by an orthodontist who is experienced in impression taking in cleft-affected babies. The maxillary impression could be made just prior to the lip repair in the operating room (Figure 7.2). Digitization of the plaster casts will facilitate measuring models and long-term storage. Currently, digital impression taking using intraoral scanning of babies seems to be a promising technique that is far more child and parent friendly than taking impressions (Benitez et al., 2022; Weise et al., 2022).

Unfortunately, the size of the scanner tip is often too big to reach easily behind the maxillary tuberosities in a newborn, as these scanners were developed for adult use (Figure 7.3). However, it will be a matter of time before scanners come onto the market with a smaller scanner tip.

In most centers, the first surgical intervention for a child with CL ± P is surgical repair of the lip, followed a couple of months later by palatal repair. To date this is a highly controversial issue and no consensus exists among centers. After the infantile period, the CLP team follows the child on an annual basis. Speech and hearing are the main issues during this period.

Neonatal maxillary infant orthopedics

Whether neonatal maxillary infant orthopedics will be part of the treatment plan prior to surgical repair of the lip depends on the treatment protocol of the team. Ever since its introduction by McNeil (1950), it has been a controversial issue. In Europe, about 54% of the operational centers used infant orthopedics (Shaw et al., 2000), while in the USA this approach has always been less popular.

Basically, infant orthopedics aims at molding the alveolar segments into the correct anatomical position, to facilitate lip repair by an intraoral acrylic appliance. Later on, the orthodontic discipline tried to justify early intervention for other reasons. Kuijpers-Jagtman and Prahl (2013) summarized the arguments of the proponents of the use of infant orthopedics, who state that this approach allows a more normalized pattern of deglutition while preventing twisting and a dorsal position of the tongue in the cleft, improves the arch form and position of the alar base, facilitates surgery, and improves outcome in general. Other alleged benefits that became *en vogue* are reduction of posterior cleft width, prevention of initial collapse after surgery, prevention of crossbites, straightening of the nasal septum, facilitation of feeding, reducing the danger of aspiration, improving speech development, nose breathing, reducing the severity and frequency of middle ear conditions, the extent of orthodontic treatment at later ages, and creating a positive psychological effect in the parents (Kuijpers-Jagtman and Prahl, 2013). Most of these benefits could not be substantiated by scientific evidence, however,

as demonstrated in several systematic reviews (Papadopoulos et al., 2012; Hosseini et al., 2017).

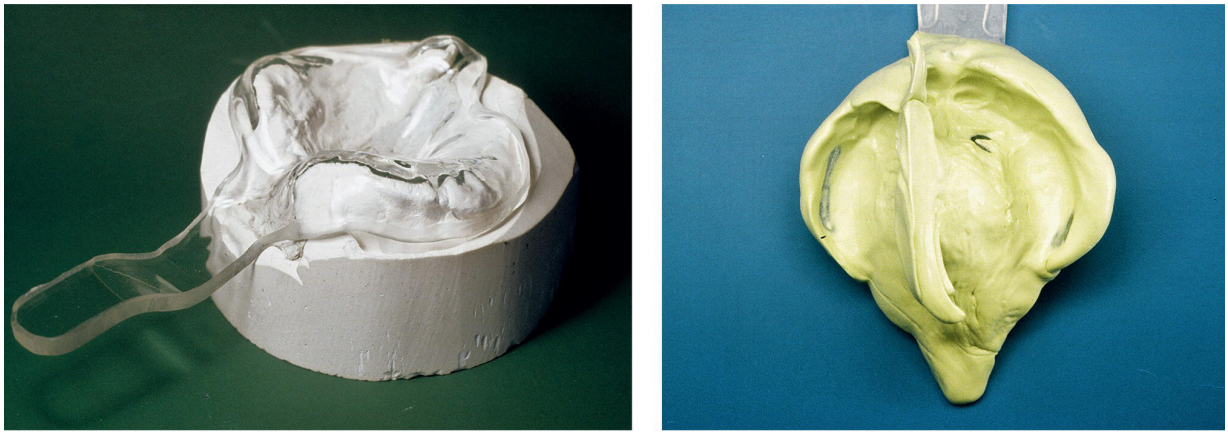


Figure 7.2 (a) Custom made baby impression tray for unilateral cleft lip and palate. (b) Baby impression with an elastomeric material.

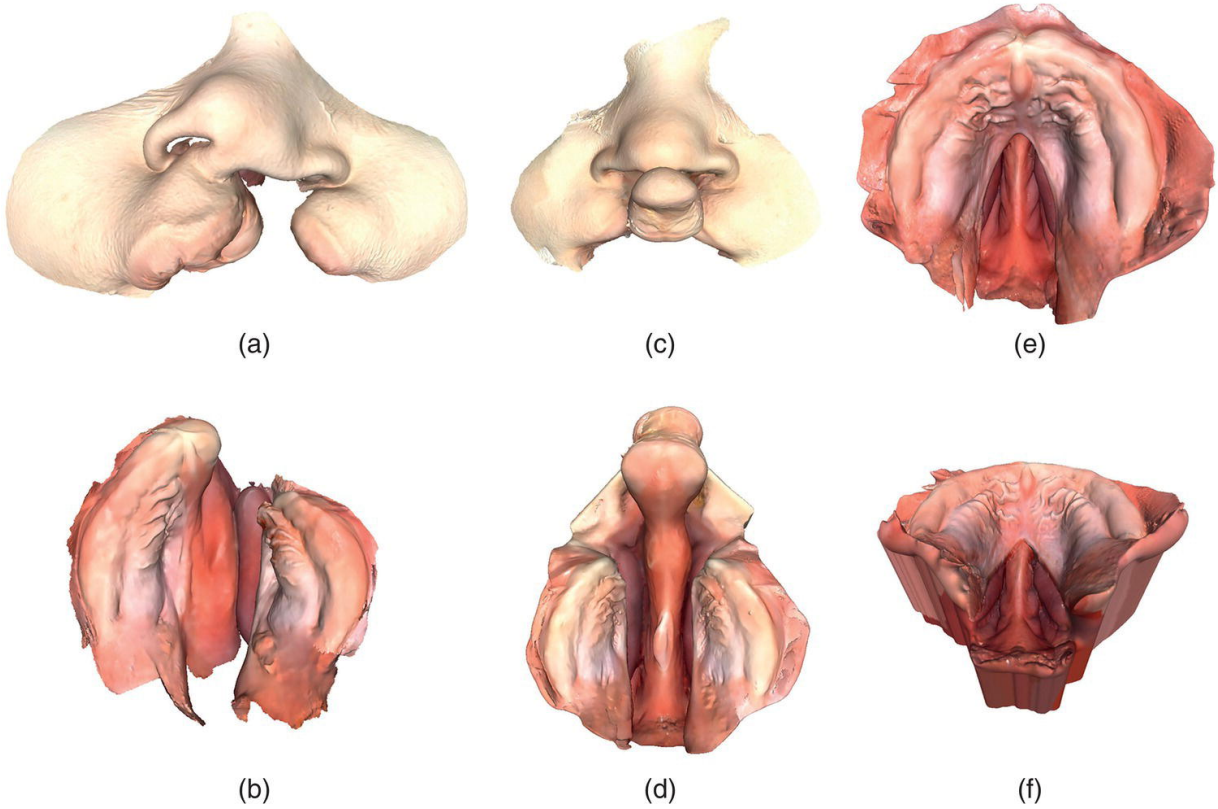


Figure 7.3 Extraoral digital scans of the nose and lip as well as intraoral digital scans of the cleft palate in infants with (a, b) unilateral cleft lip and palate; (c, d) bilateral cleft lip and palate; (e, f) cleft palate only.

Source: Benitez et al. (2022) / ELSEVIER / CC BY 4.0.

A wide range of appliances has been designed for these purposes, with pin-retained active appliances at one side of the spectrum (Georgiade and Latham, 1975) and passive appliances at the other side (Hotz and Gnoinski, 1976). Arbitrarily, they fall into three main categories: active, semi-active, and passive appliances (Kuijpers-Jagtman, 2006). *Active* appliances are constructed to apply a force to the maxillary segments, to move them in the desired direction by using an active force delivery system, like springs and screws. Additional anchorage can be obtained by pins that are driven into the maxillary bone holding the plate in position. *Semi-active* appliances are constructed by sectioning the dental cast and reorienting the maxillary segments into a more favorable position. The plate is fabricated on the reconstructed cast and forces the palatal segments in the predetermined direction when placed in the oral cavity (Figure 7.4). External strapping across the cleft can be part of the treatment protocol. These are the McNeil (1950) type of appliances. *Passive* appliances that are combined with extraoral strapping also fit into this category. They are supposed to induce arch alignment during growth by grinding away acrylic material in definitive areas of the plate, to ensure proper spontaneous development of the segments. The plate is held in position by suction and adhesion only, and no extraoral strapping is applied. The so-called Zurich approach is the best-known representative of this kind of neonatal maxillary orthopedic device (Hotz and Gnoinski, 1976).

Many different techniques for infant orthopedics have been described (for an overview, see Monga et al., 2022), and therefore it is difficult to compare treatment results. More importantly, treatment for a cleft patient consists of more than infant orthopedics alone. All treatment steps may have an influence on the final treatment outcome, and it is impossible to separate these steps when comparing results in retrospective research (e.g. Ross, 1987; Mølsted et al., 1992). So far, to our knowledge only two randomized control trials (RCTs) have been performed in this field, one in the Netherlands and one in India (Shetty et al., 2017; Garland et al. 2022). From the six-year results of the Dutch three-center trial, named DUTCHCLEFT, it can be concluded that infant orthopedics in children with a complete unilateral CLP (UCLP) with a passive appliance, as performed in this trial, is not necessary for the feeding

and nutritional status of the child, parents' satisfaction (Prahl et al., 2005), facial appearance (Bongaarts et al., 2008), facial growth (Bongaarts et al., 2009), or orthodontic reasons (Bongaarts et al., 2004, 2006). Regarding speech, a positive but very limited effect was found until the age of 2.5 years, but the speech of children with clefts remained far behind that of their noncleft peers anyway (Konst et al., 2000, 2003). Relative to the total costs of the treatment of a UCLP patient, the financial investment to reach this effect was rather limited (Konst et al., 2004). However, it is questionable whether this limited effect is important enough to justify infant orthopedics, while it should also be taken into consideration that the six-year results for speech have not been analyzed. The last publication on the results of this comprehensive RCT was in 2015 and regarded the transverse dental arch relationship until 12 years of age (Noverraz et al., 2015). No differences between the groups with or without infant orthopedics were found. The second RCT was performed in India and compared presurgical nasoalveolar molding (PNAM) starting at three different time points after birth, which is a different type of infant orthopedics that will be discussed later in the chapter (Shetty et al., 2017).

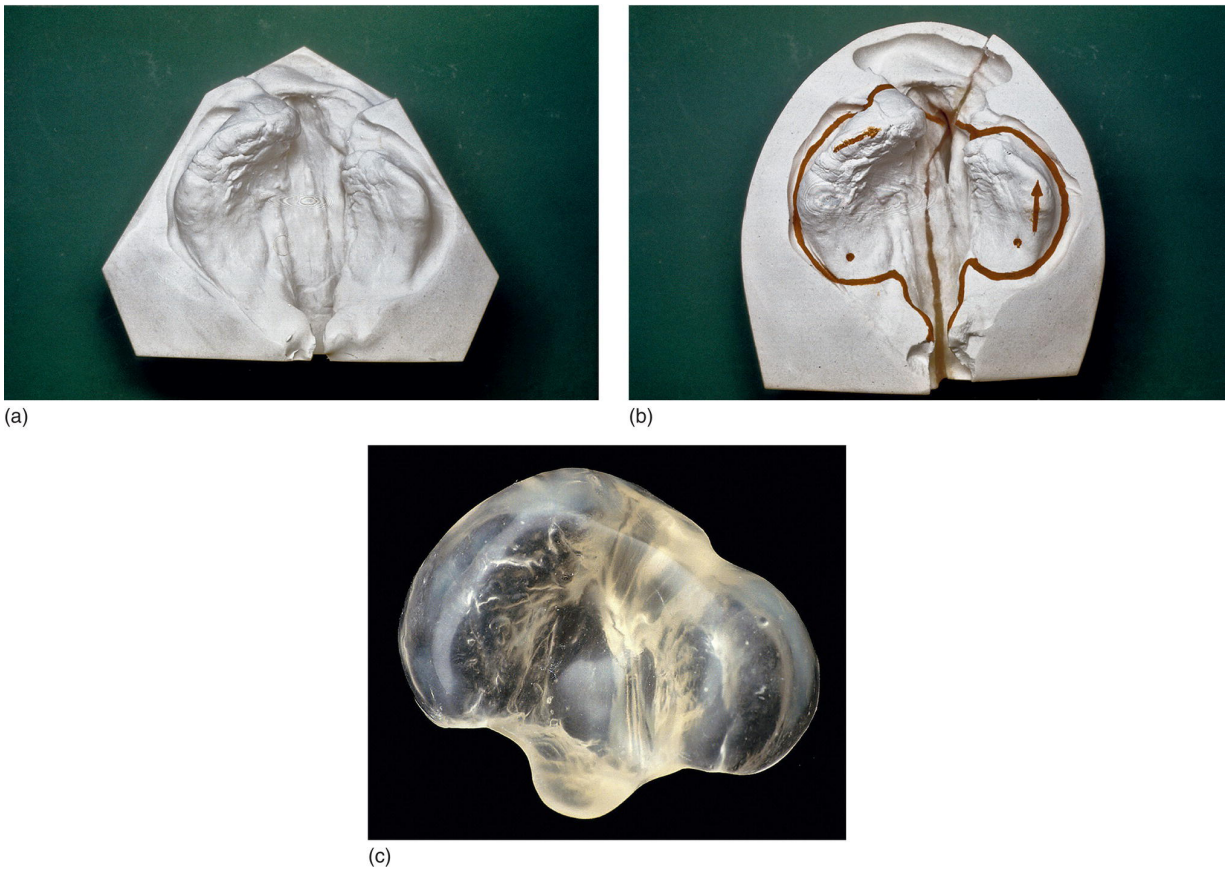


Figure 7.4 (a) Dental cast of the maxillary arch. (b) Sectioned dental cast with reoriented maxillary segments in a more favorable position. The plate is fabricated on the reconstructed cast. (c) Semi-active intraoral appliance that gently forces the palatal segments into the predetermined direction when placed in the oral cavity.

For children with bilateral clefts, no evidence-based data from RCTs are available about the effect of infant orthopedics. Based on clinical experience, it can be stated that with the therapy, good alignment of the maxillary segments can be obtained, which facilitates closure of the lip in one operation. An easier approach is preoperative lip taping only, without an intraoral appliance, which could also assist in reducing a prominent or deviated premaxilla and is also occasionally applied in wide unilateral clefts. Steri-Strips™ (3M, Saint Paul, MN, USA) or specially designed commercially available strips can be used for this purpose.

A special type of infant orthopedics that has emerged during the past three decades is nasoalveolar molding (NAM). There is a distinct

difference between the types of infant orthopedics described previously and the one that has been developed by Grayson and Cutting (Grayson et al., 1993; Cutting et al., 1998; Grayson and Cutting, 2001; Barillas et al., 2009). In the latter method, nasal stents are added to the molding plate. This appliance aims to address correction of the nasal deformity; that is, to improve nasal tip projection, and septal and lower lateral cartilage position, before cleft repair (Figure 7.5). NAM was developed to facilitate the surgical reconstruction, and primary lip surgery combined with gingivoperioplasty and rhinoplasty in the hands of an experienced surgeon are essential. In a two-center retrospective study comparing rotation advancement only (Iowa) or NAM and rotation advancement plus primary rhinoplasty (New York), less nasal asymmetry was found in the latter patients (Hosseinian et al., 2018). In bilateral CLP, the nasal stents can be used to gradually lengthen the deficient columella. The molding plate itself is mainly used to approximate the alveolar segments, to reduce the nasal deformity to a degree that enables the start of more precise nasal molding with stents (Grayson and Maull, 2006; Santiago and Grayson, 2009). Weekly or biweekly visits to the cleft orthodontist are needed to adjust the appliance.

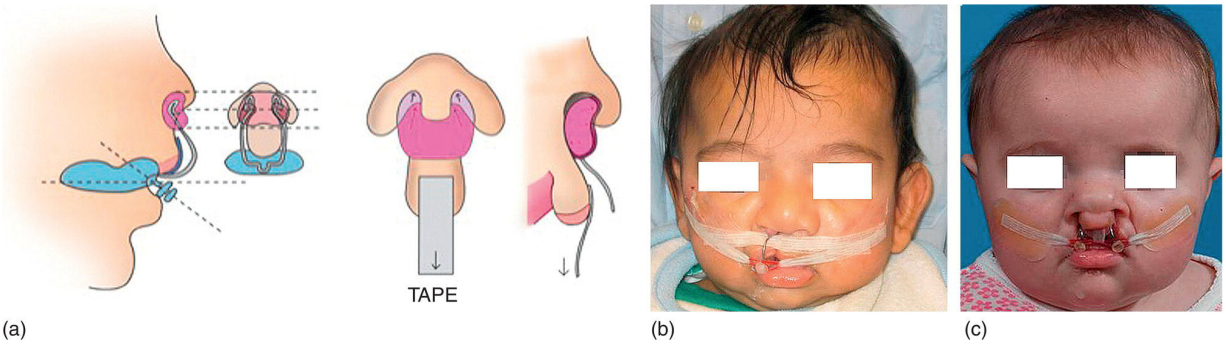


Figure 7.5 (a) Schematic drawing of a nasoalveolar molding (NAM) appliance for bilateral cleft lip and palate (BCLP) showing two nasal stents and tape adhered to the prolabium, stretched to the plate, and attached to the appliance. (b) NAM appliance for unilateral cleft lip and palate. (c) NAM appliance for BCLP.

Source: Shetty (2017) / with permission from Elsevier.

Although NAM has become very popular in the USA and in some Asian countries, it remains one of the most debated treatment

procedures in the whole treatment journey for a child with CLP, not least because of the burden of care and the costs. So far, the scientific evidence for long-term benefits of nasoalveolar molding is still weak, as can be concluded from several systematic reviews since 2011, the most recent published in 2022 (Garland et al. 2022; Padovano et al., 2022). RCTs into the short- and long-term benefits of nasoalveolar molding are needed to get an answer (Mink van de Molen et al., 2021).

Treatment during the early mixed dentition period

The development of the deciduous dentition, the presence of anterior and/or posterior crossbites, oronasal fistulae in the palate, and midfacial growth are the major concerns of the orthodontist during patients' annual team visits.

The early mixed dentition period starts with the emergence of the first permanent molars. In patients with an operated CP, special attention should be given to the first molars, as it happens quite often that their eruption pattern is directed mesially. The permanent molars are disturbed in their eruption pattern and become entrapped underneath the bulging distal surface of the second deciduous molars, leading to premature distal resorption of the maxillary second deciduous molars. The reason for this undesirable development is probably the scar tissue in the region of the tuberosities, due to the surgical palatal repair. Distal movement with a simple orthodontic device (two brackets and an opening coil) or extraction of the deciduous molars may be required in these cases.

The permanent incisor next to the cleft nearly always erupts into a rotated position. This rotation may cause a functional lateral shift of the mandible. In patients with a UCLP, the smaller segment often has a tendency to a crossbite at the deciduous canine and the first deciduous molar, which may lead to a mandibular shift. Another reason for a mandibular shift is a developing midfacial retrusion, with an end-to-end incisor relationship, resulting in an anterior posturing of the mandible. It is not always possible to correct a rotated incisor at this stage, as the root of the tooth is located very close to the alveolar cleft. Early orthodontic correction could move the incisor in the cleft space. Then it would be better to wait and

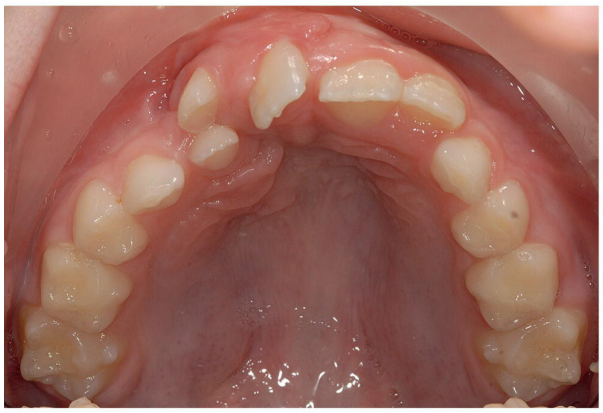
align the incisors after bone grafting of the alveolar cleft at the age of 8–10 years. A posterior crossbite with mandibular shift can be easily corrected with a removable appliance with a fan-shaped expander screw. This appliance rotates around a posterior hinge, resulting in a differential expansion, more in the front than in the back (Figure 7.6).

Large oronasal fistulae in the palate can cause hypernasal speech, as air can escape through the nose and create nasal regurgitations. During the team consultation, the speech pathologist provides the team members with the necessary information to support decision making regarding surgical or orthodontic management at this stage. If it is decided to cover the fistula temporarily, the orthodontist will make a “speech plate” covering the palate.

Developing maxillary deficiency

Despite careful monitoring of maxillary growth, midfacial retrusion remains a common finding in operated CLP patients (Figure 7.7). Delaire and coworkers (1978) have laid down the theoretical basis for the clinical application of maxillary protraction in patients with severe maxillary deficiency. Since then, numerous case reports and case series studies have been published, a majority being concerned with noncleft individuals with Class III malocclusions (Tindlund, 2006).

(a)



(b)

(c)

Figure 7.6 (a) Anterior and lateral crossbite in a patient with right-sided unilateral cleft lip and palate in the mixed dentition (age 8.2 years). (b) Occlusal view of the maxillary arch. (c) Expansion device with a fan-shape expander screw and hinge, resulting in a differential expansion, more in the front than in the back. The appliance has springs in the front to correct the anterior crossbite.

Orthopedic forces to the maxillary complex are assumed to be more effective at an early age – that is, in the deciduous and early mixed dentition periods (Tindlund, 2006) – taking into consideration the patency of the circummaxillary sutures. However, no comparative, well-controlled studies on timing of maxillary protraction in patients with CLP could be found. In a noncleft sample, comparing the result of maxillary protraction started between 5 and 8 years of age and between 8 and 12 years no difference in maxillary skeletal response was found, but the vertical response was greater in the older age group (Merwin et al., 1997).

Most of the more recent studies in patients with CLP have been conducted in Bergen, Norway, but the results published cover only a three-year period after maxillary protraction (Tindlund, 2006). Since 1977, the Bergen rationale has involved transverse expansion, anterior protraction to a tooth-borne device (either a quad-helix or a bonded maxillary plate), and fixed retention at the age of 6–7 years. The treatment procedure is assumed to normalize orofacial function and dimensional anatomy, in order to reduce detrimental functional disturbances during further growth. A significant increase of the SNA angle of 0.9° was found, together with a clockwise rotation of the mandible and an increase in lower facial height. As a result, a mean change of 2.3° in the ANB angle was found. However, the treatment response was highly variable. The short-term effect of maxillary protraction was found to be a maxillary skeletal/dentoalveolar effect, according to a ratio of 45%/55% in UCLP and 10%/90% in bilateral CLP (Tindlund and Rygh, 1993). The changes were reflected in the soft tissue profile as a mild increase in nose prominence and upper lip protrusion, as well as a reduction in lower lip and chin protrusion. During a three-year follow-up period the initial growth pattern reappeared, but the upper jaw position remained stable. The maxillo-mandibular relationship was impaired because of the normal downward and forward growth of the mandible, while the maxillary position relative to the anterior cranial base remained constant. Although the effect on the soft tissue profile had diminished, some positive effect remained (Tindlund, 2006). The results of the Bergen studies have been generally confirmed by studies from a limited number of centers around the world, but mainly short-term results have been published. Clinical experience showing that the long-term effect was disappointing and surgical advancement of the maxilla after puberty was still needed has now meant that the early protraction therapy has been mainly abandoned. Meanwhile, new treatment possibilities came onto the market using bone anchorage to protract the maxilla in the late mixed dentition and early permanent dentition, which will be described in the following.

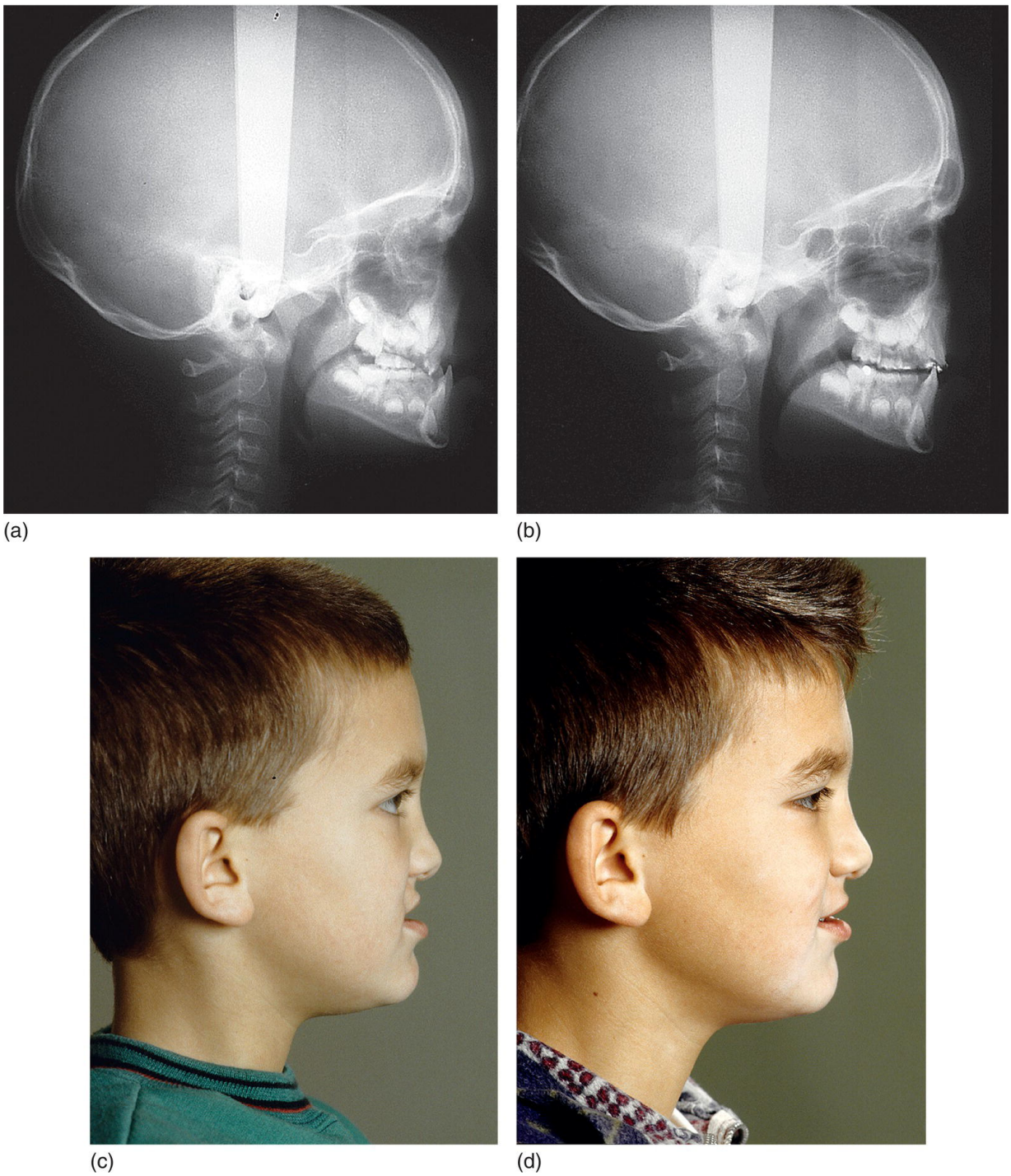


Figure 7.7 (a) Pretreatment and (b) posttreatment lateral cephalogram and (c) profile photograph of a patient. (d) During adolescence the unfavorable growth pattern reappeared and the patient had a Le Fort I osteotomy after growth had ceased.

From 8 to 15 years of age

The CLP team continues to follow the patient on an annual basis and closure of the alveolar cleft with an autologous bone graft is the next surgical intervention at this stage. Again, this is a joint decision of the team members and the parents. It is recommended to obtain standardized records at the age of 9 years, before the bone graft operation, consisting of extra- and intraoral pictures, dental casts, a cone beam computed tomography (CBCT) scan, and a 3D stereophotogrammetry facial image. The advances in 3D technology have greatly enhanced our insight into the 3D deformity of the cleft. From a CBCT a 2D head film can be reconstructed, as well as an orthopantomogram if there is a need for comparison with earlier conventional cephalometric records that are part of the patient's documentation. It has been shown that there is no clinically relevant difference between angular and linear measurements performed in conventional cephalometric radiographs, compared with measurements in cephalometric radiographs constructed from CBCT scans (Kumar et al., 2008; van Vlijmen et al., 2009). Since then, ultra-low-dose (ULD) and ultra-low-dose–low-dose (ULD-LD) CBCT protocols have been developed (van Bunningen et al., 2022). With an ULD-LD protocol an 87% reduction in radiation dose can be reached compared with the standard exposure protocols, depending on the CBCT unit (Ludlow et al., 2015]. The differences between cephalometric measurements on ULD-LD reconstructed cephalograms and conventional cephalograms were found to be negligible (van Bunningen et al., 2022). This means that CBCT-reconstructed head films can be used in longitudinal follow-up series in patients who have both 2D and 3D records.

Orthodontic treatment in relation to alveolar bone grafting

When a complete cleft of the alveolus is present, unilateral or bilateral, an early secondary bone graft is recommended between the age of 8 and 11 years, and prior to emergence of the canine at the cleft-affected side. The timing of the procedure is based on the developmental stage of the unerupted canine adjacent to the cleft, whereby its root length should be half to two-thirds of its full length (Da Silva Filho et al., 2000; Matsui et al., 2005). If a well-developed

unerupted lateral incisor is present in the cleft area that should be maintained, then the time of surgery can be brought forward. The bone is usually harvested from the iliac crest, and also from other bones such as the tibia, the cranial bones, or the mandibular symphysis (Figure 7.8). Currently, recombinant human bone morphogenetic protein (rhBMP)-2 with a demineralized bone matrix scaffold is considered as an alternative to the use of autologous bone in alveolar cleft reconstruction. Bone volume and height seem to be acceptable; however, the evidence supporting its use is still of low quality (Uribe et al., 2020).

(a)

(b)

(c)

Figure 7.8 Cone beam computer tomography scan of a patient with unilateral cleft lip and palate, two months after bone grafting of the alveolar cleft. (a) Frontal view, chin graft visible in the alveolar cleft. Note the donor site in the symphysis. (b) Lateral view depicting the canine position adjacent to the bone graft. (c) Axial view depicting maxillary bone graft.

The benefits of reconstruction of the alveolus are appreciated with respect to supporting cleft-adjacent teeth, facilitating eruption of the cleft-side canine, stabilizing the cleft maxillary segments, supporting the alar base, closing the oronasal communication, and improving the nasolabial contour (Long, 1995). Da Silva Filho et al. (2000) reviewed the literature on eruption of the cleft-side canine after bone grafting. They reported that 2–56% of the canines that were unerupted before bone grafting needed surgical exposure during the

course of orthodontic treatment after the bone grafting procedure. De Ruiter et al. (2010) found that a third of patients needed surgical assistance for eruption of the canine. An increased mesial angulation of the cleft-side canine as well agenesis of the lateral incisor at that side are early predictors for canine impaction (Simões Holz et al., 2018). These findings mean that the orthodontist should always be aware of eruption disturbances of the cleft-side canine. On the other hand, it is reassuring to know that the treatment of the impacted canine is not much different from that in a noncleft patient.

In their landmark paper, Boyne and Sands (1976) readdressed the bone grafting issue in the mixed dentition with a technique that has become standard and is still in use today in many centers. As orthodontists are always concerned about possible scar-induced growth inhibition of any type of surgery, it remains to be determined whether early secondary bone grafting affects the subsequent growth of the maxilla. A large multicenter cephalometric study found only a minor vertical deficiency of the anterior part of the maxilla (Ross, 1987). Other studies were unable to detect any differences in maxillary size or position in a secondary grafted group when compared with a group of ungrafted matched controls (Semb, 1988; Levitt et al., 1999). In general, despite the absence of any prospective, controlled trials, existing data from retrospective studies on secondary bone grafting would seem to indicate a minimal, if any, effect on maxillofacial growth.

Orthodontic preparation for the bone graft procedure is almost always needed, involving expansion of the maxillary arch to align the maxillary segments into the correct transversal and vertical relation to each other. The gingiva height should be the same at both sides of the cleft. This alignment can be performed easily with a removable maxillary expander, a quad-helix, or a fixed appliance in about 6–12 months. Caution should be exercised, however, not to overexpand the arch, as it will be very difficult for the surgeon to close the soft tissues over the bone-grafted area. A successful outcome of this procedure requires a sufficient amount of healthy attached gingiva (Iino et al., 2001). Therefore, consultation with the surgeon is indicated during the expansion phase, and the degree of expansion should be determined by the surgeon. After the proper maxillary arch form has been achieved, retention is needed. The easiest way to

establish retention is to fabricate a clear acrylic aligner that does not touch the soft tissues and is placed directly after surgery. If a quad-helix is used for the expansion, the device must be removed before surgery. Due to its flexibility it can be easily replaced 1–2 weeks after surgery.

As was mentioned earlier, the precondition for a successful bone graft is complete soft tissue closure over the bone-grafted area. This result may be difficult to achieve in patients with a wide alveolar cleft. In addition to the conventional segment osteotomy to mesialize the lateral segment, two newer approaches using distraction osteogenesis have been advocated to solve this problem. Liou et al. (2000) proposed interdental distraction osteogenesis within the alveolar process of the lateral segment, to create a new site of alveolar bone and attached gingiva. The osteotomized dental arch is transported forward, minimizing the size of the alveolar cleft. One week after distraction, the teeth adjacent to the distraction site can be moved into the newly generated bone in the dental arch. The remaining cleft is closed in a second procedure using gingivoperiosteoplasty to induce alveolar bone development in that area. The other approach is distraction osteogenesis with a bone-anchored maxillary distractor, to mesialize the lateral segment as a whole (Zemann and Pichelmayer, 2011). These distraction osteogenesis procedures are only incidentally used, and the success rate is still unclear as long-term results have not been published.

Bone-anchored maxillary protraction

De Clerck et al. (2009) presented a new approach to midfacial deficiency using skeletal anchorage with four miniplates, two at the infrazygomatic crest and two in the mandibular anterior region, and Class III elastics, called BAMP (bone-anchored maxillary protraction; Figure 7.9). These miniplates offer the possibility to apply pure bone-borne orthopedic forces between the maxilla and the mandible, using Class III elastics for 24 hours per day, avoiding any dentoalveolar compensations such as lower incisor retroclination or backward rotation of the mandible, as seen when using a face mask. Three preliminary case series studies have shown that intermaxillary Class III elastics attached to miniplates may enhance midfacial growth in young maxillary-deficient, noncleft patients (De

Clerck et al., 2009; Cevidanes et al., 2010; Heymann et al., 2010). The reader is referred to these freely available publications (through PubMed) to appreciate the treatment changes for the maxilla as assessed on 3D overlays of superimposed CBCT models and visualized with color-coded displacement maps.

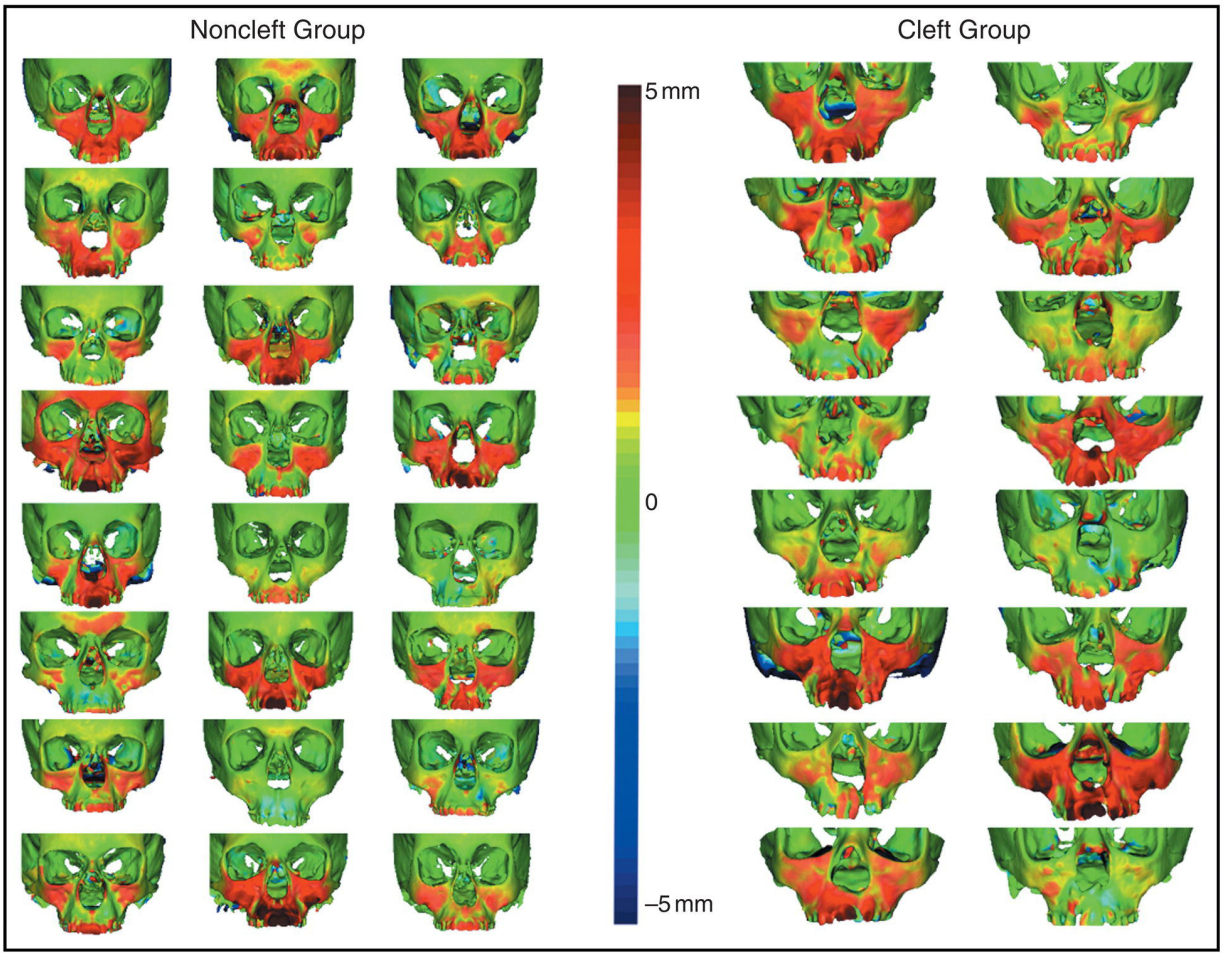


Figure 7.9 Color-map images of the antero-posterior directional changes (y component) between T1 (11.8 years) and T2 (12.8 years) in anterior views for unilateral cleft lip and palate and Class III group, both treated with bone-anchored maxillary protraction (BAMP; range −5 to +5 mm). Shades of red represent anterior displacement; shades of green no displacements; and shades of blue posterior displacement.

Source: Reproduced with permission from Yatabe et al. (2017) / Elsevier.

However, it took until 2017 for the first publication to appear on the results of application of this BAMP system in CLP patients (Yatabe et

al., 2017). In this study from the Hospital for Rehabilitation of Craniofacial Anomalies in Bauru (Brazil), the treatment response to BAMP therapy according to the De Clerck et al. (2009) approach in 24 patients with a complete UCLP was compared to that of 24 Class III noncleft patients. Treatment started at a mean age of 11.8 years and was finished at 13.2 years. The 3D evaluation with CBCT showed that BAMP resulted in a maxillary displacement (1.66 mm anteriorly and 1.21 mm caudally) in the UCLP group that was the same for the control group. However, there was a large variation in treatment response. Furthermore, in the UCLP group the upper first molars displaced medially, while in the noncleft group a lateral displacement was seen. The authors attributed this to a possible relapse of the maxillary expansion before the alveolar bone grafting. Interestingly, the zygomatic bone at the cleft side showed a larger lateral displacement than at the noncleft side (Yatabe et al., 2017; Figure 7.9). An ongoing prospective study in the Netherlands revealed a mean forward displacement of 1.5 mm of the zygomaxillary complex in a group of 18 patients after 1.5 years of treatment (Ren et al., 2019) and of 3.8 mm after 3.5 years of treatment (Steegman et al., 2022).

The second type of BAMP consists of placement of miniplates onto the left and right infrazygomatic crests and using a face mask with extraoral elastics attached to these bony anchors for protraction of the maxilla (Baek et al., 2010). The face mask should be worn at least 12 hours per day. This means that the burden of care for the patient is higher than for the previously described protraction device, which uses four miniplates with elastics worn 24 hours per day, but intraorally only. When a face mask is used in combination with maxillary miniplates, dento-alveolar compensation in the lower front region can be expected due to the chin cap of the face mask, leading to retroclination of the lower incisors (Ahn et al., 2012, 2021). On the other hand, changes in the ANB and SNA angles were shown to be more pronounced in the BAMP plus face mask group than in BAMP with Class III elastics (Jahanbin et al., 2022).

Miniplate placement surgery in young patients is complicated by the reduced height of the maxillary alveolar bone, and mandibular miniplates cannot be placed before canine emergence, therefore orthopedic traction on miniplates usually cannot start before the age

of 10 years. As miniplate surgery in young children has to be performed under general anesthesia, it should be preferably combined with the bone grafting procedure.

BAMP seems to be a promising treatment approach in growing patients with an orofacial cleft who develop a midfacial deficiency. However, long-term results are not available yet and several questions are still unanswered, such as the ideal age for this type of orthopedic traction, the possibilities of retention to prevent catch-up growth after treatment, and the incidence of a decreased need for orthognathic surgery (De Clerck et al., 2009). Moreover, combining BAMP with preloosening of the circummaxillary sutures, as described in the next section, may even produce a larger maxillary advancement.

Alt-RAMEC and maxillary protraction

Both types of maxillary protraction could be combined with rapid maxillary expansion to loosen the circummaxillary sutures and make the protraction more effective. Eric Liou from Taiwan developed the concept of alternate rapid maxillary expansion and constriction, called Alt-RAMEC (Liou and Tsai, 2005). The expansion protocol takes 7–9 weeks, alternating weeks of expansion and constriction of the screw. A few retrospective longitudinal studies have been published now on the long-term results of this approach in cleft patients (Meazzini et al., 2019) and in Class III malocclusion patients without a cleft (Meazzini et al., 2021). The latter study comprised a follow-up of a sample of 42 noncleft consecutive patients until the mean age of 19.4 years. Alt-RAMEC and maxillary protraction had started at 12.7 years of age. In these patients without a cleft, a sagittal advancement of 5.43 ± 2.71 mm at point A was found that remained stable in the long term. In the 2019 study, UCLP patients showed approximately the same advancement with stable results at 18.3 years (Meazzini et al., 2019).

Taking an overview of the results of maxillary protraction in combination with Alt-RAMEC, this may be the way to go, especially as the amount of maxillary advancement seems to be greater than with maxillary protraction alone. RCTs should provide evidence for this approach.

Adolescent orthodontic treatment

After bone grafting the orthodontic treatment continues, with the timing being dependent on the developmental stage of the dentition, especially the emergence of the canine adjacent to the cleft. Fixed appliances are nearly always necessary, and treatment takes several years to be completed. If maxillofacial growth develops favorably, this will be the final orthodontic intervention. After active treatment life-long retention is usually necessary, particularly for preserving the maxillary transverse dimension (Mink van der Molen et al., 2021; Sumardi et al., 2021).

The main problems we encounter during adolescent orthodontic treatment concern dental abnormalities, bad oral hygiene, the presence of scar tissue, and borderline skeletal relationships. Dental abnormalities are a common finding in CLP patients (das Neves et al., 2022). When compared with the general population, subjects with CLP have been found to have a higher prevalence of dental anomalies, such as variations in tooth number and position, reduced tooth size, developmental enamel defects, and taurodontism (Fonseca-Souza et al., 2022). A high prevalence of hypodontia of the permanent cleft-side lateral incisor (49.8%) as well as delayed root development in comparison with the contralateral tooth are common (Ribeiro et al., 2002). Akcam et al. (2010) found very high rates of anterior agenesis on the cleft side, varying between 70.8% and 97.1% depending on the cleft type. Dental anomalies are also more common outside the cleft area. In individuals with CL ± P, the highest incidence of dental anomalies is in the maxillary second premolars, followed by the maxillary lateral incisors and the mandibular second premolars (Menezes and Vieira, 2008). In a case of missing teeth, the orthodontic treatment plan should be developed together with the prosthodontist, who is able to determine the optimal location for future implants, veneers, and other restorations.

Poor oral hygiene, which is quite common in CLP patients, could complicate the orthodontic treatment. The prevalence of dental caries in individuals with orofacial clefts has been shown to be higher than in the noncleft population. This holds true for both the primary as well as the permanent dentition (Worth et al., 2017; Grewcock et al., 2022). For children without clefts and craniofacial anomalies, we

require good oral hygiene before orthodontic treatment is started, otherwise treatment is contraindicated. However, in children with clefts we tend to stretch thin our criteria for good oral hygiene, because these children need to be treated anyway. Unfortunately, the tolerance of poor oral hygiene can complicate the orthodontic treatment and frustrate the clinician.

Another factor that complicates orthodontic treatment is scar tissue, especially on the palate, which is associated with collapse of the transverse maxillary dimensions and can result in an omega-shaped arch form (Figure 7.10; Von den Hoff et al., 2017). Although the teeth can be aligned to a normal arch form, the tendency for relapse should be anticipated. Nearly all patients with a CP as part of the cleft anomaly show a tendency of transversal relapse, even many years after treatment. Scar tissue in the palate should be considered while planning the retention protocol in cleft patients. In patients with scarred palate, the transverse dimensions need to be retained life-long. In these patients a canine-to-canine bar, bonded to all anterior teeth, is indicated together with a Hawley retainer, which must be worn life-long at night, or even a retention frame (Sumardi et al., 2021). A preliminary study in our center showed, however, that out of a group of 39 patients with a complete cleft, only 6 were still wearing the retainer 10 years after the end of orthodontic treatment. In those 6 patients the transverse dimensions were unchanged, but in all other patients the transverse dimensions were decreased.

(a) (b)

Figure 7.10 (a) Occlusal view of an adult patient with a complete unoperated unilateral cleft lip and palate. Note the wide arch form. (b) Constricted maxillary arch in a patient with cleft palate who was operated on at a young age.

Source: Von den Hoff et al. (2017) / Reproduced from Georg Thieme Verlag KG.

Borderline skeletal relationship is one of the main problems appearing during orthodontic treatment of an adolescent with a cleft. A midfacial deficiency develops gradually during the course of the orthodontic treatment, and at a certain moment the decision has to be made as to whether the objectives still can be achieved by dental compensation only, without compromising facial esthetics (Figure 7.11). In such cases the orthodontic management of the malocclusion will be continued as camouflage orthodontic treatment. The reader is referred to Kharbanda (2022), who gives an illustrated overview of the possibilities. Unfortunately, in a considerable number of patients with clefts, a combined surgical-orthodontic correction of the skeleton is necessary after growth has ceased.

From 16 years of age into adulthood

As stated earlier, the aim of the interdisciplinary treatment approach is to create conditions that allow the affected child to grow up with an esthetically pleasing face, good hearing and speech, properly functioning and esthetically acceptable dentition, and a harmonious social-psychological development. Around the age of 16 years, these goals are reached for most of the children with mild cleft types. They are in the final stage of their treatment, perhaps requiring some

minor surgical secondary corrections of the nose and/or lip. Despite careful growth monitoring and facial orthopedic interventions, however, many patients with complete clefts end up with a midfacial deficiency after puberty that may need a combined surgical-orthodontic treatment to reach the goals described here. A recent systematic review based on 20 included studies reported the highest frequency of orthognathic surgery (38.1%) for bilateral CLP, followed by 30.2% in UCLP. For isolated CP a rate of 4.4% was found, while orthognathic surgery was reported in only 1.8% of the patients with an isolated cleft lip (Choi et al., 2021).

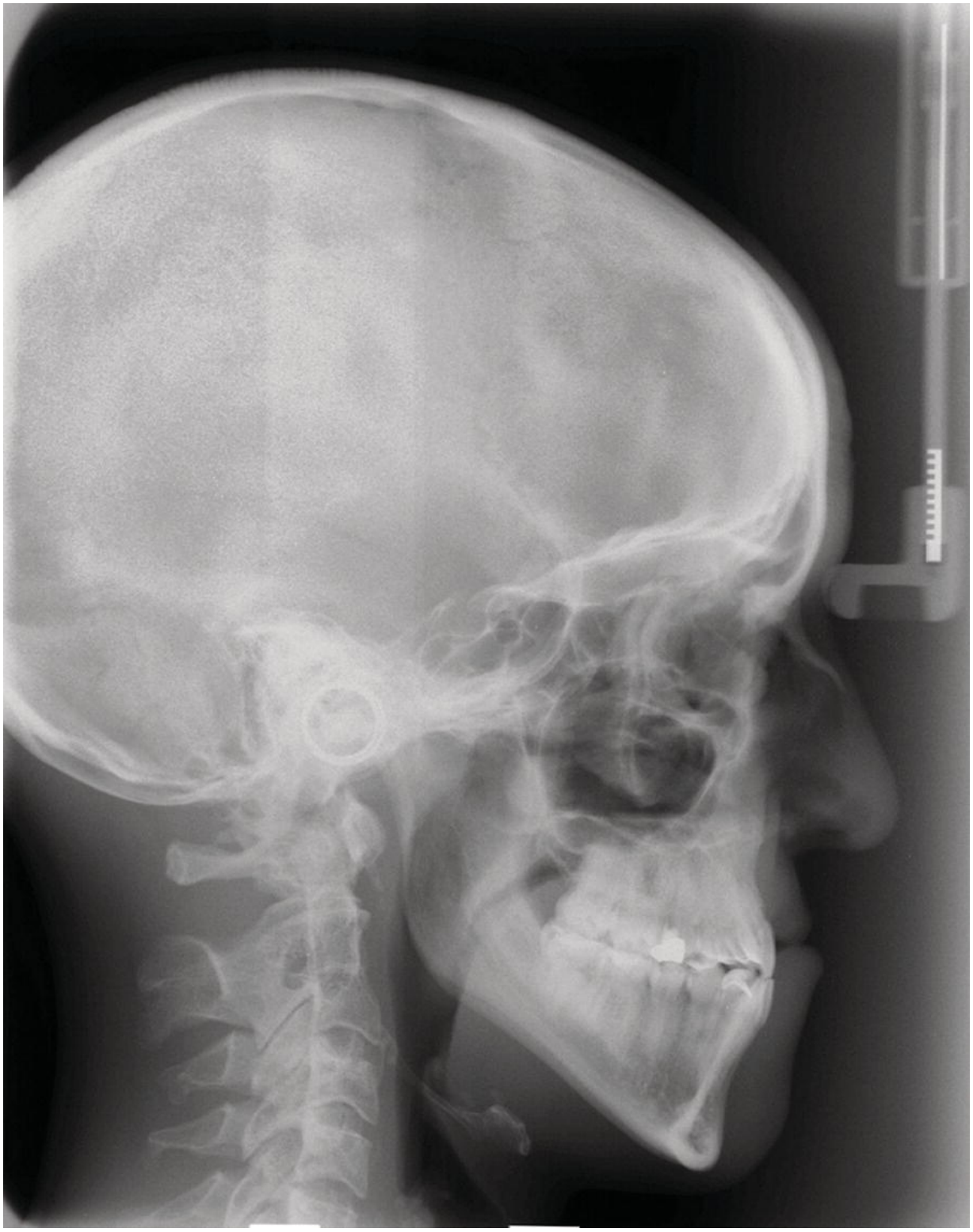


Figure 7.11 Adult individual with an operated complete unilateral cleft lip and palate. The cephalogram shows a clear midfacial deficiency with a marked maxillary retrusion. Correction was achieved by dental compensation only.

Source: Von den Hoff et al. (2017) / Reproduced from Georg Thieme Verlag KG.

There are no objective and universally accepted criteria to decide for orthognathic surgery or not. As the patient has now reached the age at which he or she can make their own decision, it is important that he or she participates in the decision-making process, rather than just the parents, the surgeon, or the cleft team. The orthodontist, surgeon, and prosthodontist need extensive documentation to be able to develop a comprehensive treatment plan together with the patient. This collaborative effort includes, but is not limited to, a thorough clinical examination with all three specialists and patient together, particularly for an assessment of the dynamic aspects of the face, by collecting and evaluating extra- and intraoral pictures, articulated dental casts, CBCT, and 3D stereophotogrammetry images of the face at rest and smiling. Postsurgical records should also be taken, to evaluate the orthodontic and surgical outcomes.

Combined orthodontic-surgical treatment in adulthood

Correction of the jaw deformity is planned for when the permanent dentition has been fully erupted, the dental arches have been aligned orthodontically, and maxillofacial growth has ceased. The correction of the midfacial deficiency can be performed either by orthognathic surgery of the maxilla alone or a bimaxillary approach, or by maxillary distraction osteogenesis if an advancement of more than 10–15 mm is needed. A Cochrane review, published in 2018, concluded that there is only very low-quality evidence regarding the long-term effect of maxillary distraction osteogenesis compared to conventional orthognathic surgery (Kloukos et al., 2018). After five years the horizontal relapse after maxillary distraction was less than after conventional surgery. However, this was based on the results of only one RCT with 42 patients in total (Chua et al., 2010).

The timing of the surgery depends on functional factors, psychosocial status, and the growth status of the patient.

Unfortunately, it is not so easy to determine the end point of facial growth. Chronological age and hand–wrist radiographs do not provide reliable information. Cervical vertebral maturation could be a good indicator for skeletal maturity, and can be easily assessed, as the vertebrae are visible on almost all lateral cephalograms (McNamara and Franchi, 2018). Although this method seems to be a valid indicator of skeletal growth during the circumpubertal period (Wong et al., 2009), providing information for timing of growth modification, it has been shown to be only modestly effective in determining the amount of postpeak circumpubertal craniofacial growth (Fudalej and Bollen, 2010).

As there is no reliable method to determine the end of facial growth, the decision should be based on individual longitudinal cephalometric data of craniofacial growth. Cephalograms should be taken at intervals of at least six months, but as the error of the method is large, longer time intervals are to be preferred. Currently, there is a tendency to operate earlier, and not to wait until late adolescence for complete definitive surgery (Posnick and Tiwana, 2006). Clearly this treatment has psychosocial advantages, as the child will not have to live through puberty with a disfigured face. Furthermore, it means that the orthodontic treatment can be performed in one stage, extending from the period after bone grafting until the surgical correction of the jaw deformity. On the other hand, it should be realized that postsurgically the maxilla is still not growing normally (Wolford et al., 2008). Long-term data are still lacking on the final outcome of orthognathic surgery or maxillary distraction to correct skeletal malformations in CLP patients before maxillofacial growth has ceased completely. Therefore, our team prefers to operate on the skeletal deformity after growth has ceased. Earlier intervention needs a thorough discussion with patient and parents. The limited predictability of the future outcome and the risk for a second surgical procedure must be mentioned.

Whatever plan is made, comprehensive pre- and postsurgical orthodontics is nearly always indicated. A wide range of orthopedic and orthodontic appliances may be used in the pre- and postsurgical orthodontic treatment stages. These include fixed appliances, palatal expansion devices, temporary anchorage devices such as miniscrews

and miniplates, inter- and intraarch elastics, removable appliances to unlock the occlusion or to support occlusal plane changes, and more. When performing midfacial distraction with intraoral distractors, a face mask is helpful in supporting and controlling movement in the three planes of space, by altering the force vectors.

After the planned presurgical dental relationships have been achieved, new orthodontic records are taken, a 3D digital surgical plan is worked out by surgeon and orthodontist that takes into consideration the viewpoints of the collaborating team specialists, and that is discussed with the patient and the patient's family. The final postsurgical orthodontic correction should be carefully planned between all team specialists involved. At this stage, the prosthodontist may want to replace missing teeth or restore hypoplastic incisors, and the plastic surgeon will perform final nose and lip corrections. A good framework of well-aligned dental arches and an optimal jaw relationship will support these late corrections.

It takes time to reach stability of the facial skeleton after this operation. Usually the skeletal structures become progressively more stable in the 12-month period after surgery. In the postsurgical orthodontic period, emphasis is placed on retaining the surgically repositioned components of the craniofacial skeleton and refining the dental occlusion. This is especially true for patients who have had large skeletal movements, or when the midface of a patient with a heavily scarred cleft palate was advanced. Therefore, interarch elastics and face-mask therapy are used to balance relapse as needed. After the orthodontic and postsurgical treatment objectives have been met, fixed appliances are removed and orthodontic retainers placed. The same considerations as explained for the previous stage of adolescent orthodontics are valid. Therefore, increased attention is given to retention appliance design and long-term stability. In view of the potential for relapse in the transverse and sagittal dimensions, lifetime retention is highly recommended (Santiago and Grayson, 2009; Mink van der Molen et al. 2021).

Conclusion

There are few greater challenges in the professional life of an orthodontist than the care of children with orofacial clefts and other

craniofacial anomalies. Over the years, the orthodontist has proven to be an essential partner in the CP team, not only responsible for the orthodontic and facial orthopedic treatment, but, more importantly, also the guardian of the child's maxillofacial growth. By their nature, orthodontists have a long-term treatment perspective in mind, which will assist the team in its consideration of treatment techniques, sequence, and timing, in relation to the effect on maxillofacial growth. Moreover, standardized records collected by the orthodontist provide a valuable basis for retrospective studies on treatment outcome and intercenter comparisons. Finally, in recent times orthodontists seem to be quite often the motor behind large-scale intercenter outcome studies such as Eurocleft (Shaw and Semb, 2006), Americleft (Long et al., 2011), and the Cleft Care UK study (Persson et al., 2015), as well as RCTs in the field of CLP like the Scandcleft trial into primary surgery of UCLP (Semb et al., 2017) and the TOPS trial of palate surgery (Shaw et al., 2019).

CLP research and/or the aggregation of existing data into meta-analyses are extremely difficult, because of problems inherent to the CLP material itself, and because of a series of inherent weaknesses in the many studies published so far. As a result of these deficiencies, it would appear as if relatively little has been accomplished over the past 50 years. However, with the negative effects of scar tissue now well accepted, the next challenge is to keep that in balance with the desire to reach outcomes as "normal" as possible, as soon as possible. To optimize treatment outcome for patients with clefts, two research approaches need to be pursued: prospective RCTs and controlled intercenter outcome studies. This target asks for standardized record taking, so that growth and treatment data between centers are consistent, to facilitate comprehensive data analysis. Moreover, it is important to include patient-reported outcome measures (PROMs) to ensure that the care delivered by the interdisciplinary team is what matters to the patient. To that end, the International Consortium for Health Outcomes Measurement (ICHOM; www.ichom.org) developed a standard set of patient-centered outcome measures for CLP (Allori et al., 2017). The ICHOM set is regularly updated (International Consortium for Health Outcomes Measurement, 2022). Also, the European Union-funded European Reference Network ERN CRANIO is working on an outcome registry with

standardized diagnosis-specific outcome sets (starting with craniosynostosis and CLP; European Reference Networks, 2022).

Over the years, craniofacial orthodontics has developed to a subspecialty of regular orthodontics. Orthodontic residents may be introduced to the field, but are not able to treat these patients independently without additional training. This has been recognized by the American Association of Orthodontists and the American Dental Association. A Fellowship in Craniofacial and Special Needs Orthodontics has been developed as a postresidency program that contains advanced education and training in a focused area of the specialty of orthodontics, including CLP patient care, syndromic patient care, orthognathic surgery, craniofacial surgery, and special care orthodontics (American Dental Association, 2022). The content of this fellowship could serve as an example for other countries desiring to improve the care for patients with clefts and craniofacial anomalies.

References

Abirami, S., Panchanadikar, N.T., Muthu, M.S. et al. (2022). Dental caries experience among children and adolescents with cleft lip and/or palate: An umbrella review. *International Journal of Clinical Pediatric Dentistry* 15(Suppl 2): S261–S268. doi: 10.5005/jp-journals-10005-2169.

Ahn, H.W., Kim, K.W., Yang, I.H. et al. (2012). Comparison of the effects of maxillary protraction using facemask and miniplate anchorage between unilateral and bilateral cleft lip and palate patients. *Angle Orthodontist*, 82(5): 935–941. doi: 10.2319/010112-1.1.

Ahn, H.W., Kim, S.J., and Baek, S.H. (2021). Miniplate-anchored maxillary protraction in adolescent patients with cleft lip and palate: A literature review of study design, type and protocol, and treatment outcomes. *Orthodontics & Craniofacial Research* 24(Suppl 1): 21–30. doi: 10.1111/ocr.12446.

Akcam, M.O., Evirgen, S., Uslu, O. et al. (2010). Dental anomalies in individuals with cleft lip and/or palate. *European Journal of*

Orthodontics 32: 207–213.

Al-Ghatam, R., Jones, T.E., Ireland, A.J. et al. (2015). Structural outcomes in the Cleft Care UK study. Part 2: Dento-facial outcomes. *Orthodontics & Craniofacial Research* 18(Suppl 2): 14–24. doi: 10.1111/ocr.12109.

Allori, A.C., Kelley, T., Meara, J.G. et al. (2017). A standard set of outcome measures for the comprehensive appraisal of cleft care. *Cleft Palate-Craniofacial Journal* 54(5): 540–554. doi: 10.1597/15-292.

American Cleft Palate-Craniofacial Association (1993). Parameters for the evaluation and treatment of patients with cleft lip/palate or other craniofacial anomalies. *Cleft Palate-Craniofacial Journal* 30(Suppl 1).

American Cleft Palate-Craniofacial Association (2018). Parameters for evaluation and treatment of patients with cleft lip/palate or other craniofacial differences. *Cleft Palate-Craniofacial Journal*, 55(1): 138–156. doi: 10.1177/1055665617739564.

American Dental Association Commission on Dental Accreditation (2022). Accreditation standards for clinical fellowship training programs in craniofacial and special care orthodontics. https://coda.ada.org/-/media/project/ada-organization/ada/coda/files/ortho_fellowship.pdf?rev=7b2498398d38465c925a9a6a25ed2bad&hash=5465B5C8DC0240DD06F27CB5414FECFD.

Baek, S.H., Kim, K.W., and Choi, J.Y. (2010). New treatment modality for maxillary hypoplasia in cleft patients. Protraction facemask with miniplate anchorage. *Angle Orthodontist* 80(4): 783–791. doi: 10.2319/073009-435.1.

Barillas, I., Dec, W., Warren, S.M. et al. (2009). Nasoalveolar molding improves long-term nasal symmetry in complete unilateral cleft lip-cleft palate patients. *Plastic and Reconstructive Surgery* 123: 1002–1006.

Bearn, D., Mildinhall, S., Murphy, T. et al. (2001). Cleft lip and palate care in the United Kingdom—the Clinical Standards Advisory Group (CSAG) Study. Part 4: Outcome comparisons, training, and conclusions. *Cleft Palate-Craniofacial Journal* 38(1): 38–43. doi: 10.1597/1545-1569_2001_038_0038_clapci_2.0.co_2.

Benitez, B.K., Brudnicki, A., Surowiec, Z. et al. (2022). Digital impressions from newborns to preschoolers with cleft lip and palate: A two-centers experience. *Journal of Plastic, Reconstructive & Aesthetic Surgery* 75(11): 4233–4242. doi: 10.1016/j.bjps.2022.08.015.

Bongaarts, C.A.M., Kuijpers-Jagtman, A.M., van't Hof, M.A. et al. (2004). The effect of infant orthopedics on the occlusion of the deciduous dentition in children with complete unilateral cleft lip and palate (Dutchcleft). *Cleft Palate-Craniofacial Journal* 41: 633–641.

Bongaarts, C.A.M., Prahl-Andersen, B., Bronkhorst, E.M. et al. (2008). Effect of infant orthopedics on facial appearance of toddlers with complete unilateral cleft lip and palate (Dutchcleft). *Cleft Palate-Craniofacial Journal* 45: 407–413.

Bongaarts, C.A.M., Prahl-Andersen, B., Kuijpers-Jagtman, A.M. (2009). Infant orthopedics and facial growth in complete unilateral cleft lip and palate until six years of age (Dutchcleft). *Cleft Palate-Craniofacial Journal* 46: 654–663.

Bongaarts, C.A.M., van 't Hof, M.A., Prahl-Andersen, B. et al. (2006). Infant orthopedics (IO) has no effect on maxillary arch dimensions in the deciduous dentition of children with complete unilateral cleft lip and palate (Dutchcleft). *Cleft Palate-Craniofacial Journal* 43: 665–672.

Boyne, P.J., and Sands, N.R. (1976). Combined orthodontic-surgical management of residual palato-alveolar cleft defect. *American Journal of Orthodontics* 70: 20–37.

Brons, S., Darroudi, A., Nada, R. et al. (2019a). Influence of involuntary facial expressions on reproducibility of 3D

stereophotogrammetry in children with and without complete unilateral cleft lip and palate from 3 to 18 months of age. *Clinical Oral Investigations* 23(3): 1041–1050. doi: 10.1007/s00784-018-2520-0.

Brons, S., Meulstee, J.W., Loonen, T. et al. (2019b). Three-dimensional facial development of children with unilateral cleft lip and palate during the first year of life in comparison with normative average faces. *PeerJ* 7: e7302. doi: 10.7717/peerj.7302.

Cevidanes, L., Baccetti, T., Franchi, L. et al. (2010). Comparison of two protocols for maxillary protraction: Bone anchors versus face mask with rapid maxillary expansion. *Angle Orthodontist* 80: 799–806.

Choi, K.J., Wlodarczyk, J.R., Nagengast, E.S. et al. (2021). The likelihood of orthognathic surgery after orofacial cleft repair. *Journal of Craniofacial Surgery* 32(3): 902–906. doi: 10.1097/SCS.0000000000007262.

Christ, J.E., and Meininger, M.G. (1981). Ultrasound diagnosis of cleft lip and cleft palate before birth. *Plastic and Reconstructive Surgery* 68: 854–859.

Chua, H.D., Hägg, M.B., and Cheung, L.K. (2010). Cleft maxillary distraction versus orthognathic surgery—which one is more stable in 5 years? *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics* 109(6): 803–814. doi: 10.1016/j.tripleo.2009.10.056.

Cutting, C.B., Grayson, B.H., Brecht, L. et al. (1998). Presurgical columellar elongation and retrograde nasal reconstruction in one-stage bilateral cleft lip and nose repair. *Plastic and Reconstructive Surgery* 101: 630–639.

Da Silva Filho, O.G., Teles, S.G., Ozawa, T.O. et al. (2000). Secondary bone graft and eruption of the permanent canine in patients with alveolar clefts: Literature review and case report. *Angle Orthodontist* 70: 174–178.

das Neves, L.T., de Carvalho, I., Cobourne, M.T. et al. (2022). Dental anomalies in non-syndromic orofacial clefts: A clinical approach. *Oral Diseases* 28(5): 1351–1368. doi: 10.1111/odi.14226.

Day, D.W. (1981). Perspectives on care: The interdisciplinary team approach. *Otolaryngology Clinics of North America* 14: 769–775.

De Clerck, H.J., Cornelis, M.A., Cevidanes, L.H. et al. (2009). Orthopedic traction of the maxilla with miniplates: A new perspective for treatment of midface deficiency. *Journal of Oral and Maxillofac Surgery* 67: 2123–2129.

Delaire, J., Verdon, P., and Flour, J. (1978). Möglichkeiten und Grenzen extraoraler Züge in postero-anteriorer Richtung unter Verwendung der orthopädischen Maske bei der Behandlung von Fällen der Klasse III. *Fortschritte der Kieferorthopädie* 39: 27–45.

De Ruiter, A., van der Bilt, A., Meijer, G. et al. (2010). Orthodontic treatment results following grafting autologous mandibular bone to the alveolar cleft in patients with a complete unilateral cleft. *Cleft Palate-Craniofacial Journal* 47: 35–42.

European Reference Networks (2022). ERN CRANIO registry and outcome measurement. https://ern-cranio.eu/for-clinicians/ern-cranio-registry-and-outcome-measurement.

Fonseca-Souza, G., de Oliveira, L.B., Wambier, L.M. et al. (2022). Tooth abnormalities associated with non-syndromic cleft lip and palate: Systematic review and meta-analysis. *Clinical Oral Investigations* 26(8): 5089–5103. doi: 10.1007/s00784-022-04540-8.

Frederick, R., Hogan, A.C., Seabolt, N. et al. (2022). An ideal multidisciplinary cleft lip and cleft palate care team. *Oral Diseases* 28(5): 1412–1417. doi: 10.1111/odi.14213.

Fudalej, P., and Bollen, A.M. (2010). Effectiveness of the cervical vertebral maturation method to predict postpeak circumpubertal growth of craniofacial structures. *American Journal of Orthodontics and Dentofacial Orthopedics* 137: 59–65.

Gani, B., Kinshuck, A.J., and Sharma, R. (2012). A review of hearing loss in cleft palate patients. *International Journal of Otolaryngology* 2012: 548698. doi: 10.1155/2012/548698.

Garland, K., McNeely, B., Dubois, L. et al. (2022). Systematic review of the long-term effects of presurgical orthopedic devices on patient outcomes. *Cleft Palate-Craniofacial Journal* 59(2): 156–165. doi: 10.1177/1055665621998176.

Georgiade, N.G., and Latham, R.A. (1975). Maxillary arch alignment in the bilateral cleft lip and palate infant, using pinned coaxial screw appliance. *Plastic and Reconstructive Surgery* 56(1): 52–60. doi: 10.1097/00006534-197507000-00011.

Grayson, B.H., and Cutting, C.B. (2001). Presurgical nasoalveolar orthopedic molding in primary correction of the nose, lip, and alveolus of infants born with unilateral and bilateral clefts. *Cleft Palate-Craniofacial Journal* 38: 193–198.

Grayson, B.H., Cutting, C.B., and Wood, R. (1993). Preoperative columella lengthening in bilateral cleft lip and palate. *Plastic and Reconstructive Surgery* 92: 1422–1423.

Grayson, B.H., and Maull, D. (2006). Nasoalveolar molding for infants born with clefts of the lip, alveolus and palate. In: S. Berkowitz (ed.), *Cleft Lip and Palate: Diagnosis and Management*. Berlin: Springer Verlag, pp. 451–458.

Grewcock, R.E., Innes, N., Mossey, P.A. et al. (2022). Caries in children with and without orofacial clefting: A systematic review and meta-analysis. *Oral Diseases* 28(5): 1400–1411. doi: 10.1111/odi.14183.

Heymann, G.C., Cevidanes, L., Cornelis, M. et al. (2010). Three-dimensional analysis of maxillary protraction with intermaxillary elastics to miniplates. *American Journal of Orthodontics and Dentofacial Orthopedics* 137: 274–284.

Hosseini, H.R., Kaklamanos, E.G., and Athanasiou, A.E. (2017). Treatment outcomes of pre-surgical infant orthopedics in patients with non-syndromic cleft lip and/or palate: A systematic review

and meta-analysis of randomized controlled trials. *PloS One* 12(7): e0181768. doi: 10.1371/journal.pone.0181768.

Hosseinian, B., Rubin, M.S., Clouston, S. et al. (2018). Comparative analysis of three-dimensional nasal shape of casts from patients with unilateral cleft lip and palate treated at two institutions following rotation advancement only (Iowa) or nasoalveolar molding and rotation advancement in conjunction with primary rhinoplasty (New York). *Cleft Palate-Craniofacial Journal* 55(10): 1350–1357. doi: 10.1177/1055665618765524.

Hotz, M., and Gnoinski, W. (1976). Comprehensive care of cleft lip and palate children at Zürich University: A preliminary report. *American Journal of Orthodontics* 70: 481–504.

Hubbard, T.W., Paradise, J.L., McWilliams, B.J. et al. (1985). Consequences of unremitting middle-ear disease in early life. Otologic, audiologic, and developmental findings in children with cleft palate. *New England Journal of Medicine* 312: 1529–1534.

Iino, M., Fukuda, M., Murakami, K. et al. (2001). Vestibuloplasty after secondary alveolar bone grafting. *Cleft Palate-Craniofacial Journal* 38: 551–559.

Institute of Medical Illustrators (2021). National guidelines: Cleft lip and palate. https://www.imi.org.uk/resources/professional-resources/national-guidelines.

International Consortium for Health Outcome Measurement (2022). Patient-centered outcome measures: Cleft lip & palate. https://connect.ichom.org/patient-centered-outcome-measures/cleft-lip-palate.

IPDTOC Working Group (2011). Prevalence at birth of cleft lip with or without cleft palate. Data from the International Perinatal Database of Typical Oral Clefts (IPDTOC). *Cleft Palate-Craniofacial Journal* 48: 66–81.

Jahanbin, A., Shafaee, H., Pahlavan, H. et al. (2022). Efficacy of different methods of bone-anchored maxillary protraction in cleft lip and palate children: A systematic review and meta-analysis.

Journal of Craniofacial Surgery Aug 30. doi: 10.1097/SCS.0000000000008972.

Kadir, A., Mossey, P.A., Blencowe, H. et al. (2017). Systematic review and meta-analysis of the birth prevalence of orofacial clefts in low- and middle-income countries. *Cleft Palate-Craniofacial Journal* 54(5): 571–581. doi: 10.1597/15-221.

Kasten, E.F., Schmidt, S.P., Zickler, C.F. et al. (2008). Team care of the patient with cleft lip and palate. *Current Problems in Pediatric and Adolescent Health Care* 38: 138–158.

Kharbanda, O.P. (ed.) (2022). *Cleft Orthodontics: A Holistic and Interdisciplianry Approach*. Delhi: Thieme Medical and Scientific Publishers.

Kloukos, D., Fudalej, P., Sequeira-Byron, P. et al. (2018). Maxillary distraction osteogenesis versus orthognathic surgery for cleft lip and palate patients. *Cochrane Database of Systematic Reviews* 8(8): CD010403. doi: 10.1002/14651858.CD010403.pub3.

Konst, E.M., Prahl, C., Weersink-Braks, H. et al. (2004). Cost-effectiveness of infant orthopedic treatment regarding speech in patients with complete unilateral cleft lip and palate: A randomized three-center trial in the Netherlands (Dutchcleft). *Cleft Palate-Craniofacial Journal* 41: 71–77.

Konst, E.M., Rietveld, T., Peters, H. et al. (2003). Use of perceptual evaluation instrument to assess the effects of infant orthopedics on the speech of toddlers with cleft lip and palate. *Cleft Palate-Craniofacial Journal* 40: 597–605.

Konst, E.M., Weersink-Braks, H., Rietveld, T. et al. (2000). An intelligibility assessment of toddlers with cleft lip and palate who received and did not receive presurgical infant orthopedic treatment. *Journal of Communication Disorders* 33: 483–501.

Kuijpers, M.A.R., Brons, S., and Kuijpers-Jagtman, A.M. (2022). Three-dimensional surface imaging of the face in patients with cleft lip and palate. In: O.P. Kharbanda (ed.), *Cleft Orthodontics:*

A Holistic and Interdisciplinary Approach. Delhi: Thieme Medical and Scientific Publishers, pp. 226–233.

Kuijpers-Jagtman, A.M. (2006). The orthodontist, an essential partner in CLP treatment. *B-ENT* 2(Suppl 4): 57–62.

Kuijpers-Jagtman, A.M., and Prahl, C. (2013). History of neonatal orthopedics: Past to present. In: S. Berkowitz (ed.), *Cleft Lip and Palate. Diagnosis and Management*. Heidelberg: Springer Verlag, pp. 455–472.

Kumar, V., Ludlow, J., Soares Cevidanes, L.H. et al. (2008). In vivo comparison of conventional and cone beam CT synthesized cephalograms. *Angle Orthodontist* 78: 873–879.

Kuo, C.L., Tsao, Y.H., Cheng, H.M. et al. (2014). Grommets for otitis media with effusion in children with cleft palate: A systematic review. *Pediatrics* 134(5): 983–994. doi: 10.1542/peds.2014-0323.

Levitt, T., Long, R.E., Jr., and Trotman, C.A. (1999). Maxillary growth in patients with clefts following secondary alveolar bone grafting. *Cleft Palate-Craniofacial Journal* 36: 398–406.

Liou, E.J., Chen, P.K., Huang, C.S. et al. (2000). Interdental distraction osteogenesis and rapid orthodontic tooth movement: A novel approach to approximate a wide alveolar cleft or bony defect. *Plastic and Reconstructive Surgery* 105: 1262–1272.

Liou, E.J., and Tsai, W.C. (2005). A new protocol for maxillary protraction in cleft patients: Repetitive weekly protocol of alternate rapid maxillary expansions and constrictions. *Cleft Palate-Craniofacial Journal* 42(2): 121–127. doi: 10.1597/03-107.1.

Long, R.E., Jr. (1995). Factors affecting the success of secondary alveolar bone grafting in patients with complete clefts of the lip and palate. In: C.A. Trotman and J.A. McNamara Jr. (eds.), *Orthodontic Treatment: Outcome and Effectiveness, Monograph 30. Craniofacial Growth Series*. Ann Arbor, MI: Center for

Human Growth and Development, University of Michigan, pp. 271–295.

Long, R.E., Jr., Hathaway, R., Daskalogiannakis, J. et al. (2011). The Americleft study: An inter-center study of treatment outcomes for patients with unilateral cleft lip and palate. Part 1: Principles and study design. *Cleft Palate-Craniofacial Journal* 48(3): 239–243. doi: 10.1597/09-180.1.

Ludlow, J.B., Timothy, R., Walker, C. et al. (2015). Effective dose of dental CBCT—a meta-analysis of published data and additional data for nine CBCT units. *Dento-maxillofacial Radiology* 44(1): 20140197. doi: 10.1259/dmfr.20140197.

Maarse, W., Bergé, S.J., Pistorius, L. et al. (2010). Diagnostic accuracy of transabdominal ultrasound in detecting prenatal cleft lip and palate: A systematic review. *Ultrasound in Obstetrics and Gynecology* 35: 495–502.

Maarse, W., Rozendaal, A.M., Pajkrt, E. et al. (2012). A systematic review of associated structural and chromosomal defects in oral clefts: When is prenatal genetic analysis indicated? *Journal of Medical Genetics* 49(8): 490–498. doi: 10.1136/jmedgenet-2012-101013.

Matsui, K., Echigo, S., Kimizuka, S. et al. (2005). Clinical study on eruption of permanent canines after secondary alveolar bone grafting. *Cleft Palate-Craniofacial Journal* 42: 309–313.

McNamara, J.A., Jr., and Franchi, L. (2018). The cervical vertebral maturation method: A user's guide. *Angle Orthodontist* 88(2): 133–143. doi: 10.2319/111517-787.1.

McNeil, C.K. (1950). Orthodontic procedures in the treatment of congenital cleft palate. *Dental Record* 70: 126–132.

Meazzini, M.C., Torre, C., Cappello, A. et al. (2021). Long-term follow-up of late maxillary orthopedic advancement with the Liou-Alternate rapid maxillary expansion-constriction technique in patients with skeletal Class III malocclusion. *American Journal of*

Orthodontics and Dentofacial Orthopedics 160(2): 221–230. doi: 10.1016/j.ajodo.2020.04.027.

Meazzini, M.C., Zappia, L.B., Tortora, C. et al. (2019). Short- and long-term effects of late maxillary advancement with the Liou-Alt-RAMEC protocol in unilateral cleft lip and palate. *Cleft Palate-Craniofacial Journal* 56(2): 159–167. doi: 10.1177/1055665618772395.

Menezes, R., and Vieira, A.R. (2008). Dental anomalies as part of the cleft spectrum. *Cleft Palate-Craniofacial Journal* 45: 414–419.

Merwin, D., Ngan, P., Hägg, U. et al. (1997). Timing for effective application of anteriorly directed orthopedic force to the maxilla. *American Journal of Orthodontics and Dentofacial Orthopedics* 112: 292–299.

Mink van der Molen, A.B., van Breugel, J., Janssen, N.G. et al. (2021). Clinical practice guidelines on the treatment of patients with cleft lip, alveolus, and palate: An executive summary. *Journal of Clinical Medicine* 10(21): 4813. doi: 10.3390/jcm10214813.

Mølsted, K., Asher-McDade, C., Brattström, V. et al. (1992). A six-center international study of treatment outcome in patients with clefts of the lip and palate: Part 2. Craniofacial form and soft tissue profile. *Cleft Palate-Craniofacial Journal* 29: 398–404.

Monga, N., Kharbanda, O.P., Dave, H. et al. (2022). Presurgical infant orthopaedics and nasoalveolar molding. In: O.P. Kharbanda (ed.), *Cleft Orthodontics: A Holistic and Interdisciplinary Approach*. Delhi: Thieme Medical and Scientific Publishers, pp. 101–117.

Mossey, P.A., Little, J., Munger, R.G. et al. (2009). Cleft lip and palate. *Lancet* 374(9703): 1773–1785. doi: 10.1016/S0140-6736(09)60695-4.

Noverraz, R.L., Disse, M.A., Ongkosuwito, E.M. et al. (2015). Transverse dental arch relationship at 9 and 12 years in children with unilateral cleft lip and palate treated with infant orthopedics:

a randomized clinical trial (DUTCHCLEFT). *Clinical Oral Investigations* 19(9): 2255–2265. doi: 10.1007/s00784-015-1451-2.

Padovano, W.M., Skolnick, G.B., Naidoo, S.D. et al. (2022). Long-term effects of nasoalveolar molding in patients with unilateral cleft lip and palate: A systematic review and meta-analysis. *Cleft Palate-Craniofacial Journal* 59(4): 462–474. doi: 10.1177/10556656211009702.

Papadopoulos, M.A., Koumpridou, E.N., Vakalis, M.L. et al. (2012). Effectiveness of pre-surgical infant orthopedic treatment for cleft lip and palate patients: A systematic review and meta-analysis. *Orthodontics & Craniofacial Research* 15(4): 207–236. doi: 10.1111/j.1601-6343.2012.01552.x.

Persson, M., Sandy, J.R., Waylen, A. et al. (2015). A cross-sectional survey of 5-year-old children with non-syndromic unilateral cleft lip and palate: The Cleft Care UK study. Part 1: Background and methodology. *Orthodontics & Craniofacial Research*, 18(Suppl 2): 1–13. doi: 10.1111/ocr.12104.

Posnick, J., and Tiwana, P.S. (2006). Cleft-orthognathic surgery. In: S. Berkowitz (ed.), *Cleft Lip and Palate: Diagnosis and Management*. Berlin: Springer Verlag, pp. 573–585.

Prahl, C., Kuijpers-Jagtman, A.M., van't Hof, M.A. et al. (2005). Infant orthopedics in UCLP: Effect on feeding, weight and length: A randomized clinical trial (Dutchcleft). *Cleft Palate-Craniofacial Journal* 42: 171–177.

Ren, Y., Steegman, R., Dieters, A. et al. (2019). Bone-anchored maxillary protraction in patients with unilateral complete cleft lip and palate and Class III malocclusion. *Clinical Oral Investigations* 23(5): 2429–2441. doi: 10.1007/s00784-018-2627-3.

Ribeiro, L.L., das Neves, L.T., Costa, B. et al. (2002). Dental development of permanent lateral incisor in complete unilateral

cleft lip and palate. *Cleft Palate-Craniofacial Journal* 39: 193–196.

Ross, R.B. (1987). Treatment variables affecting facial growth in complete unilateral cleft lip and palate. *Cleft Palate Journal* 24: 5–77.

Sagar, R., and Sahu, A. (2022). Psychological aspects and psychological counselling in cleft subjects. In: O.P. Kharbanda (ed.), *Cleft Orthodontics: A Holistic and Interdisciplianry Approach*. Delhi: Thieme Medical and Scientific Publishers, pp. 451–462.

Sandy, J., Davies, A., Humphries, K. et al. (2020). Cleft lip and palate: Care configuration, national registration, and research strategies. *Journal of the World Federation of Orthodontists* 9(Suppl 3): S40–S44. doi: 10.1016/j.ejwf.2020.09.003.

Santiago, P.E., and Grayson, B.H. (2009). Role of the craniofacial orthodontist on the craniofacial and cleft lip and palate team. *Seminars in Orthodontics* 15: 225–243.

Semb, G. (1988). Effect of alveolar bone grafting on maxillary growth in unilateral cleft lip and palate patients. *Cleft Palate Journal* 25: 288–295.

Semb, G., Enemark, H., Friede, H. et al. (2017). Scandcleft randomised trials of primary surgery for unilateral cleft lip and palate: 1. *Planning and management. Journal of Plastic Surgery and Hand Surgery* 51(1): 2–13. doi: 10.1080/2000656X.2016.1263202.

Shaw, W.C., Asher-McDade, C., Brattström, V. et al. (1992a). A six-center international study of treatment outcome in patients with clefts of the lip and palate: Part 1. Principles and study design. *Cleft Palate-Craniofacial Journal* 29: 393–397.

Shaw, W.C., Dahl, E., Asher-McDade, C. et al. (1992b). A six-center international study of treatment outcome in patients with clefts of the lip and palate: Part 5. General discussion and conclusions. *Cleft Palate-Craniofacial Journal* 29: 413–418.

Shaw, W.C., and Semb, G. (2006). Eurocleft – an experiment in intercenter collaboration. In: S. Berkowitz (ed.), *Cleft Lip and Palate: Diagnosis and Management*. Berlin: Springer Verlag, pp. 765–776.

Shaw, W., Semb, G., Lohmander, A. et al. (2019). Timing Of Primary Surgery for cleft palate (TOPS): Protocol for a randomised trial of palate surgery at 6 months versus 12 months of age. *BMJ Open* 9(7): e029780. doi: 10.1136/bmjopen-2019-029780.

Shaw, W.C., Semb, G., Nelson, P. et al. (2000). *The EUROCLEFT Project 1996–2000: Standards of Care for Cleft Lip and Palate in Europe*. Amsterdam: IOS Press.

Shetty, V., Agrawal, R.K., and Sailer, H.F. (2017). Long-term effect of presurgical nasoalveolar molding on growth of maxillary arch in unilateral cleft lip and palate: Randomized controlled trial. *International Journal of Oral and Maxillofacial Surgery* 46(8): 977–987. doi: 10.1016/j.ijom.2017.03.006.

Simões Holz, I., Martinelli Carvalho, R., Lauris, J.R. et al. (2018). Permanent canine eruption into the alveolar cleft region after secondary alveolar bone grafting: Are there prediction factors for impaction? *American Journal of Orthodontics and Dentofacial Orthopedics* 154(5): 657–663. doi: 10.1016/j.ajodo.2018.01.016.

Steegman, R., Schoeman, A., Dieters, A. et al. (2022). Three-dimensional volumetric changes in the airway of growing unilateral complete cleft lip and palate patients after bone-anchored maxillary protraction. *American Journal of Orthodontics and Dentofacial Orthopedics* 162(6): 850–860. doi: 10.1016/j.ajodo.2021.07.021.

Stock, N.M., Costa, B., White, P. et al. (2020). Risk and protective factors for psychological distress in families following a diagnosis of cleft lip and/or palate. *Cleft Palate-Craniofacial Journal* 57(1): 88–98. doi: 10.1177/1055665619862457.

Stock, N.M., Costa, B., Williams, J.R., et al. (2019a). Breaking the news: Parents' experiences of receiving an antenatal diagnosis of

cleft lip. *Cleft Palate-Craniofacial Journal* 56(9): 1149–1156. doi: 10.1177/1055665619830884.

Stock, N.M., Costa, B., Williams, J. et al. (2019b). Parental views of antenatal testing and termination following a diagnosis of cleft lip. *Psychology, Health & Medicine* 24(4): 456–469. doi: 10.1080/13548506.2018.1529328.

Strauss, R.P. (1999). The organization and delivery of craniofacial health services: The state of the art. *Cleft Palate-Craniofacial Journal* 36: 189–195.

Sumardi, S., Latief, B.S., Kuijpers-Jagtman, A.M. et al. (2021). Long-term follow-up of mandibular dental arch changes in patients with complete non-syndromic unilateral cleft lip, alveolus, and palate. *PeerJ* 9: e12643. doi: 10.7717/peerj.12643.

Tindlund, R.S. (2006). Protraction facial mask for the correction of midfacial retrusion: The Bergen Rationale. In: S Berkowitz (ed.), *Cleft Lip and Palate: Diagnosis and Management*. Berlin: Springer Verlag, pp. 486–502.

Tindlund, R.S., and Rygh, P. (1993). Maxillary protraction: Different effects on facial morphology in unilateral and bilateral cleft lip and palate patients. *Cleft Palate-Craniofacial Journal* 30: 208–221.

Uribe, F., Alister, J.P., Zaror, C. et al. (2020). Alveolar cleft reconstruction using morphogenetic protein (rhBMP-2): A systematic review and meta-analysis. *Cleft Palate-Craniofacial Journal* 57(5): 589–598. doi: 10.1177/1055665619886142.

van Bunningen, R.H., Dijkstra, P.U., Dieters, A. et al. (2022). Precision of orthodontic cephalometric measurements on ultra low dose-low dose CBCT reconstructed cephalograms. *Clinical Oral Investigations* 26(2): 1543–1550. doi: 10.1007/s00784-021-04127-9.

van Vlijmen, O.J., Bergé, S.J., Swennen, G.R. et al. (2009). Comparison of cephalometric radiographs obtained from cone-

beam computed tomography scans and conventional radiographs. *Journal of Oral and Maxillofacial Surgery* 67: 92–97.

Von den Hoff, J.W., Ongkosuwito, E.M., Kuijpers-Jagtman, A.M. et al. (2017). Vom Nutzen der Chirurgie und vom Nachteil der Narben [The benefit of surgery, the drawback of scars]. *Informationen aus Orthodontie und Kieferorthopädie* 49: 286≠294. doi: 10.1055/s-0043-122640.

Weise, C., Frank, K., Wiechers, C. et al. (2022). Intraoral scanning of neonates and infants with craniofacial disorders: Feasibility, scanning duration, and clinical experience. *European Journal of Orthodontics* 44(3): 279–286. doi: 10.1093/ejo/cjab068.

Wolford, L.M., Cassano, D.S., Cottrell, D.A. et al. (2008). Orthognathic surgery in the young cleft patient: Preliminary study on subsequent facial growth. *Journal of Oral and Maxillofacial Surgery* 66(12): 2524–2536. doi: 10.1016/j.joms.2008.06.104.

Wong, R.W., Alkhal, H.A., and Rabie, A.B. (2009). Use of cervical vertebral maturation to determine skeletal age. *American Journal of Orthodontics and Dentofacial Orthopedics* 136: 484.e1–6.

World Health Organization (2002) Global strategies to reduce the health-care burden of craniofacial anomalies: Report of WHO Meetings on International Collaborative Research on Craniofacial Anomalies, Geneva, Switzerland, 5–8 November 2000; Park City, Utah, USA, 24–26 May 2001. Geneva: World Health Organization. http://whqlibdoc.who.int/publications/9241590386.pdf.

Worley, M.L., Patel, K.G., and Kilpatrick, L.A. (2018). Cleft lip and palate. *Clinics in Perinatology* 45(4): 661–678. doi: 10.1016/j.clp.2018.07.006.

Worth, V., Perry, R., Ireland, T. et al. (2017). Are people with an orofacial cleft at a higher risk of dental caries? A systematic review and meta-analysis. *British Dental Journal* 223(1): 37–47. doi: 10.1038/sj.bdj.2017.581.

Yatabe, M., Garib, D.G., Faco, R. et al. (2017). Bone-anchored maxillary protraction therapy in patients with unilateral complete cleft lip and palate: 3-dimensional assessment of maxillary effects. *American Journal of Orthodontics and Dentofacial Orthopedics* 152(3): 327–335. doi: 10.1016/j.ajodo.2016.12.024.

Zemann, W., and Pichelmayer, M. (2011). Maxillary segmental distraction in children with unilateral clefts of lip, palate, and alveolus. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics* 111(6): 688–692. doi: 10.1016/j.tripleo.2010.08.002.

8

Multidisciplinary Management of Craniofacial Malformations

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Summary

Craniofacial malformations describe a diverse group of congenital disorders, varying from simple craniosynostosis involving single sutural fusion to complex syndromes marked by multiple sutural fusions, from simple clefts of the lip and palate to complex facial clefts, and branchial arch syndromes. This vast array of dysmorphic conditions involves abnormalities of craniofacial development and may result in minor or major abnormalities of the craniofacial skeleton and its appendages. There might be difficulties in maintaining an airway, feeding issues, reduced vision or hearing, delayed development of speech, and impaired neurological development. These malformations can result in abnormalities or malfunctioning of other organ systems as well. Children with complex craniofacial anomalies require the skills of a variety of medical and dental professionals, to observe and assess their development and to intervene at the right time. They need to be under the constant care of this team, from birth to adolescence or even beyond. The involved family also will require long-term support, as a child with such conditions can impose a huge financial and psychological burden. This chapter aims to provide a concise description of the commonly encountered craniofacial anomalies and their multidisciplinary management, with stress on the craniofacial orthodontics.

The head, face, and neck develop through a complex process of embryogenesis, with the involvement of many genes. Any disturbances or interruptions in cell growth, migration, differentiation, and apoptosis, any changes in the genes encoding for these processes, and environmental influences result in craniofacial malformations (CFMs; Leslie and Marazita 2013; Twigg and Wilkie, 2015; Miller et al., 2017), and about one-third of these congenital deformities involve the face and skull (Wiechers et al., 2021), with considerable morbidity among affected children.

CFMs can be broadly classified into craniofacial dysplasias and craniofacial dysplasias of other origins. The craniofacial dysplasias – an abnormality in the development of craniofacial structures,

especially the bone and soft tissues – comprise conditions such as clefts, craniosynostosis, dysostoses (abnormal facial bone development), or combinations. Craniofacial syndromes such as Apert, Crouzon, and Pfeiffer come into this category. Vascular anomalies and neurofibromatosis affecting the craniofacial skeleton and soft tissues contribute to dysplasia of other origins (van der Meulen et al., 1983).

The complex etiology and involvement of multiple anatomical regions complicate the management of CFMs. Attainment of normalcy, which was never there, requires comprehensive and coordinated care from infancy through adolescence and long-term follow-up (Kapp, 1979; Kapp-Simon, 1995). The child may experience problems with breathing, feeding, speech and hearing, and social integration (Yoon et al., 2016). The team should ideally consist of a geneticist, pediatrician, otolaryngologist, craniofacial surgeon, neurosurgeon, dentist, orthodontist, oral and maxillofacial surgeon, audiologist, speech-language pathologist, and social services provider (Bohm et al., 2016).

A craniofacial orthodontist is an integral part of the team, and carries the power to modify the growth and development of these inherently anomalous conditions. The value of the orthodontist in the craniofacial surgery team could be understood when McCarthy (2009: 222–223) said: "I was impressed by the role of other orthodontists in the evolution of this surgical field …. From my perspective, what began as a collaborative professional relationship almost 40 years ago has evolved into an incredible story. I have been witness to the genesis of a new professional discipline – craniofacial orthodontics – recently recognized as a Postgraduate Fellowship in Orthodontics by the Commission on Dental Accreditation of the American Dental Association and the American Association of Orthodontists." According to the American Dental Association, craniofacial orthodontics is that area of orthodontics that treats patients with congenital and acquired deformities of the integument and its underlying musculoskeletal system within the maxillofacial area and associated structures (Santiago and Grayson, 2009).

General principles in the diagnosis and management of craniofacial malformations

Prenatal screening

The presence of a CFM has a devastating effect on the child and the parents. Most of the time, the birth of such an infant may come with various issues, the most pressing of them being respiratory and feeding disorders. Though prenatal diagnosis of an anomaly might increase parental distress, it prepares them to accept the condition in a more objective manner (Sreejith et al., 2018) and helps the clinicians to anticipate and manage potentially life-threatening issues (Evans et al., 2011) in the immediate postnatal period. Prenatal diagnosis is hugely beneficial in antenatal care, delivery, and postnatal planning, parental counseling, parental decision making, and management of parental expectations (Descamps et al., 2010; Maarse et al., 2018). This may even allow the prenatal referral of a case to a higher-level center.

A prenatal ultrasonogram in the second trimester is the standard modality for screening and identification of fetal abnormalities (Mak and Leung, 2019), with an identification rate of 0–70% for cleft lip and palate deformities (Maarse et al., 2010), 7–72% for Robin sequence (Di Pasquo et al., 2017), and up to 60% for craniosynostosis syndromes (Harada et al., 2019). The huge variation in the predictive value of transabdominal ultrasound has been attributed to sonographer experience and challenges in cases involving decreased amniotic fluid volume, difficult fetal positioning, and maternal obesity. Moreover, the evaluation of the head, face, and neck can be limited by the interposition of the tongue and the acoustic shadowing caused by the ossification of facial structures (Zugazaga Cortazar and Martínez, 2012).

Fetal magnetic resonance imaging (MRI) is emerging as a potentially beneficial adjunct imaging modality for the prenatal diagnosis of congenital anomalies. The advantages of fetal MRI over ultrasound are increased soft tissue contrast and multiplanar capability, images that are not affected by amniotic fluid levels, maternal obesity, or fetal positioning (Descamps et al., 2010; Maarse et al., 2018), and the

technique being less operator dependent. Fetal MRI has 91.7% sensitivity in the assessment of cleft palate, 100% sensitivity in the diagnosis of micrognathia associated with Robin sequence (Laifer-Narin et al., 2019), and 88.9% sensitivity in cases of central nervous system anomalies (Gonçalves et al., 2016).

Support groups

The birth of an infant with CFM creates a psychological impact on the family and numerous centers have developed counseling and family support groups (Barden et al., 1989). These support groups educate and reassure parents that their baby will be well cared for, in a structured team environment, over several years, from birth to adulthood. This gaining of the parents' trust forms an essential component of the integrated team approach, as parents should be active participants in the treatment protocol, preparing themselves and their child to confront the challenges that might arise in the ensuing years. Parents appreciate discussing issues with others who have had similar experiences and reviewing pre- and posttreatment records. This approach adds to the complex interdisciplinary interaction that aims to achieve more complete integration of all parties concerned with the care and pays attention to the needs of the extended family.

Genetic counseling

A CFM can occur as an isolated entity or be part of a syndrome. It is always beneficial to have a working knowledge of syndromology and medical genetics, as this will assist in looking for less visible abnormalities that are commonly associated with more visible cranial or facial aberrant features. For example, microtia, the second most common congenital CFM (Zim et al., 2017), is associated with other organ system disorders in up to 40% of cases (Wang et al., 2001) – 16% of which are renal structural abnormalities needing follow-up (Koenig et al. 2018). Hence the team working closely with a clinical geneticist is very important, as it will assist in diagnosing the specific syndrome, which is important in the overall care of the patient. A genetic diagnosis will also throw light on the possibility of recurrence in future pregnancies. Recent advances in molecular

genetics have made elucidation of the pathogenesis of many CFMs easier (Marazita, 2012; Yoon et al., 2016).

The clinical genetic examination starts by taking a careful history, doing a three-generation pedigree, and conducting a complete physical examination and specific tests according to need. Karyotype analysis and fluorescent *in situ* hybridization (FISH), which have been used traditionally, look at the chromosome number and specific deletions and duplications. The newest technologies are specific enough to look at the individual base pairs of the DNA-encoding proteins (Yoon et al., 2016).

Neonatal care

All infants born with CFMs should be examined from head to toe in a systematic manner. Particular attention should be paid to the cranial vault shape and suture patency, maxillomandibular relation, palatal clefting, tongue position, presence of stridor, and overall work of breathing (Bohm et al., 2016). Anomalies of the fetal head, face, and neck can result in severe functional impairment, many of which demand immediate attention – compromised airway, feeding difficulties, and issues with raised intracranial tension would lead to severe morbidity and mortality if left untreated.

The signs of acute airway obstruction include nasal flaring, tracheal tug, and intercostal, subcostal, or sternal recession. The raised intracranial pressure may be reflected as papilledema. A computed tomography (CT) scan of the head and face will throw light on the bony anatomy and help in planning the surgery. MRI is beneficial in cases of suspected central nervous system anomalies – hydrocephalus or Chiari malformation. The initial acute needs are addressed by the neurosurgeon, neonatologist, otolaryngologist, pediatric/maxillofacial surgeon, and a specialized intensive care unit.

Airway and feeding

Children with CFMs are uniquely prone to upper airway obstruction, due either to abnormalities in the position of the adjacent structures or anomalies in the airway itself. The presentation of a blocked or compromised airway could vary from mild stridor to sudden upper

airway obstruction. The reported incidence of obstructive sleep apnea (OSA) in children with craniofacial anomalies is 28.2–50% (Pijpers et al., 2004; Lam et al., 2010; Paliga et al., 2014). The child may not be able to tolerate a supine position even in an awake state, or may turn cyanotic on feeding or crying. The baseline oxygen saturation on room air may be low, necessitating continuous oxygen support.

The team that manages these children should always be alert to the possibility of a blocked airway, especially in the neonatal period. Any failure to identify the condition or a delay in management would have devastating effects on the quality of life for these children. In addition to a detailed physical examination, bilateral nasal endoscopy can assist in assessing the patency of nasal passages – pyriform aperture stenosis or choanal atresia and a posteriorly placed tongue due to micrognathia are the most common causes for a compromised airway in children with CFMs (Bohm et al., 2016). Moreover, children with CFMs are highly susceptible to repeated respiratory tract infections, which can further compromise their airways. Children with CFMs are more prone to anomalies of the laryngotracheal complex. In cases where regular airway measures fail to maintain an adequate airway, the presence of tracheal stenosis or tracheal cartilaginous sleeve should be suspected, which could be confirmed with rigid bronchoscopy (Bohm et al., 2016). The possibility of further compromising the airway should be kept in mind in cases where some intraoral procedures like impression taking for a feeding plate are contemplated.

The management of a compromised airway is always customized depending on the degree of severity and the anatomical site of the obstruction. The decision to intervene early depends on clinical findings of difficulty in maintaining saturation, as well as feeding problems (Bohm et al., 2016). The necessary interventions could vary from positioning maneuvers – keeping the child in a prone position – to a surgical airway.

Congestion due to respiratory infections can be managed with topical vasoconstrictors. Noninvasive positive-pressure ventilation or bag–valve–mask ventilation serve as short-term measures of ventilation in cases where emergency intubation is not required. But maxillary

hypoplasia and exorbitism (protrusion of the eyeball due to a decrease in capacity of the orbital container) make the fit of the mask difficult and the mouth might have to be held in an open position to get a seal (Nargozian, 2004). A nasopharyngeal airway is another temporary measure to deal with a short period of airway compromise, but carries the disadvantage of being a bulky measure in an already narrowed airway and may incite mucosal inflammation.

In cases of mandibular hypoplasia, patient positioning alleviates the airway block in a large majority of cases and a prone position is well tolerated in infants (Marques et al., 2001; Schaefer et al., 2004; Meyer et al., 2008). Additional measures to advance the mandible or floor-of-mouth musculature might be helpful to open up the airway. Lip–tongue adhesion (Kirschner et al., 2003; Denny et al., 2004; Rogers et al., 2011), glossopexy (Argamaso, 1992; Evans et al., 2006), and hyoid suspension among others are techniques aiming to advance the tongue and floor of the mouth to open the airway. As the patient is being prepared for these procedures, a tongue suture can be applied with which the tongue can be physically pulled to keep the airway open.

Acute airway obstruction not responding to these measures would require definitive airway management – orotracheal intubation or, in a case of long-term requirement for airway intervention, a tracheostomy. Though orotracheal intubation is a straightforward procedure, it may pose difficulties in cases where there are congenital anomalies of the vertebral column. In infants with spine issues, extending the head for intubation would not be possible or would be hazardous. In such cases surgical airway/tracheostomy alone would be the option. Among children with CFMs, about 20% require tracheostomy and for a long duration, with a mean of 6.7 years (Perkins et al., 1997; Sculerati et al., 1998). The presence of a tracheostomy tube necessitates frequent care of the tube, as it carries the risk of accidental decannulation, tube block, infection, hemorrhage, pneumothorax, and issues with speech and swallowing (Carron et al., 2000; Carr et al., 2001).

Distraction osteogenesis (DO) is being increasingly used to advance the midface or mandible to relieve the airway obstruction in

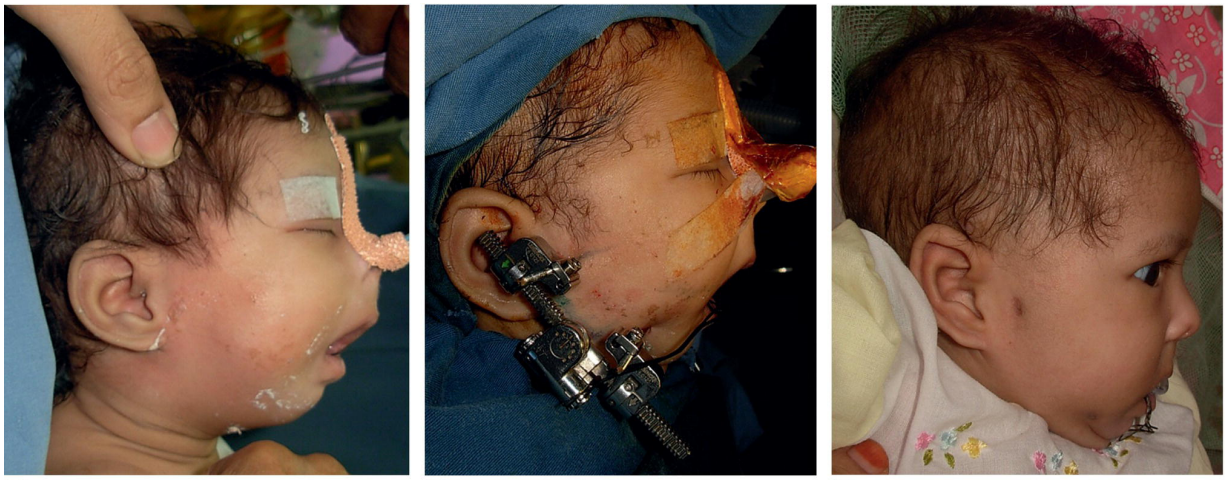
neonates with CFMs (Scott et al., 2011; Collins et al., 2014; Figures 8.1 and 8.2). The increase in airway dimensions allows for prevention or early decannulation of the tracheostomy. The complications of DO – namely, hardware failure, scar, and infection – are far fewer than the complications of long-term maintenance of a tracheostomy (Bohm et al., 2016).

Pyriform aperture stenosis and choanal atresia are two other causes of airway obstruction in infants with CFMs that need thorough evaluation clinically and radiologically (Belden et al., 1999; Robson and Hudgins, 2003). The presence of both would require surgical correction, as infants are obligate nasal breathers and would fail to thrive if these were uncorrected. As the skull base may be abnormal, care should be exercised while doing endoscopic perforation and widening of choanal atresia to prevent an intracranial injury (Ramsden et al., 2009).

Because of the abnormal position/shape of the facial bones, especially the maxilla or mandible or both, nourishment may be inadequate, leading to failure to gain weight. They would require Ryle's tube feeding if it is for a short period or feeding gastrostomy if the support is required for longer.

(a) (b) (c)

Figure 8.1 Apert syndrome. (a) Severe maxillary hypoplasia and exorbitism leading to airway compromise and exposure keratitis; (b) after midface distraction osteogenesis; (c) seven years post distraction of the midface – further advancement of the midface is required.



(a) (b) (c)

Figure 8.2 Pierre Robin sequence. (a) Severe mandibular retrognathia leading to airway compromise; (b) after mandibular distractor fixation; (c) after distractor removal. The advancement of the mandible can be appreciated.

Raised intracranial tension

CFMs may involve premature fusion of one or more cranial sutures, causing craniosynostoses leading to raised intracranial pressure

(ICP), visual impairment, and disturbances in functional and cognitive developments. The reduced intracranial volume, impaired cerebrospinal fluid (CSF) circulation and absorption, upper airway obstruction, and intracranial venous congestion contribute to an increase in ICP.

In the vast majority of cases symptoms of raised ICP may be nonspecific, like headache, irritability, vomiting, or bulging of the fontanelle. But in up to 38% of multisutural craniosynostoses (Figure 8.3), raised ICP may lead to symptoms such as visual impairment that require immediate intervention (Thompson et al., 1995; Stavrou et al., 1997; Langvatn et al., 2019).

The indicators for raised ICP are papilledema, a deflecting head circumference curve, headache, aggressive behavior, indentations/extensive endocortical erosions on imaging ("copper-beaten appearance"; Figure 8.4), altered morphology of ventricles, and Chiari malformation (CM; Woods et al., 2009). Papilledema has been cited as a reliable indicator for the presence of raised ICP, though its absence does not rule out the condition (Tuite et al.,1996). The presence or absence of papilledema is detectable with routine fundoscopic examination. Visual evoked potential and ocular coherence tomography are more sensitive in the early diagnosis of intracranial hypertension (Swanson et al., 2020; Yamada et al., 2020).

Figure 8.3 Pan-craniosynostosis leading to a Kleeblatt Schädel skull deformity (clover-shaped head). (a) Frontal views showing bilateral temporal bulges and frontal bulge with prominent scalp veins. The increased transverse and vertical dimensions of the head can be discerned from this view. (b) Lateral views showing the shortened antero-posterior dimension and increased vertical dimension of the head. The knotty appearance of the calvarium can be appreciated.

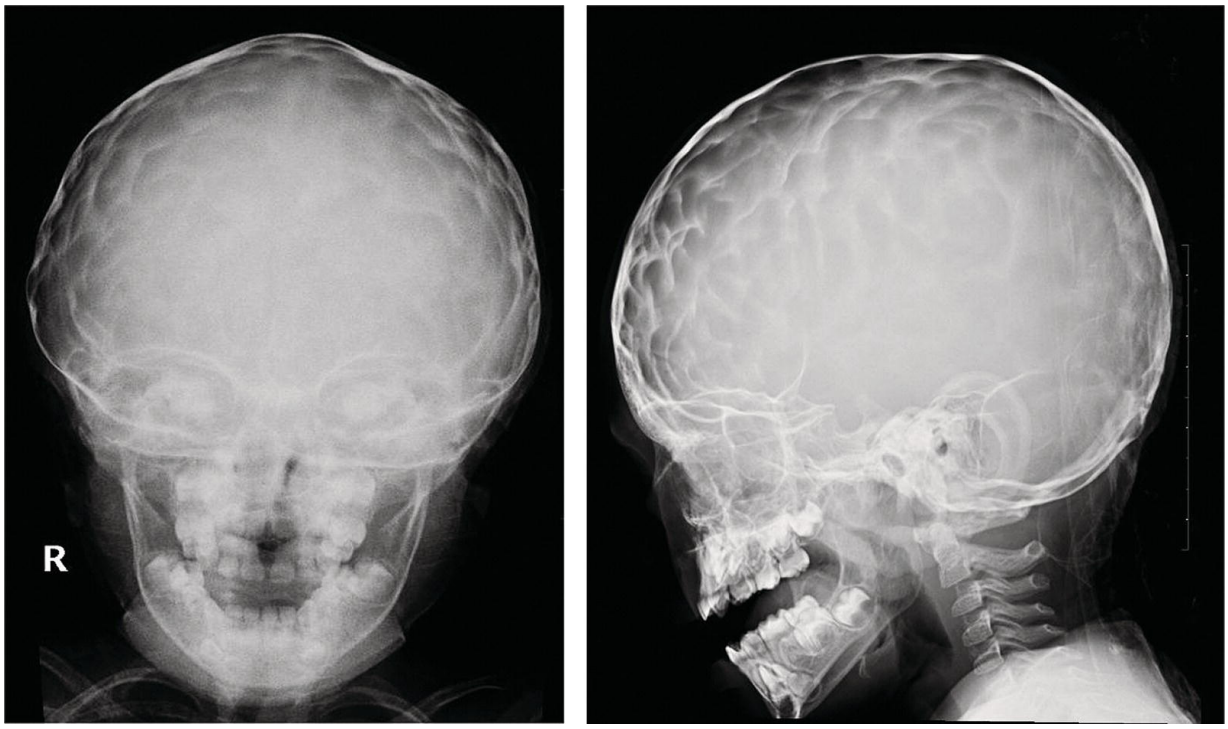


Figure 8.4 Posterior cranial fossa hypoplasia (crowding). Skull x-rays showing extensive indentations suggestive of cortical resorption due to raised intracranial pressure – "copper-beaten" appearance.

CM is considered to result from underdevelopment of the posterior cranial fossa, although its hypoplasia does not necessarily lead to

CM. CM can be present in a normal-volume posterior cranial fossa as well (Sgouros et al., 2007; Loukas et al., 2011). CM type I is associated with CFMs and involves downward displacement of the cerebellar tonsils by more than 4 mm, beneath the foramen magnum into the cervical spinal canal. This displacement may block the normal pulsations of CSF between the spinal canal and the intracranial space. This mechanical obstruction of the CSF may result in hydrocephalus developing in 7–10% of cases of CM (Greitz, 2004).

The raised ICP warrants immediate intervention to reduce the elevated pressure by releasing the synostosed sutures and/or expanding the cranial volume by osteotomy or distraction osteogenesis. Strip craniectomy/suturectomy releases the synostosis and allows normal growth of the brain to mold the calvarium. In certain cases, molding with helmets may be needed (Figure 8.5) after suturectomy. The expansion of the crowded posterior cranial fossa can be achieved by osteotomy (Figure 8.6) or distraction osteogenesis (Figure 8.7). Following the release of pressure in the cranial fossa, it has been noted that the herniated cerebellar tonsils regain their normal position (Figure 8.8).

Follow-up

Once the acute conditions – namely, airway patency, feeding efficiency, and intracranial tension – have been successfully managed, there follows a long period of follow-ups. The issues to be addressed in these visits include esthetic appearance, speech forming, hearing ability, dental health, proper food intake, and psychological well-being. Specialist clinicians should play their roles at specific times appropriate for the patient's particular needs. These needs are established and constantly reviewed at regular team meetings of the interdisciplinary group, and this excellent level of coordinated communication is the keystone to interdisciplinary, interactive care. The importance of long-term follow-ups in a multispecialty center should be stressed to the patient and family, rather than there being several individual consultations.

Figure 8.5 Suturectomy/strip craniectomy followed by helmet molding. (a) Preoperative computed tomographic scan showing synostosis of sagittal and left coronal sutures; (b) right-side frontal bossing to compensate for left coronal synostosis; (c) strip craniectomy where fused sutures have been released; (d) cranial molding with helmet; (e) changes in the forehead contour after three months of strip craniectomy and helmet molding.

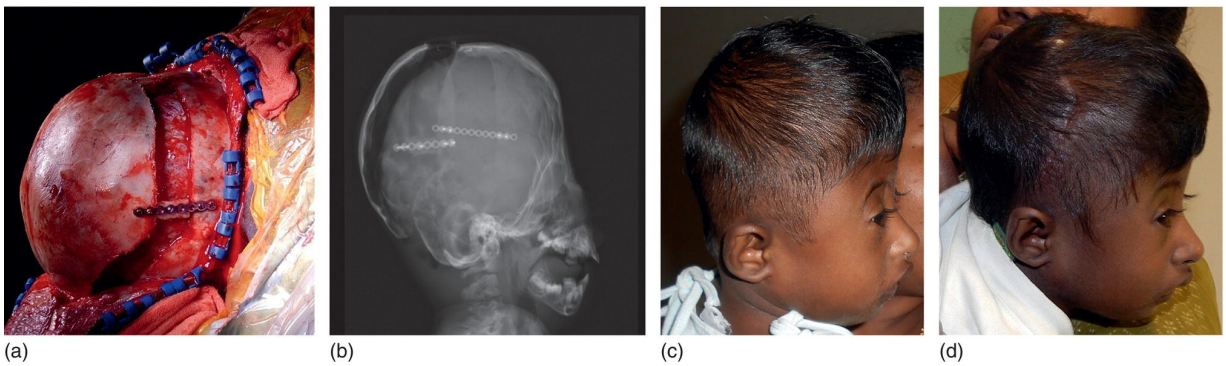


Figure 8.6 Expansion of posterior cranial fossa by osteotomy. (a) Expansion obtained during the operation; (b) lateral skull x-ray showing the posterior expansion; (c) preoperative lateral view showing reduced antero-posterior dimension; (d) postoperatively the skull has attained normal dimensions.

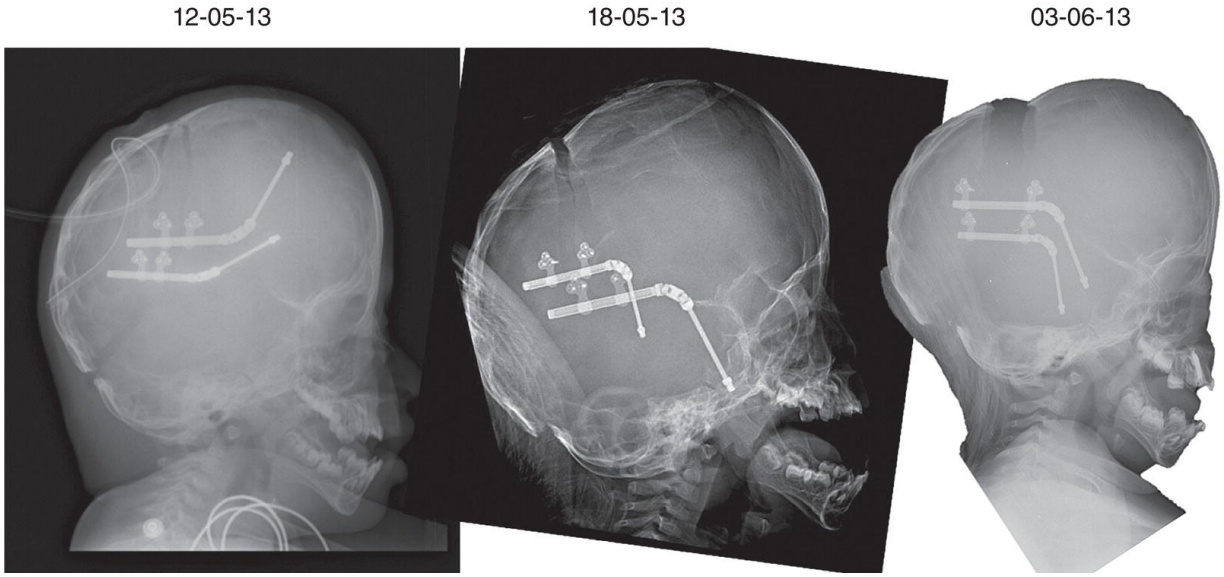


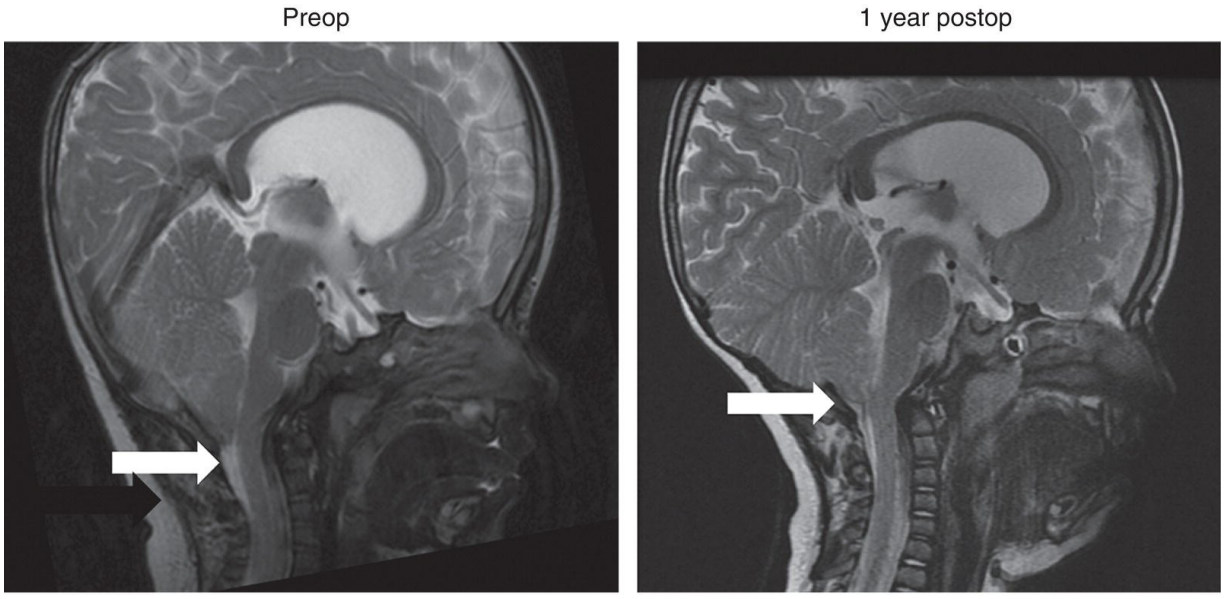
Figure 8.7 Expansion of posterior cranial fossa by distraction osteogenesis.

The psychosocial needs of children with craniofacial anomalies and their families need to be constantly addressed. Speech and effective communication are other areas that need long-term intervention. Speech issues could be precipitated by oral anomalies, respiratory compromises, or pharyngeal and laryngeal anomalies. Speech-language pathologists aim to correct the abnormalities related to speech, production, fluency, language, cognition, voice, resonance, and hearing (Susanu et al., 2018).

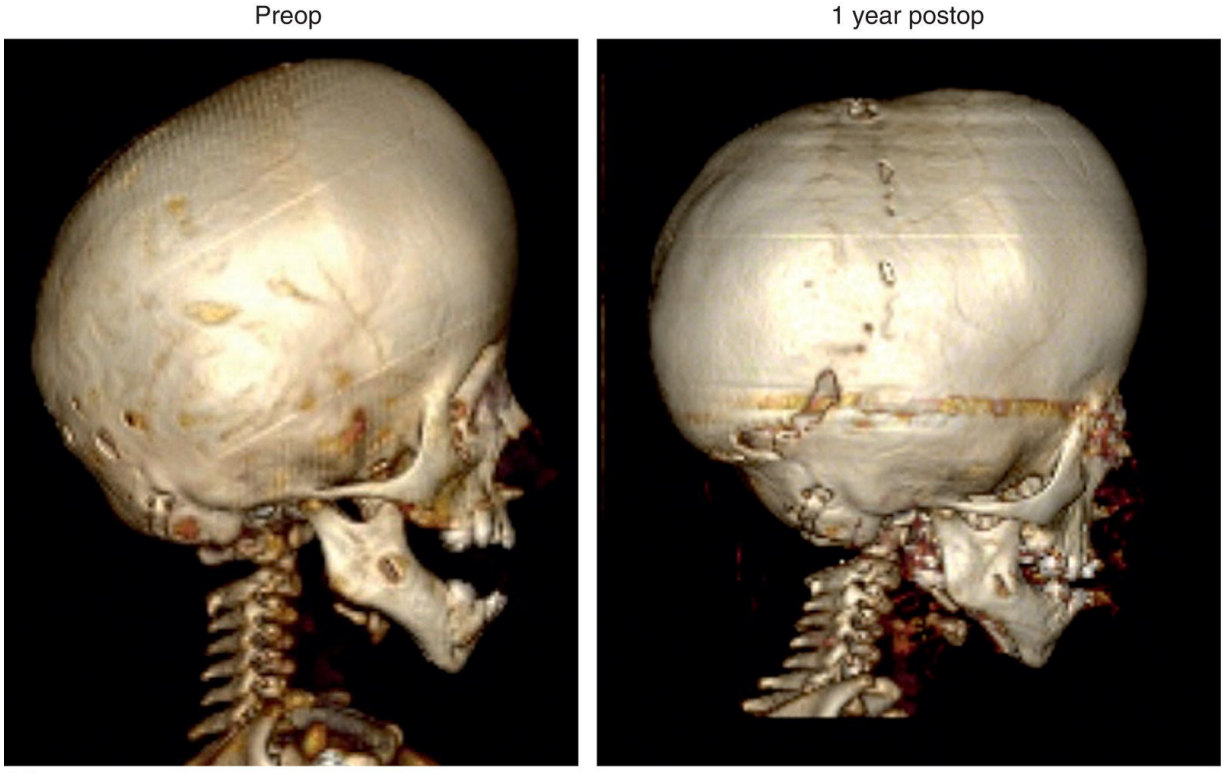
Inability to maintain oral hygiene leading to mutilated dentition needs to be addressed early with the help of a pedodontist or restorative dentist. As almost all craniofacial anomalies involve jaw deformities, which are amenable to timely functional orthopedic and orthodontic treatment, orthodontists play an intrinsic role in their care (McCarthy, 2007). They are actively involved in infant presurgical orthopedics, early mixed dentition treatment, dentofacial orthopedics and orthodontics, adolescent/adult orthodontics,

preprosthetic orthodontics, and pre- and postsurgical orthodontics. The yearly dental follow-ups involve oral hygiene measures, restorations, obtaining needed radiographs, and identifying discrepancy in the growth pattern of the jaws or the eruption pattern of teeth, followed by the required interventions.

The rest of this chapter provides an overview of interdisciplinary team management of the most common CFMs, other than cleft lip and palate that forms the basis of Chapter 7. This chapter outlines major congenital orofacial malformations under the headings of otofacial malformations and craniosynostosis, with particular emphasis on the role of orthodontists in the interdisciplinary team.



(a)



(b)

Figure 8.8 Correction of Chiari malformation with posterior calvarial fossa expansion. (a) The magnetic resonance imaging scan showing herniation of the cerebellar tonsils inferiorly due to the posterior cranial fossa crowding in the preoperative scan. In the one-year postoperative scan, the cerebellar tonsils have ascended to their normal position. (b) The computed tomographic scan showing the change in the skull shape and dimensions.

Otofacial malformations

Craniofacial microsomia

The term craniofacial microsomia, formerly also named hemifacial microsomia, describes a complex spectrum of congenital anomalies that primarily involve structures derived from the first and second branchial arches, either unilaterally or bilaterally (Ross, 1975; Converse et al., 1979; Kaban et al., 1981; Posnick, 2000). It is the second most common congenital syndrome of the head and neck region, after cleft lip and palate, with an incidence as high as 1 in 3500 live births (Munro and Lauritzen, 1985). The hypoplasia can manifest itself in any of the structures derived from the first and second branchial arches, accounting for the wide spectrum of deformities observed in this syndrome. This variable expression had resulted in numerous alternate names, such as Goldenhar syndrome, dysostosis otomandibularis, and occulo-auriculovertebral dysplasia (Gorlin et al., 1990). The currently used terminology of craniofacial microsomia encompasses the varying degrees of presentation, such as underdevelopment of the mandible, maxilla, ear, orbit, facial soft tissue, and/or facial nerve leading to feeding difficulties, compromised airway, asymmetrical facial movements, and altered facial appearance. There could be asymmetry at the skull base itself.

Over the years, several methods of classification have been developed, describing the anatomical regions and grades of involvement (Posnick, 2000). The most accepted classifications are the Orbit, Mandible, Ear, Nerve, and Soft tissue (OMENS) classification (Vento et al., 1991; Table 8.1) and the SAT method, where S stands for skeleton, A for auricle, and T for soft tissue (David et al., 1987).

The etiology of this anomaly has been related to defects of neural crest cells (Johnston and Bronsky, 1995), and the most accepted mechanism involved in the etiopathogenesis is that of a vascular insult, with hemorrhage and hematoma formation in the developing stapedial artery in the first and second branchial arches, and subsequent maldevelopment (Poswillo, 1975; Soltan and Holmes, 1986). The mandible has long been considered the “cornerstone” of hemifacial microsomia (Kaban et al., 1981; Vento et al., 1991), as it is always involved and contributes to the natural course of skeletal asymmetry (Kaban et al.,1981, 1988; Polley et al., 1997; Kearns et al., 2000). The restricted growth potential of the affected hemimandible inhibits ipsilateral vertical maxillary development, resulting in progressive facial asymmetry (Figure 8.9). Mandibular hypoplasia may range from mild flattening of the condylar head to complete agenesis of the condyle, ascending ramus, and glenoid fossa. Because of the hypoplastic ramus, the mandibular plane angle is increased, the chin is deviated toward the affected side, and there is a corresponding cant of the mandibular occlusal plane, which is reflected onto the maxillary occlusal plane, as well as the levels of pyriform apertures (Figure 8.10).

Table 8.1 OMENS classification for craniofacial anomalies.

Orbit
O0: Normal orbital size, position
O1: Abnormal orbital size
O2: Abnormal orbital position
O3: Abnormal orbital size and position
Mandible
M0: Normal mandible
M1: Small mandible and glenoid fossa with short ramus
M2: Ramus short and abnormally shaped
2A: Glenoid fossa in anatomical acceptable position
2B: Temporomandibular joint inferiorly, medially, anteriorly displaced, with severely hypoplastic condyle
M3: Complete absence of ramus, glenoid fossa and temporomandibular joint
Ear
E0: Normal ear
E1: Minor hypoplasia and cupping with all structures present
E2: Absence of external auditory cannel with variable hypoplasia of the concha
E3: Malposition of the lobule with absent auricle, lobular remnant usually inferiorly anteriorly displaced
Facial nerve

N0: No facial nerve involvement

N1: Upper facial nerve involvement (temporal or zygomatic branches)

N2: Lower facial nerve involvement (buccal, mandibular, or cervical)

N3: All branches affected

Soft tissue

S0: No soft tissue or muscle deficiency

S1: Minimal tissue or muscle deficiency

S2: Moderate tissue or muscle deficiency

S3: Severe tissue or muscle deficiency

Variable hypoplasia of the ipsilateral zygomatico-orbital region is a common finding, occasionally resulting in orbital dystopia (Gougoutas et al., 2007). Because of their proximity, secondary involvement of skeletal structures not directly derived from the first and second brachial arch derivatives, like temporal bone, frontal bone, styloid, mastoid, and pterygoid processes, and cervical vertebrae, is inevitable (Converse et al., 1973). Involvement of the auricle occurs in most patients (Meurman, 1957; Figure 8.11). A combination of cutaneous and subcutaneous connective and neuromuscular tissue deficiency is most evident in the region of the external ear and eye, and the temporal, malar, and masseteric regions of the face, giving rise to a characteristic temporal hollowing and malar flattening (Figure 8.12). This characteristic appearance may be accentuated by muscular hypoplasia involving the muscles of mastication. Masticatory muscle function on the affected side may likewise be impaired. The maxillary and mandibular dentoalveolar complexes are reduced in the vertical dimension on the affected side, and exhibit crowding, delayed eruption of the deciduous and permanent teeth, and sometimes missing molars (Figure 8.13). Macrostomia or clefting through the oral commissure and hypoplasia of the parotid gland may also be present (Whitaker and Bartlett,

1990; Figure 8.14). Facial palsies have been estimated to occur in 22–45% of patients (Bergstrom and Baker, 1981; McCarthy, 1997; Figure 8.15).

Management

Management of hemifacial microsomia requires a comprehensive evaluation of the extent of the deformity. It is possible that functional appliance treatment and dental compensation may suffice in minor skeletal discrepancies, but moderate to severe skeletal problems will require surgical intervention. Treatment must proceed depending on the severity of the dysmorphism and the age of the child (Silvestri et al., 1996).

Figure 8.9 Characteristic facial features in craniofacial microsomia.

Figure 8.10 Canting of the occlusal plane in a craniofacial microsomia patient.

Figure 8.11 A patient showing malformation of the external ear (microtia) as part of craniofacial microsomia.

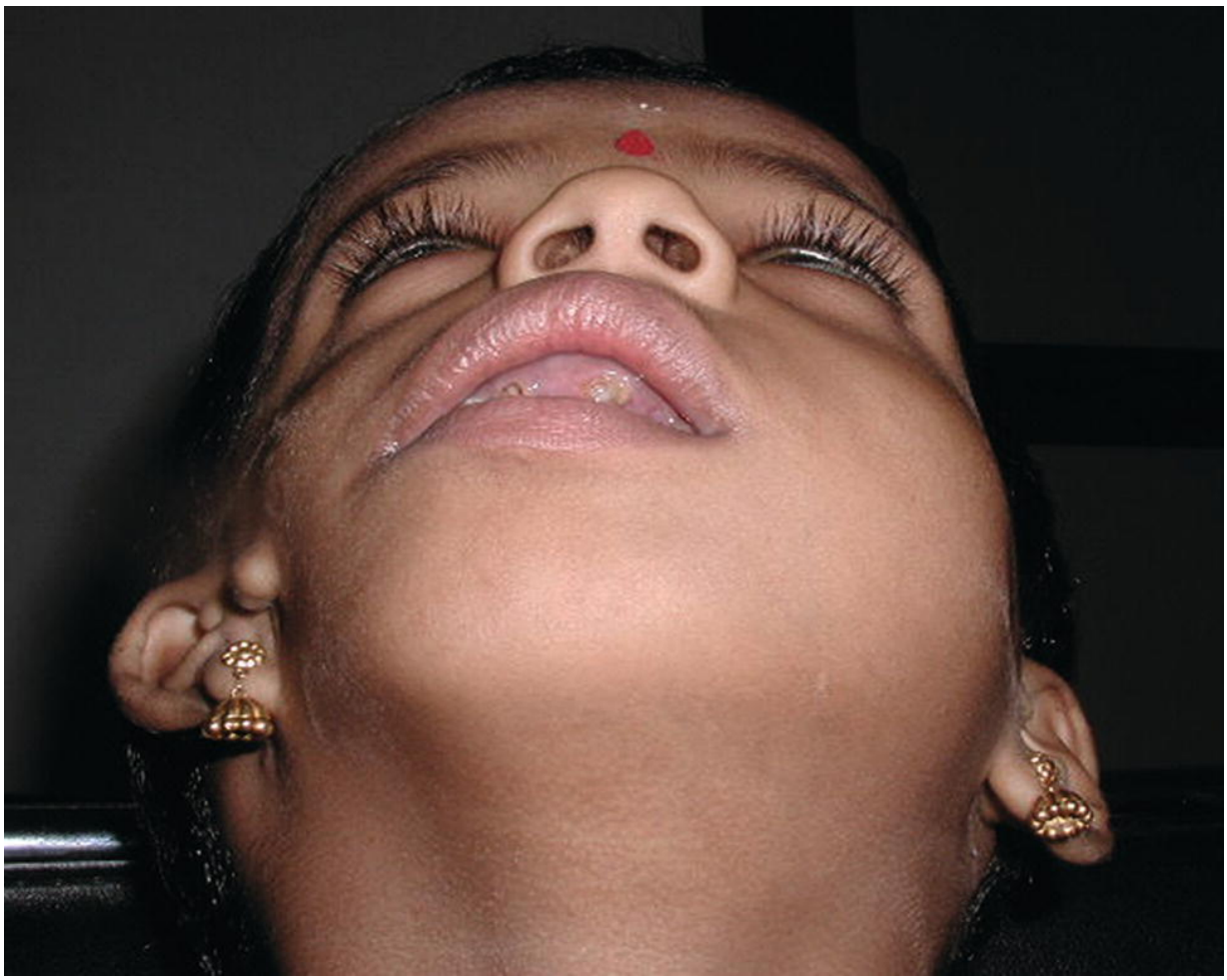
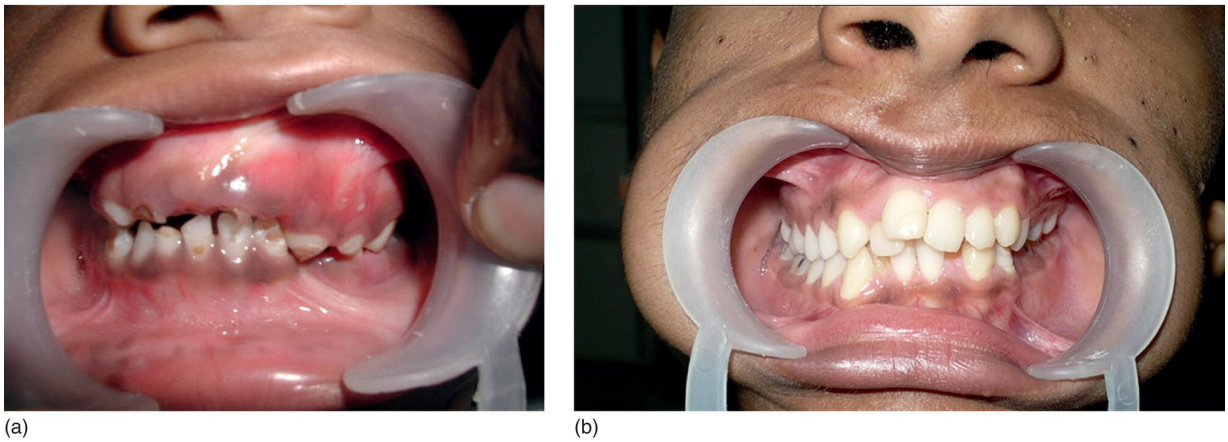


Figure 8.12 Characteristic malar flattening in craniofacial microsomia.



(a) (b)

Figure 8.13 (a, b) Occlusion in two craniofacial microsomia patients.

Figure 8.14 Macrostomia and ear anomaly in a baby affected with craniofacial microsomia.

Figure 8.15 A patient with facial palsy as part of craniofacial microsomia syndrome. (a) Frontal view; (b) frontal view showing incomplete eye closure and deviation of the angle of the mouth toward the normal left side; (c) worm's-eye view showing malar flattening and deviation of the angle of the mouth.

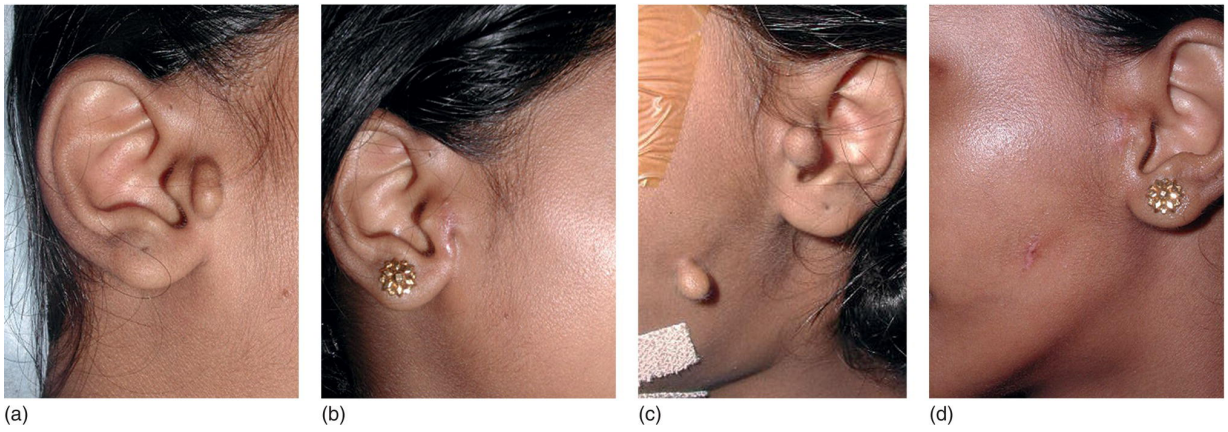


Figure 8.16 Ear tag excision as part of initial treatment in hemifacial microsomia patients: (a, c) preoperative and (b, d) postoperative photographs.

At a very young age no surgery is indicated, unless there is an airway disruption due to mandibular micrognathia, which is usually dealt with by tracheostomy or mandibular distraction (McCarthy et al., 1992; Boston and Rutter, 2003), as has already been discussed. But

often excision of the preauricular skin tags and cartilage remnants, as well as macrostomia correction, is quite satisfying to the parents, because it removes some of the stigmata of the syndrome (McCarthy, 2007; Figure 8.16). Assessment of hearing and the provision of hearing aids also need attention during early childhood.

The widely followed treatment protocol is by Silvestri et al. (1996), based on the SAT classification system (David et al., 1987). It emphasizes functional treatment during growth, followed by surgery to reposition the skeleton and grafting. The objectives of early intervention, however, include providing growth stimulus for the affected side of the maxilla, associated dentoalveolus, and soft tissues.

Distraction osteogenesis in adolescents with craniofacial microsomia

With effective mandibular lengthening and correction of facial asymmetry reported with DO it has become the treatment of choice, especially in growing children (McCarthy et al., 1992; Cascone et al., 2005). DO is beneficial, especially in patients with psychological or functional impairment, as it improves function and appearance during growth, creating an almost normal interim status. The distraction of the ramus opens a vertical and anterior space into which the undererupted maxillary teeth can be guided, thereby reducing or even correcting the asymmetry.

There are conflicting reports regarding the growth potential of the mandible after DO. Initially early reconstruction was advocated to prevent secondary deformities (Kaban et al., 1981, 1988; Grayson and Santiago, 1999). It was believed that overcorrection of the affected mandible by DO to compensate for the lack of/reduced growth potential would be sufficient to prevent maxillary asymmetry from happening. Though growth of the mandible after DO has been reported by few authors (Sheyte et al., 2006), most report that the degree of asymmetry remains constant (Polley et al., 1997; Iseri et al., 2008). Moreover, studies and systematic reviews have shown varying degrees of relapse of the distracted bone, sometimes as high as 100% (Iseri et al., 2008; Wan et al., 2011; Meazzini et al., 2012; Pluijmers et al., 2014). In cases of severe facial asymmetry a staged

procedure is advocated, with DO of the mandible in the growing years to negate any serious functional or psychological issues (Dufton et al., 2011; Pluijmers et al., 2014). The patient would also require a series of soft tissue procedures to compensate for the hypoplasia and ear malformations (Brent, 1992; Longaker and Siebert, 1995; Wang and Andres, 1999; **(**Figure 8.17).

Surgical correction in adults with craniofacial microsomia

In postadolescent patients, DO procedures are reserved for the more severe skeletal anomalies, and it is not uncommon for the patient to receive mandibular distraction, as the major defect usually lies in the mandible, followed by maxillary surgery and revision surgery on the mandible, to obtain its final position (Figure 8.18). The maxilla and mandible may be simultaneously distracted to effect three-dimensional (3D) changes if required (Ortiz-Monasterio et al., 1997; Sant'Anna et al., 2015). Maxillomandibular DO brings about leveling of the occlusal plane.

Figure 8.17 Pre- and postdistraction treatment records in an adolescent craniofacial microsomia patient. (a) Pretreatment extraoral photograph; (b) postdistraction extraoral photograph; (c) soft tissue corrections performed with a temporo-parietal flap; (d) pretreatment orthopantomogram – note the discrepancy between the right- and left-side rami in the vertical plane (arrows); (e) postdistraction orthopantomogram showing nearly symmetrical rami after distraction (arrows).

Orthodontic treatment in craniofacial microsomia

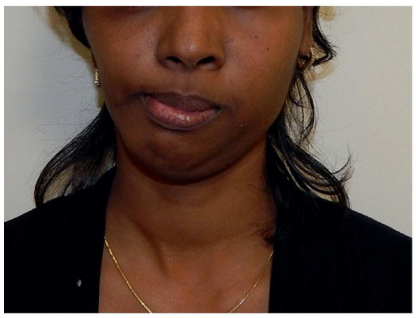
The best possible treatment results can be achieved if the orthodontist and the surgeon agree on a carefully designed and customized treatment plan. Both should be aware of the treatment objectives, limitations, and risks. The importance of a staged treatment plan should be explained to the patient and the family.

The orthodontic treatment phases can be broadly divided into pre-DO orthodontic treatment, orthodontic treatment during DO and

consolidation, and postconsolidation orthodontics.

Predistraction planning and orthodontics

This phase of treatment is carried out in the growing child, where the aim of DO is to decrease the quantum of facial asymmetry. Vector planning is crucial in this stage, depending on the lengthening of the mandible required in the vertical, sagittal, or oblique plane. The decision about the type of movement that would be required, and the associated position of the distractor, is determined in a combined clinic, where the operating surgeon and orthodontist participate (Hanson and Melugin, 1999). With the advances in computer-aided surgery, the planning of the surgical procedure, the position of the distractors, direction of the vector, and the probable postsurgical soft tissue position can be assessed and the virtual plan can be translated into accurate surgery with the help of 3D-printed cutting and positioning guides (Steinbacher, 2015; Steinberg et al., 2016), confirmed with intraoperative navigation systems (Mazzoni et al., 2010).



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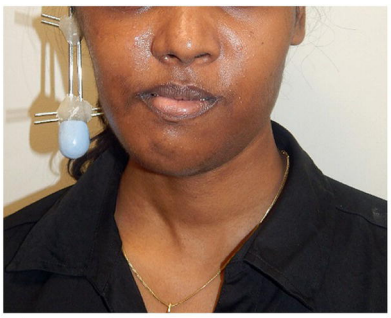

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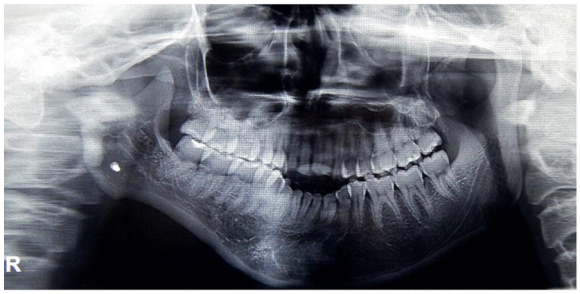

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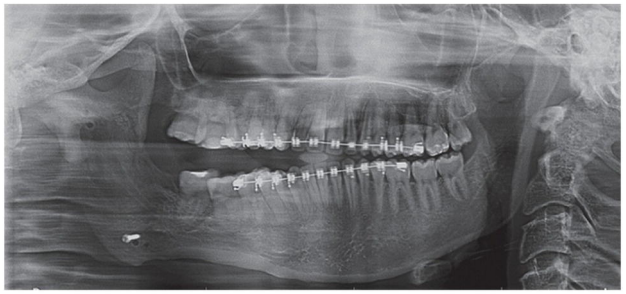

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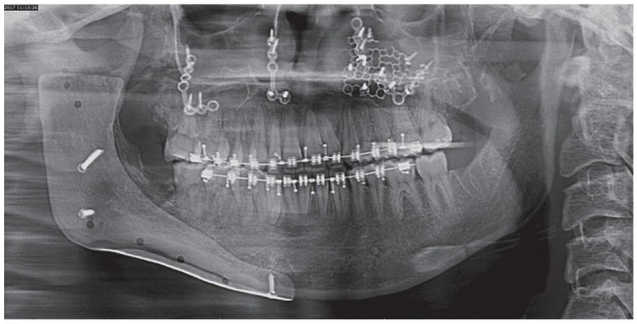

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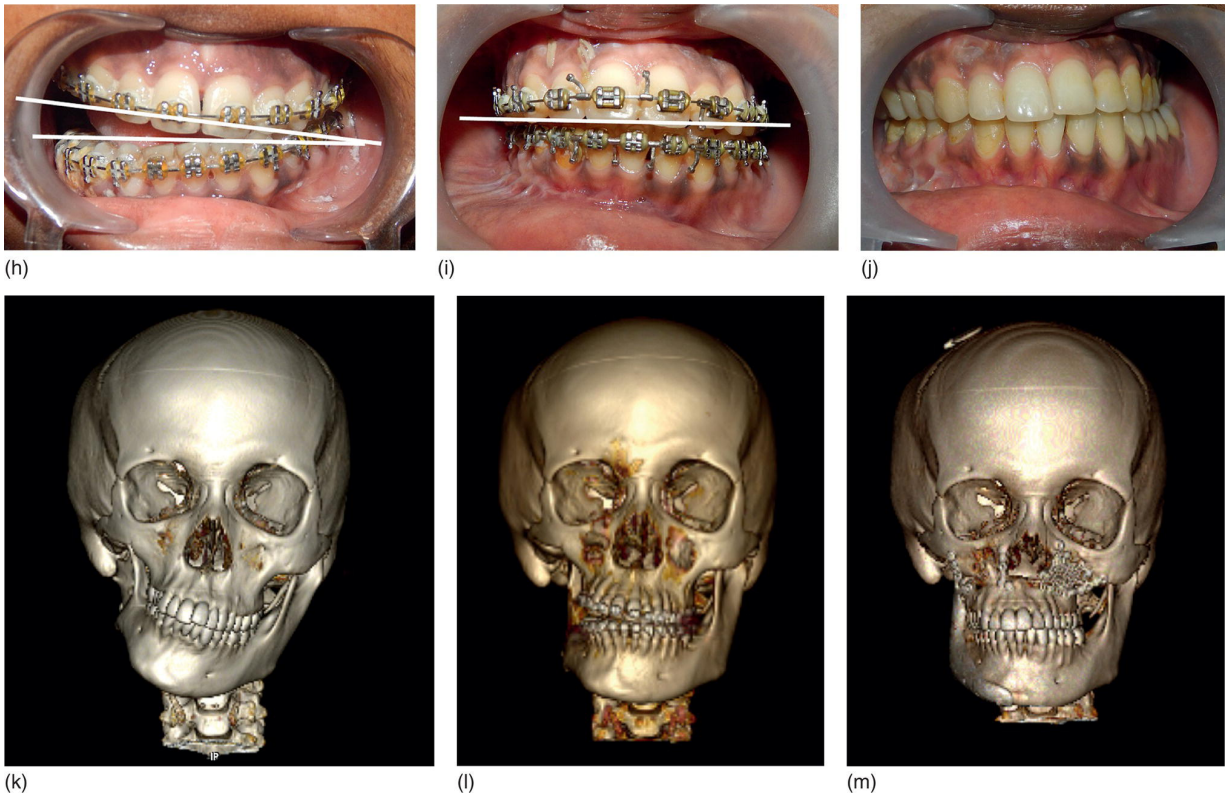

Figure 8.18 Pre- and posttreatment records in an adult craniofacial microsomia patient. Facial photographs: (a) at presentation; (b) post distraction of mandible; (c) after maxillary osteotomy and ramal implant insertion. Orthopantomograms: (d) at presentation; (e) post distraction of mandible; (f) after maxillary osteotomy and ramal implant insertion. Occlusion: (g) at presentation; (h) post distraction mandible; (i) after maxillary osteotomy; (j) after debonding. Three-dimensional computed tomography: (k) at presentation; (l) post distraction of mandible; (m) after maxillary osteotomy and ramal implant insertion.

It is always advantageous as part of predistraction to use stabilization appliances, which help in elastic traction (Hanson and Melugin, 1999). This treatment also facilitates vector control and maintenance of the transverse relationship between the maxilla and mandible, preventing lateral displacement of the dental segment.

Orthodontics during distraction osteogenesis

The aim of orthodontic treatment during DO is to control the vector and to direct the growth of the mandible to an advantageous

position. As DO progresses the ramus lengthens vertically, resulting in a posterior open bite. In this stage, the mandibular occlusal cant is corrected and the vertical symmetry is established. But as the posterior open bite increases, the patient might find it difficult to occlude and shift the mandible to the unaffected side. This situation can be observed clinically, as the dental midline shifts away from the distracted side and a buccal crossbite on the distracted side is corrected, while a crossbite evolves on the unaffected side (laterognathism).

Orthopedic forces are required to correct the laterognathism. The force of the elastics might be opposite to the distraction forces, and so the distraction force must be greater than the elastic traction. Elastic traction can also be used to coordinate the dental arches and correct the dental midline shifts (Figure 8.19). Orthodontists should maintain all records for future re-evaluations and planning treatment progression.

Postdistraction orthodontics

In the growing child, post-DO orthodontics is extremely important. Guided eruption of teeth, correction of laterognathism with elastics, and controlled vertical closure of the unilateral posterior open bite are the main objectives of this stage of treatment, along with stabilizing the corrected mandibular occlusal plane. Failure to stabilize the occlusal plane leads to overeruption of both maxillary and mandibular teeth, and re-establishment of the previous maxillary and mandibular occlusal cant. The corrected mandibular occlusal plane is maintained by the selective eruption of the maxillary teeth, and can be performed with an occlusal acrylic wafer that is reduced one tooth at a time, to allow controlled eruption of the maxillary teeth. Santiago and Grayson (2009) inserted a bite block that fills the open bite on the distracted side soon after active distraction, providing a bilateral balanced occlusion (Figure 8.20). Another possibility is to use a functional appliance with lingual shields, to provide lateral control of the mandibular position. A bite plane is also included, which is adjusted to allow serial eruption of maxillary teeth. Elastic traction is often added to the appliance, which has been shown to decrease treatment time (Hanson and Melugin, 1999).

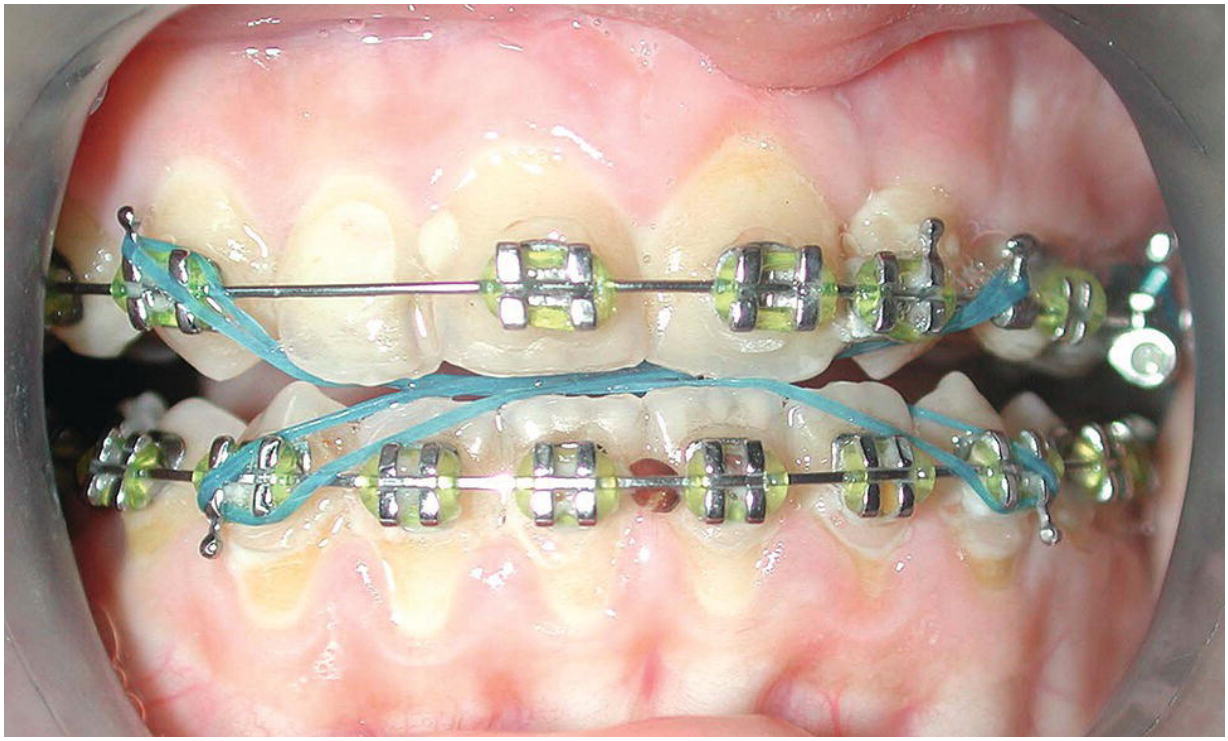

Figure 8.19 Midline oblique elastics to coordinate dental arches during distraction osteogenesis.

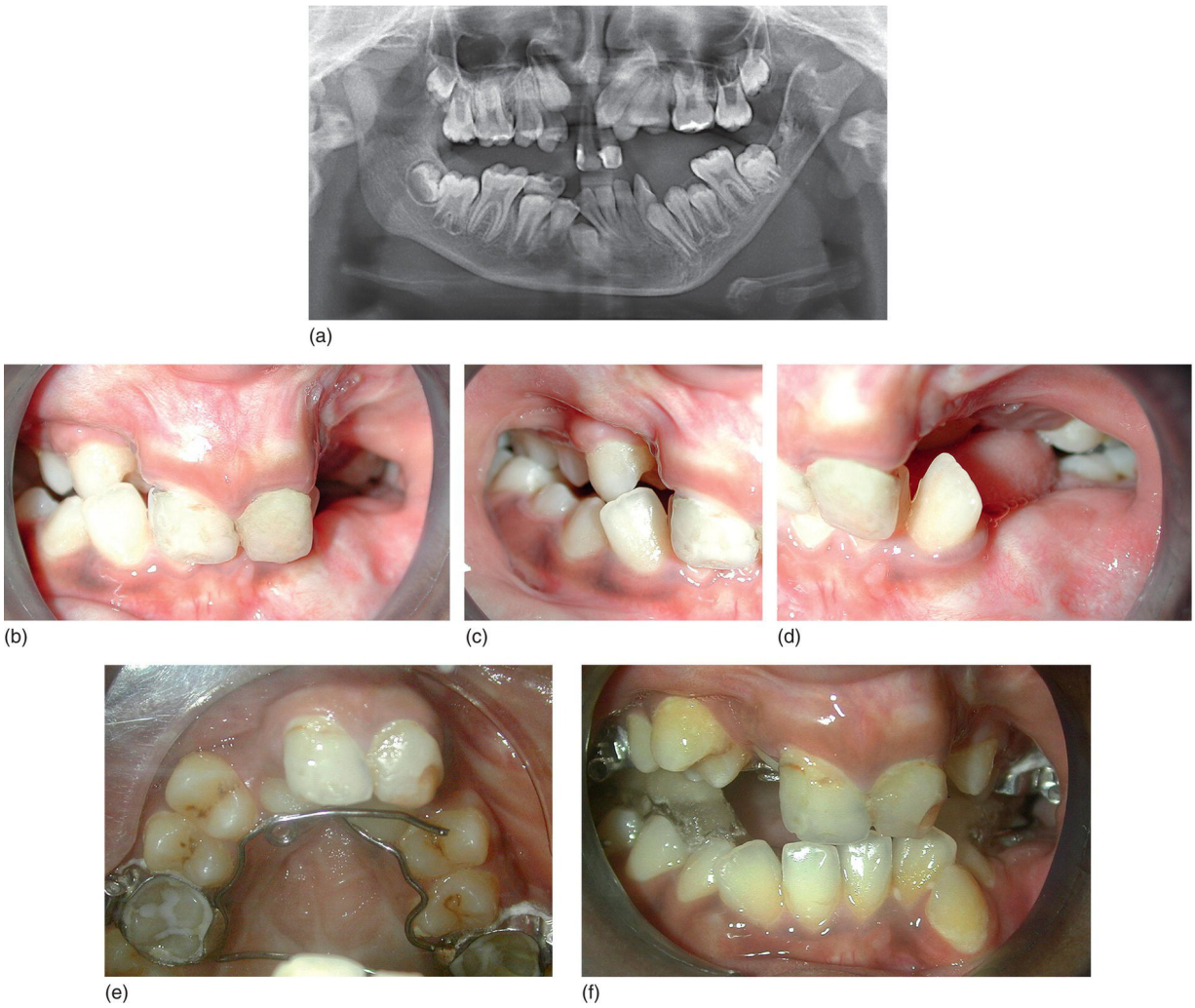

Figure 8.20 Sequential steps in orthodontic treatment following distraction osteogenesis in a growing child with craniofacial microsomia and bilateral cleft palate. (a) Pretreatment orthopantomogram. (b–d) Occlusion after distraction osteogenesis of the mandible was performed. Note the bilateral posterior crossbite that is evident. (e) Fabrication and placement of a soldered custom-made expansion appliance with extension to procline the central incisors. The right maxillary canine can be seen erupting behind the central incisor. (f) A bite block in the mandibular arch for promoting controlled eruption of the maxillary teeth.

The role of functional appliances

The aim of functional therapy is to stimulate the impaired stomatognathic system, to substitute for absent structures, and to

promote differential growth on both sides of the face (Silvestri et al., 1996). There are mixed reports on the efficacy of functional appliance in the postdistraction period. Maintenance of the vertical increase in the ramus and corrected occlusal plane have been pointed out as the definitive advantages (Takashima et al., 2003; Shetye et al., 2006). But later literature reports that the return of asymmetry is only slowed down by the functional appliances (Meazzini et al., 2008, 2012).

The functional appliances alone are more effective in the milder form of the malformation than in patients with severe malformation, where the functional appliances must be combined with further orthodontics and surgery. But even in these cases, some authors (including those of this chapter) feel that functional therapy is useful, as it corrects the dentoalveolar disorders and prepares the neuromuscular system for the new position adopted by the skeletal structures after surgical intervention. The postsurgical open bite, when functional appliance treatment is followed by surgical intervention, could be treated with the help of comprehensive orthodontic treatment.

Silvestri et al. (1996) have successfully used an asymmetrical functional activator (AFA) to induce harmonious maxillomandibular growth. A wax bite is taken with the mandible protruded and deviated contralaterally to the side of the microsomia, with an occlusal rise greater than the rotation of the occlusal plane. The activator consists of a body of monobloc resin, with an occlusal rise contralateral to the malformation that acts as a guide for the mandible when closed. To prevent the muscular forces from acting, the appliance has a shield in the vestibule on the side of the microsomia and two small inferior shields. In this fashion, all the growth stimuli are directed toward the side of the microsomia, while inhibiting the growth of the maxilla and mandible on the healthy side (Figure 8.21).

Orthodontics in the skeletally mature patient

Distraction is the treatment of choice in skeletally mature patients when the deformity is severe. Orthodontic treatment in these patients is performed in three stages:

- *Predistraction orthodontics*. The aim of predistraction orthodontics is to achieve a functional and esthetic occlusion. It involves moving teeth to the ideal positions relative to basal bone, so that the maxillomandibular skeletal relationship is not compromised by the dental compensations. It is critical to ascertain that the maxillary and mandibular arches are coordinated. For instance, in severe mandibular retrognathia, as the mandible is moved forward the maxillary transverse deficiency might get unmasked, which requires a preoperative expansion approach for its correction. Rigid, full-sized rectangular stainless steel wires, filling the bracket slots, should be in place. If possible, lingual cleats need to be welded to the bands, which may help in using elastics during the distraction phase.

(a)

(b)

(c)

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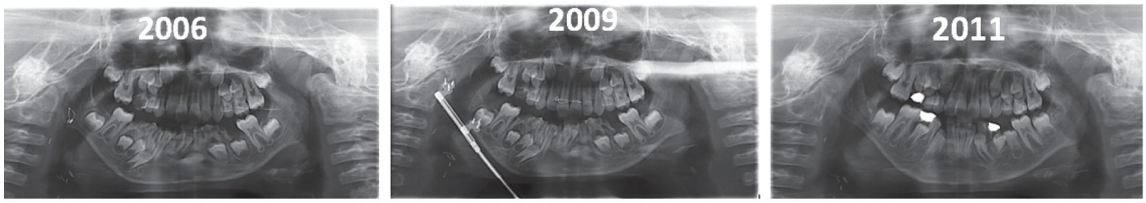
(e)



(f)

Figure 8.21 A growing child with craniofacial microsomia treated with distraction osteogenesis and a hybrid appliance. (a) Occlusion before distraction osteogenesis. (b) Distractor in place. (c) Occlusion after distraction at the start of functional therapy. Note that the upper and lower midlines are not coincident with each other. (d) Hybrid functional appliance in place. Note the upper and lower midlines coinciding when the functional appliance is inserted. (e) Changes in occlusion with distraction osteogenesis and the hybrid appliance. (f) Correction of the mandibular ramal length.

- *Orthodontics during distraction*. This involves close monitoring during the distraction process. Any occlusal interferences with the free movement of the distracted segment might need to be addressed. Bite planes can be used to prevent occlusal

interferences and elastic traction can be applied for correcting transverse discrepancy and occlusal cant. Elastics can be used in a cross-arch or midline-oblique fashion. Sometimes expansion appliances might be needed to correct transverse discrepancies (Figure 8.22).

- *Postdistraction*. Some patients might require further orthognathic surgery to fully correct the deformity. In these instances, presurgical preparation should be commenced. Otherwise, this phase involves correction of transverse discrepancies, midline shifts, and the cant of the occlusal plane. If unilateral mandibular distraction is the treatment choice, controlled vertical closure of the bite, using elastic traction or other means, is performed at this stage (Figure 8.23).

Orthognathic surgery

Many patients treated with early distraction require an orthognathic surgical procedure at a later stage, as the mandibular asymmetry reappears (Nagy et al., 2009). The role of orthodontists at this stage involves participating in the planning of the surgery and performing pre- as well as postsurgical orthodontics.

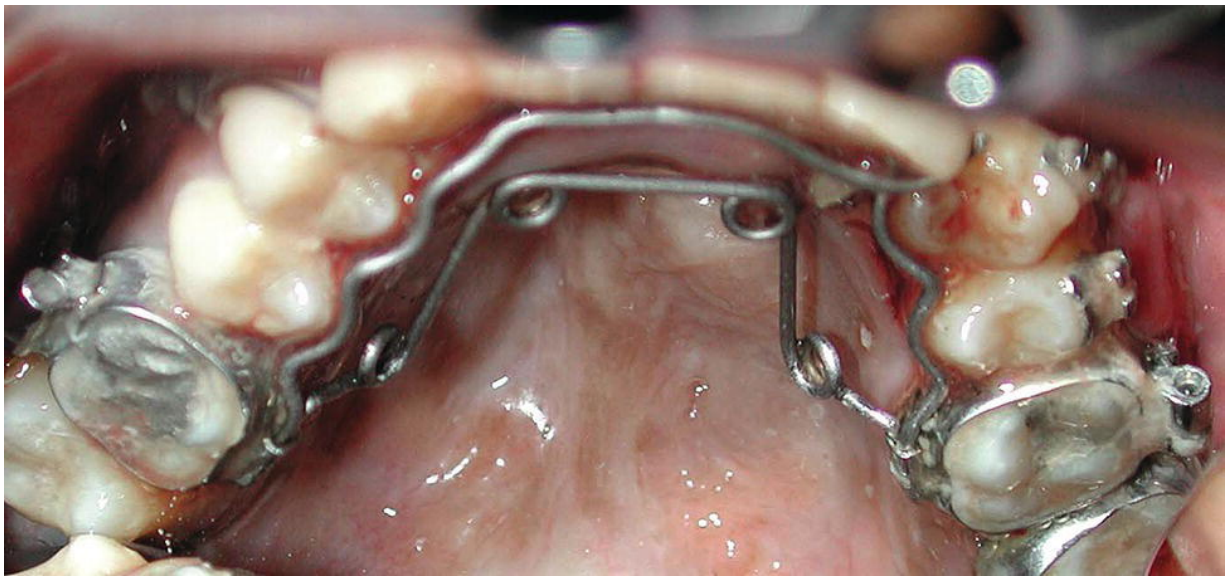


Figure 8.22 Orthodontic treatment with a modified quad-helix during distraction to correct the transverse discrepancy. A posterior bite plane could be used along with expansion devices so that occlusal interferences during distraction procedures can be avoided.

Treacher Collins syndrome (mandibulofacial dysostosis)

Mandibulofacial dysostosis, or Treacher Collins syndrome (TCS), is an autosomal dominant disorder that arises from aberrations in the development of first and second branchial arches, with an incidence of 1 in 50,000 live births (Gorlin et al., 1990). TCS occurs because of destruction of neural crest cells before they migrate to form facial structures (Van Vierzen et al., 1995). TCS is named after Edward Treacher Collins (1862–1932), an English surgeon and ophthalmologist who described two patients with lower eyelid and malar deformities. Tessier (1971a) described TCS as the expression of bilateral 6, 7, and 8 craniofacial clefts, which accounts for the absent or malformed zygomas, eyelid coloboma, and ear and oral malformations (Figure 8.24).

TCS can be recognized at birth, given the characteristic facial appearance (Trainor et al., 2009). The most frequent clinical characteristics include hypoplasia of facial bones, mandible, and zygoma, antimongoloid slant of the palpebral fissure, eyelid coloboma, total or partial absence of lower eyelashes, external ear malformations and conductive hearing loss, cleft palate with shortened soft palate, tongue-shaped process of hair in the face, macrostomia, and obstructive apnea (25% of cases). The convex profile and prominent retruding chin give the characteristic bird facies or fish facies of TCS patients (Franceschetti and Klein, 1949) (Figure 8.25). Dental malalignment with an anterior open bite is common.

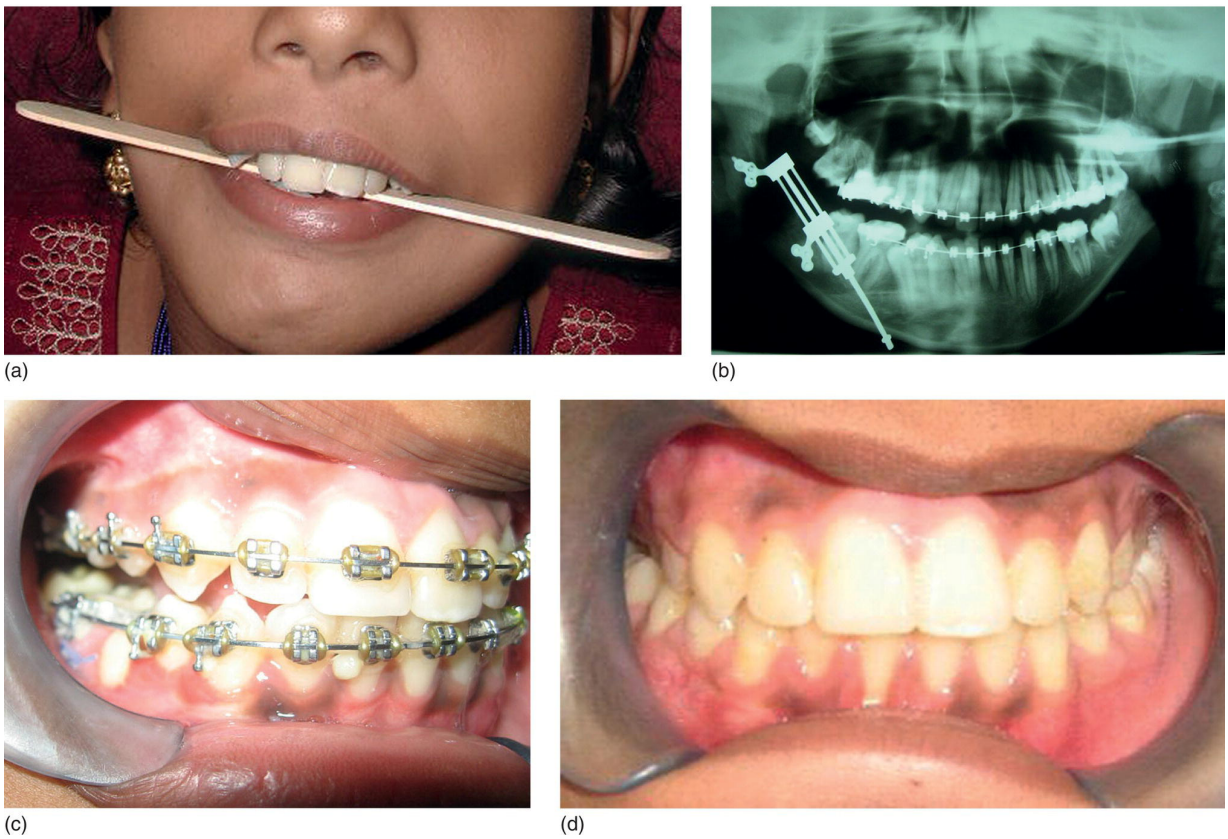


Figure 8.23 Orthodontics in a skeletally mature patient after unilateral mandibular distraction at the right side. (a) Occlusal cant before distraction. (b) Orthopantomogram showing distractor in place. (c) Open bite following unilateral distraction. (d) Occlusion at debonding. The unilateral open bite was closed with conventional orthodontic treatment.

Management

Early diagnosis of TCS allows appropriate management of the functional deficiencies and esthetic concerns in these patients. Ameliorating the outward signs of TCS gives these patients the opportunity to have an improved social life. All members of the craniofacial team need to evaluate the infant with TCS. The hypoplastic mandible and sometimes the maxilla, along with pharyngeal incompetence and choanal atresia, are reasons for concern about the pharyngeal airway and oral alimentation (Dufresne, 1992). Obstructive sleep apnea (OSA) may manifest in infants and adults and its severity may vary from mild to severe. Prone positioning may be all that is required in alleviating milder

airway issues. As severity increases, various interventions such as positive-pressure air, intubation, or tracheostomy may become necessary. The incidence of OSA in TCS is 25–41% (Plomp et al., 2012; Akre et al., 2012).

An experienced pediatric otolaryngologist needs to perform an audiology test to allow early fitting of hearing aids. With TCS 93–96% unilateral or bilateral conductive hearing loss has been reported (Plomp et al., 2016). The speech/swallow team is integral for assistance in learning better communication skills. Speech errors are common in TCS due to the structural anomalies of the dentition and skeleton, choanal atresia, and smaller nasal cavities (Vallino- Napoli, 2002). A pediatric neuro-ophthalmological evaluation of eyelid deformities, ocular muscles, and visual acuity is important. Structural deformities of the periorbital soft tissues may require management to prevent complications such as exposure keratitis. TCS patients are often dissatisfied with the esthetic appearance of the periorbital region, necessitating Z-plasties, musculocutaneous transposition flaps, and lateral canthopexy (Plomp et al., 2013, 2016).

Figure 8.24 (a, b) Characteristic absence of eyelashes in the medial two-thirds of the lower eyelid because of a Tessier number 6 cleft in Treacher Collins syndrome.

Figure 8.25 Characteristic facies in Treacher Collins syndrome. (a) Frontal facial photograph showing bilateral malar flattening because of a Tessier number 7 cleft and anti-mongoloid slant of palpebral fissures due to lack of lateral orbital support because of a Tessier number 8 cleft. (b, c) Lateral facial views showing microtia and anterior displacement of sideburns because of a Tessier number 7 cleft.

DO of the mandible in infancy allows for relief of the issues with breathing and nutrition. In the growing child, distraction allows the mandible to move down and forward, theoretically allowing the maxilla to descend vertically. If maintaining airway patency is not a

major concern, the surgical intervention is delayed to make use of any residual native growth potential and to decrease the total number of surgeries required. A significant amount of relapse has been reported with growth in cases where DO has been performed in childhood.

A definitive procedure at skeletal maturity helps to resolve the problems with occlusion. Often a maxillary osteotomy is needed for esthetics and to restore occlusion. Onlay grafts or patient-specific implants would be required to augment the deficient zygomas (Plomp et al., 2016). Specialized maxillary procedures have been reported to reduce the relative prominence of the central midface (Tulsane and Tessier, 1986; Fuento del Campo et al., 1994).

Staged repair of ear deformities is usually combined with distraction procedures. Split rib and calvarial bone onlay grafts or vascularized bone flaps are needed, depending on the severity of the mandibular and zygomatic hypoplasia. Rhinoplasty and genioplasty are usually carried out along with or after the final bone correction procedure.

Orthodontic management

An experienced multidisciplinary team of orthodontists and maxillofacial surgeons is necessary for good results, since the method of choice in the treatment of TCS is DO associated with preoperative and postoperative orthodontic treatment (Opitz et al., 2004).

A modified treatment schedule advocated by Opitz et al. (2004) included therapeutic measures in the following sequence: preoperative alignment of the maxillary and mandibular dental arches, with extractions if needed to relieve crowding; extraction of all third molars; mandibular advancement by sagittal osteotomy of the ramus; bilateral zygomatic augmentation; genioplasty; rhinoplasty; and postoperative adjustment of the occlusion. Functional appliances for mandibular advancement and protrusion had proved to be only moderately effective.

For DO precise treatment planning and preoperative alignment of the dental arches are needed, to prevent or reduce deviations of the occlusal plane, and to carry out targeted encouragement of vertical

growth, thereby eliminating the dental compensations (Opitz et al., 2004). Orthodontic treatment is usually performed with acrylic splints or functional appliances, with selected bite planes that perform individual occlusal adjustment with selective extrusion of the molars and premolars on the affected side. This also regulates the transverse position of the mandible, especially in cases of unilateral dysplasia. DO demands intensive, often long-term orthodontic aftercare, to achieve correct alignment of the teeth and controlled closure of lateral open bite. Simultaneous or subsequent treatment with intermaxillary elastics is typically used to modify the regenerate bone to be shaped according to need before consolidation.

Presurgical orthodontics commences at around skeletal maturity, and is followed by postsurgical orthodontics after osteotomy, to align the teeth in the best possible relation to the basal bone and to get final occlusal settling.

Craniosynostosis

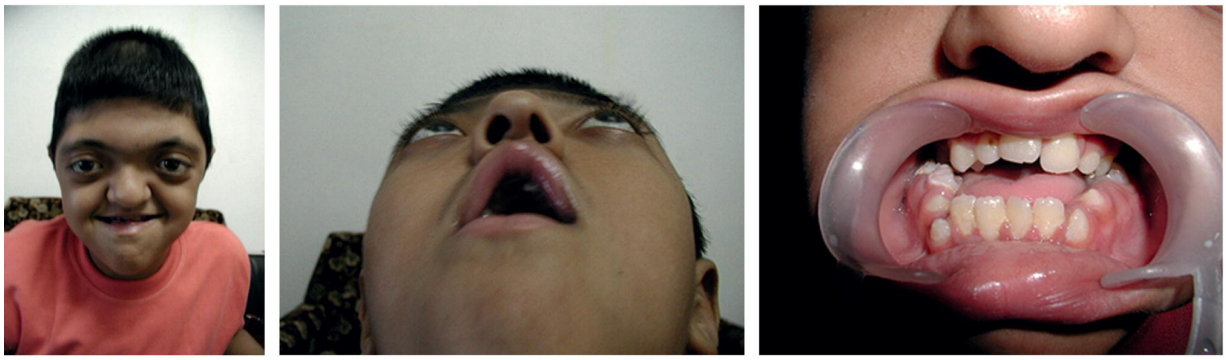
Craniosynostosis characterizes premature closure of the calvarial sutures. There are over 100 recognized syndromes, which include craniosynostoses of various types (Gorlin et al, 1990). Syndromic craniosynostosis is most often genetic in nature. The synostosis of the cranial sutures, and probably a mesenchymal defect in the cranial base, contributes to the abnormal craniofacial features in these syndromic children. Out of more than 100 reported syndromes, the Apert (1 in 25,000 live births) and Crouzon (1 in 25,000 live births) syndromes represent the more commonly identified ones (Cohen, 1986). The craniosynostosis is sometimes present even at birth. All these craniosynostoses may have varying degrees of fusion of the calvarial sutures, which may result in progressive increase in ICP and development of characteristic hypertelorism, exophthalmos, midface deficiency, and a Class III malocclusion (Bartlett, 2007; (Figures 8.26 and 8.27).

These familial syndromes share many common craniofacial features, and the digital anomalies of the hands may be the only differentiating feature. Premature fusion of both coronal sutures results in a brachycephalic head, with a flat, elongated forehead, bitemporal widening, and occipital flattening (Bartlett, 2007).

As the cranial base sutures are frequently involved, forward translation of the midfacial region/maxilla is restricted, resulting in midface hypoplasia. Patients will often present with a concave profile, shallow orbits with exorbitism, along with obstructive sleep apnea (Nout et al., 2008). A skeletal Class III relationship with anterior crossbite is a common finding in these patients (Figure 8.28). The palate is often high arched and constricted, exhibiting lateral palatal swellings containing excess mucopolysaccharides (Solomon et al., 1973; Pruzansky, 1974; Cohen, 1986; Kreiborg and Cohen, 1992) that increase in size with age, especially in Apert syndrome (Figure 8.29). The hard palate is shorter than normal, and the soft palate is longer and thicker (Peterson-Falzone et al., 1981). A cleft of the soft palate, or bifid uvula, occurs in 75% of patients (Kreiborg and Cohen, 1992). As the maxillary arch width is reduced, there is severe crowding and ectopic eruption of teeth (Nurko and Quinones, 2004). Associated with the narrow maxilla, there will be tongue thrust swallow and anterior open bite. In both Apert and Crouzon syndromes, the saliva is thick and mucinous. Patients with Apert syndrome exhibit short clinical crowns, along with thick and fibrous gingival tissue.

(a) (b) (c)

Figure 8.26 Craniosynostosis – Crouzon syndrome. (a) Lateral view showing midface hypoplasia and exorbitism; (b) bird's-eye view of the same patient showing retruded position of the forehead and exorbitism; (c) worm's-eye view showing midface hypoplasia and exorbitism.



(a) (b) (c)

(d) (e)

Figure 8.27 Craniosynostosis – Apert syndrome. (a) Frontal view showing midface hypoplasia and exorbitism; (b) worm's-eye view showing midface hypoplasia and exorbitism; (c) class III occlusal relationship; (d, e) syndactyly in upper and lower limbs.

Apert syndrome, in addition, manifests symmetrical syndactyly of both hands and feet, most often involving fusion of the second, third, and fourth fingers as well as toes. These hand anomalies are so severe and functionally debilitating that referral to a hand surgeon with special expertise in this area is essential (Bartlett, 2007; Figure 8.27).

Figure 8.28 Characteristic Class III skeletal relationship with anterior crossbite and open bite in a patient with Apert syndrome.

Figure 8.29 Palatal swellings seen in the same patient as in Figure 8.28.

Management

Surgical procedures for the correction of craniofacial deformities in patients with syndromic craniosynostosis can be divided into those procedures that are performed early in life (4–12 months: suture release, cranial vault decompression, and upper orbital reshaping/advancement) and those that are performed at a later age (4–12 years for midface deformities at Le Fort III level) and jaw surgery (14–18 years; Bartlett, 2007). These patients often require multiple surgeries, which may include suture release and fronto-orbital advancement (Tessier, 1971b; Cohen, 1986; Whitaker and Bartlett, 1990; Figure 8.30), or distraction of the fused sutures to accommodate the enlarging brain (Sugawara et al., 1998; Kobayashi et al., 1999; Figure 8.7) and advancement of the midface by

osteotomy or distraction (Ortiz-Monasterio et al., 1978; Converse and Telsey, 1971; McCarthy et al., 1990; Polley et al., 1995; Polley and Figueroa, 1997; Cohen et al., 1997; Figure: 8.31). Definitive surgery usually occurs in the postadolescence stage, when a combination of distraction of the maxilla and possibly setback of the mandible may be considered to establish well- or relatively well-balanced skeletal relationships. Definitive surgery to address any residual skeletal issues is dictated by the individual's morphological needs. The exact timing and sequence for each of the surgical procedures are dependent on both the functional and the psychological needs of the patient (Bartlett, 2007).

Skull deformities may require early intervention by a neurosurgeon, so that the elevated ICP and papilledema are relieved, and airway issues necessitating tracheostomy or timely advancement of the midface are carried out (Boston and Rutter, 2003; Hoeve et al, 2003; Pijpers et al., 2004). Chiari formation is another indication for early intervention (Mathijssen, 2021). The early intervention aims at improvement or prevention of deterioration of neurocognition and vision. Esthetic improvement may or may not happen with the early decompression surgeries. Ocular proptosis in these patients results in exposure keratitis (Figure 8.32) and infection leading to corneal ulceration and cataract (Khan et al., 2003). Ocular (sub-)luxation, necessitating reduction of the globe and tarsorrhaphy to contain the globe in the most severe cases, is performed to prevent developing complications (Figure 8.33; Tay et al., 2006).

(a) (b)

Figure 8.30 Craniosynostosis of coronal suture and fronto-orbital advancement. (a) Preoperative lateral photograph; (b) postoperative lateral view. The healed incision line can be seen and advancement of the fronto-orbital region can be appreciated.

(a) (b)

Figure 8.31 Midface distraction in Apert syndrome. (a) Predistraction photograph. Note the scar from previous fronto-orbital advancement. (b) Lateral view with distractor for midface advancement.

Figure 8.32 Exposure keratitis seen in a patient with Apert syndrome – the same patient as in Figure 8.1.

Orthodontic treatment in craniosynostosis

The orthodontist, as part of the team, should be involved from the beginning to monitor the growth and development of the craniofacial complex. It is to be kept in mind that orthodontic treatment alone will not be enough to correct the skeletal and dental deformities. Orthodontics prepares the dentition to match with future jaw positions and is carried out in multiple stages. A close association between the orthodontist and the treating surgeon is essential to establish treatment goals and achieve the desired results in the shortest time possible (Mathijssen and Working Group Guideline Craniosynostosis, 2021). Adherence to strict oral hygiene measures is very important, especially after the beginning of orthodontics, because the orthodontic appliance may lead to difficulties in maintaining hygiene along with the behavioral and functional issues the patient might be having, like reduced manual dexterity due to hand abnormalities.

Orthodontic treatment during childhood

It is necessary at this stage to keep a close eye on the erupting pattern of teeth. Due to the prevalent crowding, it might often be necessary to extract primary teeth to allow permanent teeth to erupt. Primary canines are the most extracted teeth to make space for the erupting laterals or permanent canines. Care should be taken that the extraction of the primary teeth does not bring about a shift in the midline. When the primary canines are extracted in the mandibular arch, a lingual arch might be needed to prevent loss of space. In the maxilla, expansion is often necessary, and a lingual arch or trihelix could be used, because jackscrew expansion in these patients is impossible.

During childhood, in some cases correction of midface deficiency with either monobloc or Le Fort III osteotomy or distraction is performed, as the change in appearance might have a psychological effect on the child (Tessier, 1971b; McCarthy et al., 1990; Polley and Figueroa, 1997). The aim is to correct the fronto-orbital–midface position in these patients. It would be ideal at this stage to wait for the permanent first molars to erupt and for the canines to drop a little so that the teeth are not damaged during osteotomy.

(a) (b)

Figure 8.33 Orbital complications as part of Crouzon syndrome. (a) Globe dislocation because of hypoplastic bony orbits; (b) postreduction photograph with tarsorrhaphy to contain the globe.

All orthodontic procedures during this stage are performed with minimal fixed appliances, such as 2×4 appliances. Once in

rectangular rigid wires, hooks can be attached or a stabilization appliance (Hanson and Melugin, 1999) can be used. These procedures help in the construction of the surgical splint, necessary at the time of performing osteotomy or distraction. The occlusion is not finalized at this stage.

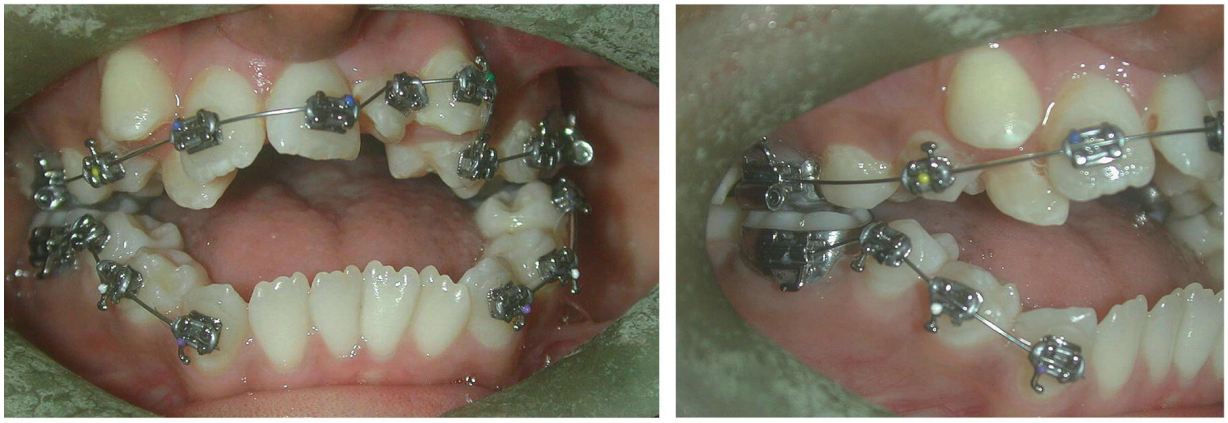
Orthodontic treatment during adolescence

Once growth is over, a Le Fort I osteotomy will be necessary to correct the skeletal Class III relationship (Bachmayer et al., 1986). Orthodontic decompensation must be performed, keeping in mind that movement of teeth will be considerably slower than in normal patients. This slow pace must be explained to the patient and family before initiating the treatment itself. Sometimes it is necessary to perform gingivectomy before bonding, as the clinical crown height is low and the gingiva is thick and fibrous. Sometimes unerupted teeth might need to be exposed with this procedure. During the course of treatment, sometimes the gingivectomy must be repeated due to gingival hyperplasia, because of poor oral hygiene.

Due to pressure from the tongue, the buccal and incisor segments will be at different occlusal levels (Figure 8.34). The alignment procedure in these situations is often initiated with sectional arch orthodontics, and gradually progressed to full archwires (Figure 8.35). In extreme cases orthodontic treatment might have to be finished in sectional wires. In the maxillary arch, exposing the unerupted teeth and gradually aligning them into the dental arch is a major step. With multiple missing teeth, use of implants to obtain the necessary anchorage might be a favorable option (Figure 8.36). Like in normal decompensation, if there is severe crowding extractions become necessary. Correction of midline shifts should be kept in mind while extracting teeth in these patients, making an asymmetrical extraction pattern a good option (Figure 8.37). In the mature adolescent child with severe crowding, surgically assisted palatal expansion (SAPE) is a better alternative (Figure 8.38). Once the teeth are aligned, osteotomy will correct the Class III appearance as well as the decompensated occlusion.

(a) (b) (c)

Figure 8.34 Apert syndrome and occlusion at different occlusal levels. (a) Frontal view; (b) right lateral view; (c) left lateral view.



(a) (b)

Figure 8.35 Sectional arch mechanics in a patient with Apert syndrome to align the different occlusal levels. (a) Frontal occlusal view; (b) right lateral view.

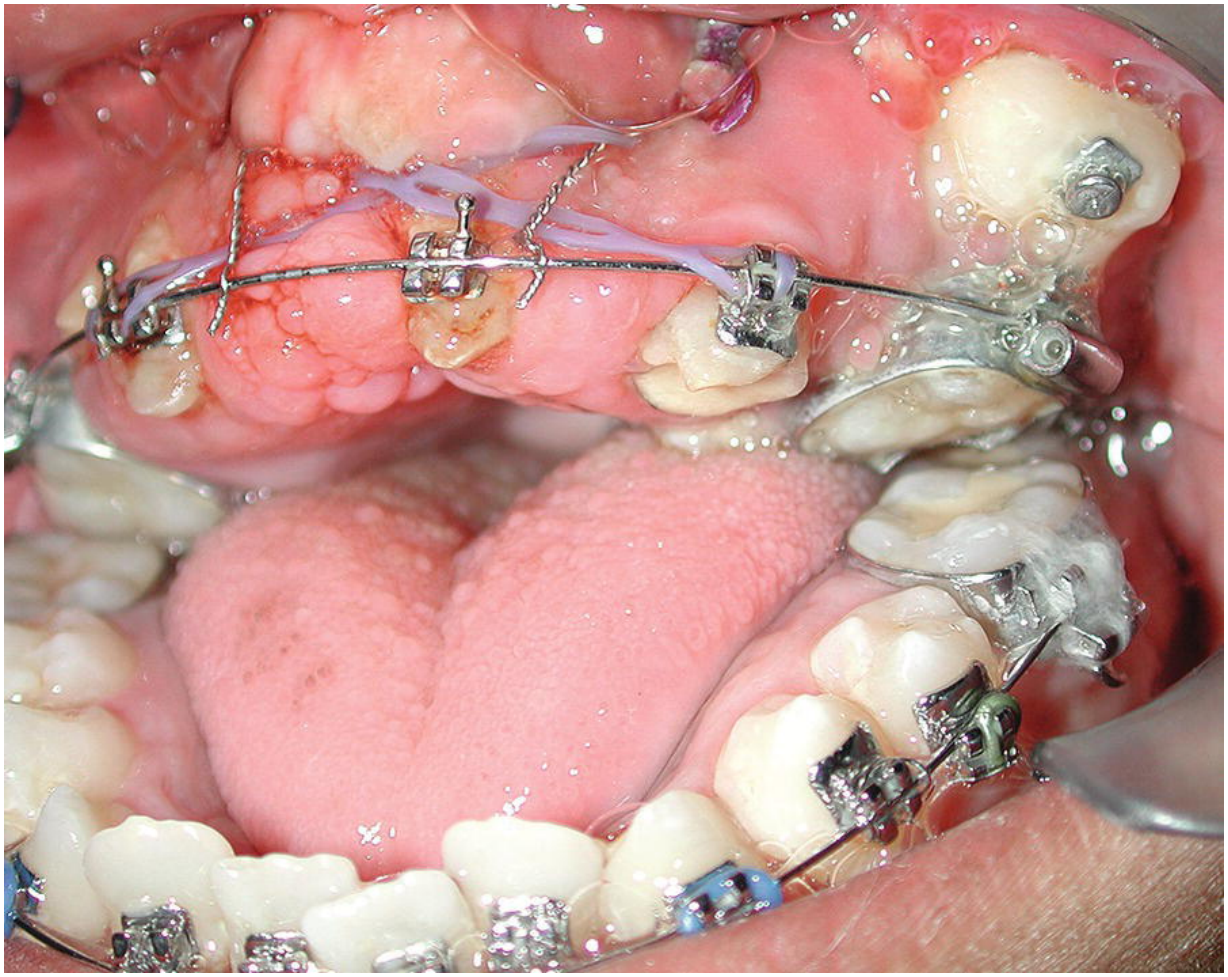
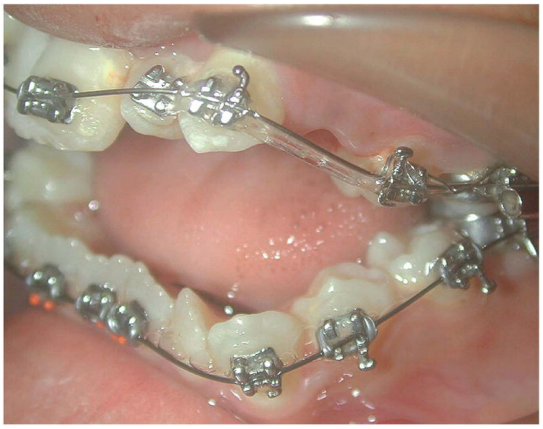


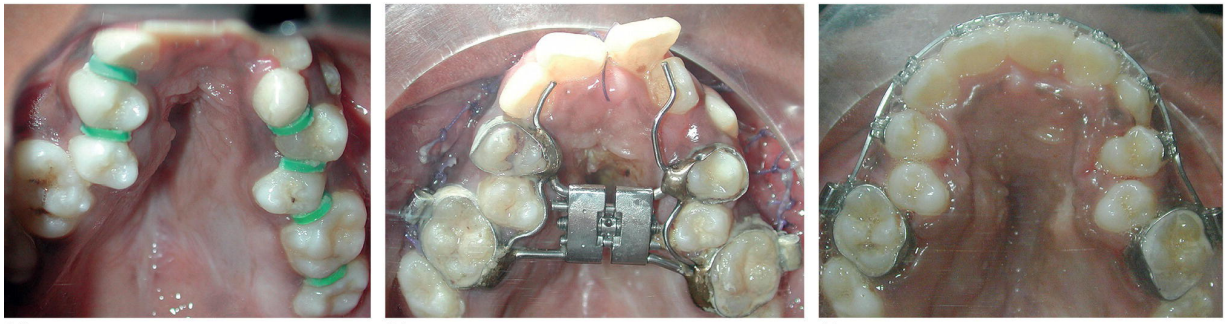
Figure 8.36 Implants placed in the retromolar area to be used as a source of anchorage to distalize the left maxillary molar in a patient with Apert syndrome. Note the chain seen from the first molar distally to the implant placed in the retromolar area.

(a)



(b)

Figure 8.37 (a) The maxillary midline shifted toward the right side in a patient with Apert syndrome. The patient is in the alignment and leveling stage. Note the sectional mechanics used in the lower arch due to different occlusal planes anteriorly and posteriorly. (b) Asymmetrical extraction performed (left maxillary first premolar only) in order to correct the midline.



(a) (b) (c)

Figure 8.38 Crouzon syndrome – treatment with surgically assisted rapid palatal expansion. (a) Severely constricted and high-vaulted palate. Note the placement pattern of the elastic separators to accommodate the bands soldered with the Hyrax. (b) Hyrax in place. (c) Expansion obtained after surgically assisted rapid palatal expansion (SARPE) with Hyrax. Overexpanded rectangular archwire in place to maintain the expansion achieved. The maxillary second premolars need to be aligned and there is a lack of space to accommodate the right maxillary canine, even after performing SARPE.

Postsurgical orthodontics

Postsurgical orthodontics aims mainly at preventing relapse and coordinating the arches. The archwires might need to be changed from rectangular stabilizing wires to working wires to achieve good arch coordination and occlusion. Elastics are used in different directions for occlusal settling and to prevent relapse. In Apert and Crouzon patients, it might be useful to apply a reverse pull headgear to prevent relapse of the Class III skeletal pattern. Box elastics are also used to close open bites and in patients with a tendency toward anterior open bite. For patients with persistent tongue thrusting, habit correction should be considered important (Santiago and Grayson, 2009). Depending on the severity of the initial deformity,

the timing of postsurgical orthodontics may vary, and the treatment stops once the occlusion is stable. Just as in conventional treatment, retention is an important part of treatment of craniofacial microsomia and craniosynostosis patients and due to the potential for relapse, life-long retention is recommended.

Conclusion

Patients with craniofacial anomalies present with multiple skeletal and soft tissue deformities and medical conditions, and an interdisciplinary team approach is the standard of care in most developed nations. Craniofacial units have been established to centralize care and create a critical mass of resources necessary for efficient coordinated therapy. This interactive effort requires timely and careful consideration toward intervention, supported by specific evidence-based protocols, to ensure that the affected individual receives the best care possible. Orthodontists play a unique role in this team, with expertise in assessing, monitoring, and influencing the growth and development of the craniofacial structures. They are active participants in data collection, clinical examination, diagnosis, and treatment planning, and have the opportunity to make a significant contribution at specific times in the management of the child with a craniofacial anomaly.

References

Akre, H., Øverland, B., Åsten, P. et al. (2012). Obstructive sleep apnea in Treacher Collins syndrome. *European Archives of Otorhinolaryngology* 269: 331–337.

Argamaso, R.V. (1992). Glossopexy for upper airway obstruction in Robin sequence. *Cleft Palate-Craniofacial Journal* 29(3): 232–238.

Bachmayer, D.I., Ross, R.B., and Munro, I.R. (1986). Maxillary growth following Le Fort III advancement surgery in Crouzon, Apert, and Pfeiffer syndromes. *American Journal of Orthodontics and Dentofacial Orthopedics* 90: 420–430.

Barden, R.C., Ford, M.E., Jensen, A.G. et al. (1989) Effects of craniofacial deformity in infancy on the quality of mother-infant interactions. *Child Development* 60: 819–824.

Bartlett, S.P. (2007). Craniosynostosis syndromes. In: C.H. Thorne (ed.), *Grabb & Smith's Plastic Surgery*, 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins, pp. 237–247.

Belden, C.J., Mancuso, A.A., and Schmalfuss, I.M. (1999). CT features of congenital nasal piriform aperture stenosis: Initial experience. *Radiology* 213(2): 495–501.

Bergstrom, L., and Baker, B.B. (1981). Syndromes associated with congenital facial paralysis. *Otolaryngology Head and Neck Surgery* 89: 336–342.

Bohm, L.A., Sidman, J.D., and Roby, B. (2016). Early airway intervention for craniofacial anomalies. *Facial Plastic Surgery Clinics of North America* 24: 427–436.

Boston, M., and Rutter, M.J. (2003). Current airway management in craniofacial anomalies. *Current Opinion in Otolaryngology & Head and Neck Surgery* 11: 428–432.

Brent, B. (1992). Auricular repair with autogenous rib cartilage grafts: Two decades of experience with 600 cases. *Plastic and Reconstructive Surgery* 90: 355– 374.

Carr, M.M., Poje, C.P., Kingston, L. et al. (2001). Complications in pediatric tracheostomies. *Laryngoscope* 111: 1925–1928.

Carron, J.D., Derkay, C.S., Strope, G.L. et al. (2000). Pediatric tracheotomies: Changing indications and outcomes. *Laryngoscope* 110(7): 1099–1104.

Cascone, P., Gennaro, P., Spuntarelli, G. et al. (2005). Mandibular distraction: Evolution of treatment protocols in hemifacial microsomy. *Journal of Craniofacial Surgery* 16: 563–571.

Cohen, M.M., Jr. (ed.) (1986) *Craniosynostosis: Diagnosis, Evaluation, and Management*. New York: Raven Press.

Cohen, S.R., Burstein, F.D., Stewart, M.B. et al. (1997). Maxillary-midface distraction in children with cleft lip and palate: A preliminary report. *Plastic and Reconstructive Surgery* 99: 1421–1428.

Collins, B., Powitzky, R., Robledo, C. et al. (2014). Airway management in Pierre Robin sequence: Patterns of practice. *Cleft Palate-Craniofacial Journal* 51(3): 283–289.

Converse, J.M., Coccaro, P.J., and Becker, M. (1973). On hemifacial microsomia – the first and second branchial arch syndrome. *Plastic and Reconstructive Surgery* 51: 268–279.

Converse, J.M., McCarthy, J.G., Coccaro, PJ. et al. (1979). Clinical aspects of craniofacial microsomia. In: J.M. Converse, J.G. McCarthy, and D. Wood-Smith (eds.), *Symposium on Diagnosis and Treatment of Craniofacial Anomalies*. St. Louis, MO: Mosby, pp. 461–462.

Converse, J.M., and Telsey, D. (1971). The tripartite osteotomy of the mid-face for orbital expansion and correction of the deformity in craniostenosis. *British Journal of Plastic Surgery* 24: 365–374

David, J.D., Mahatumarat, C., and Cooter, R.D. (1987). Hemifacial microsomia: A multisystem classification. *Plastic and Reconstructive Surgery* 80: 525–533.

Denny, A.D., Amm, C.A., and Schaefer, R.B. (2004). Outcomes of tongue-lip adhesion for neonatal respiratory distress caused by Pierre Robin sequence. *Journal of Craniofacial Surgery* 15(5): 819–823.

Descamps, M.J., Golding, S.J., Sibley, J. et al. (2010). MRI for definitive in utero diagnosis of cleft palate: A useful adjunct to antenatal care? *Cleft Palate-Craniofacial Journal* 47: 578–585.

Di Pasquo, E., Amiel, J., Roth, P. et al. (2017). Efficiency of prenatal diagnosis in Pierre Robin sequence. *Prenatal Diagnosis* 37: 1169–1175.

Dufresne, C. (1992). Treacher Collins syndrome. In: C. Dufresne (ed.), *Complex Craniofacial Problems: A Guide to Analysis and Treatment*. New York: Churchill Livingstone, p. 169.

Dufton, L.M., Speltz, M.L., and Kelly, J.P. (2011). Psychosocial outcomes in children with hemifacial microsomia. *Journal of Pediatric Psychology* 36: 794–805.

Evans, A.K., Rahbar, R., Rogers, G.F. et al. (2006). Robin sequence: A retrospective review of 115 patients. *International Journal of Pediatric Otorhinolaryngology* 70(6): 973–980.

Evans, K.N., Sie, K.C., Hopper, R.A. et al. (2011). Robin sequence: From diagnosis to development of an effective management plan. *Pediatrics* 127: 936–948.

Franceschetti, A., and Klein, D. (1949). The mandibulofacial dysostosis. A new hereditary syndrome. *Acta Ophthalmologica* 27: 143–224.

Fuento del Campo, A., Elizondo, M.M., and Arnaud, E. (1994). Treacher Collins syndrome (mandibulofacial dysostosis). *Clinics of Plastic Surgery* 21: 613–623.

Gonçalves, L.F., Lee, W., Mody, S. et al. (2016). Diagnostic accuracy of ultrasonography and magnetic resonance imaging for the detection of fetal anomalies: A blinded case–control study. *Ultrasound in Obstetrics and Gynecology* 48(2): 185–192.

Gorlin, R.J., Cohen, M.M., and Levin, L.S. (1990). *Syndromes of the Head and Neck*, 3rd ed. Oxford: Oxford University Press.

Gougoutas, A.J., Singh, D.J., Low, D.W. et al. (2007). Hemifacial microsomia: Clinical features and pictographic representations of the OMENS classification system. *Plastic and Reconstructive Surgery***120**: 112e–113e.

Grayson, B.H., and Santiago, P.E. (1999). Treatment planning and vector analysis of mandibular distraction osteogenesis. *Atlas of the Oral and Maxillofacial Surgery Clinics of North America* 7: 1–13.

Greitz, D. (2004). Radiological assessment of hydrocephalus: New theories and implications for therapy. *Neurosurgical Review* 27: 145–165.

Hanson, P., and Melugin, M.B. (1999). Orthodontic management of the patient undergoing mandibular distraction osteogenesis. *Seminars in Orthodontics* 5: 25–34.

Harada, A., Miyashita, S., Nagai, R. et al. (2019). Prenatal sonographic findings and prognosis of craniosynostosis diagnosed during the fetal and neonatal periods. *Congenital Anomalies* 59: 132–141.

Hoeve, L.J., Pijpers, M., and Joosten, K.F. (2003). OSAS in craniofacial syndromes: An unsolved problem. *International Journal of Pediatric Otorhinolaryngology* 67: S111–S113.

Iseri, H., Kisnisci, R., and Altug-Atac, A.T. (2008). Ten-year follow-up of a patient with hemifacial microsomia treated with distraction osteogenesis and orthodontics: An implant analysis. *American Journal of Orthodontics and Dentofacial Orthopedics* 134: 296–304.

Johnston, M.C., and Bronsky, P.T. (1995). Prenatal craniofacial development: New insights on normal and abnormal mechanisms. *Critical Reviews in Oral Biology and Medicine* 6: 368–422.

Kaban, J.C., Mulliken, J.B., and Murray, J.E. (1981). Three-dimensional approach to analysis and treatment of hemifacial microsomia. *Cleft Palate Journal* 18: 90–99.

Kaban, L.B., Moses, M.H., and Mulliken, J.B. (1988). Surgical correction of hemifacial microsomia in the growing child. *Plastic and Reconstructive Surgery* 82: 9–19.

Kapp, K. (1979). Self concept of the cleft lip and or palate child. *Cleft Palate Journal* 16: 171–176.

Kapp-Simon, K.A. (1995). Psychological interventions for the adolescent with cleft lip and palate. *Cleft Palate-Craniofacial*

Journal 32: 104–108.

Kearns, G.J., Padwa, B.L., Mulliken, J.B. et al. (2000). Progression of facial asymmetry in hemifacial microsomia. *Plastic and Reconstructive Surgery* 105: 492–498.

Khan, S.H., Nischal, K.K., Dean, F. et al. (2003). Visual outcomes and amblyogenic risk factors in craniosynostotic syndromes: A review of 141 cases. *British Journal of Ophthalmology* 87: 999–1003.

Kirschner, R.E., Low, D.W., Randall, P. et al. (2003). Surgical management in Pierre Robin sequence: Is there a role for tongue-lip adhesion? *Cleft Palate-Craniofacial Journal* 40(1): 13–18.

Kobayashi, S., Honda, T., Saitoh, A. et al. (1999). Unilateral coronal synostosis treated by internal forehead distraction. *Journal of Craniofacial Surgery* 10: 467–472.

Koenig, J.L., Amoils, M., Grade, M.M. et al. (2018). Renal ultrasound abnormalities in children with syndromic and non-syndromic microtia. *International Journal of Pediatric Otorhinolaryngology* 113: 173–176.

Kreiborg, S., and Cohen, M.M., Jr. (1992). The oral manifestations of Apert syndrome. *Journal of Craniofacial Genetics and Developmental Biology* 12: 41–48.

Laifer-Narin, S., Schlechtweg, K., Lee, J. et al. (2019). A comparison of early versus late prenatal magnetic resonance imaging in the diagnosis of cleft palate. *Annals of Plastic Surgery* 82: 242–246.

Lam, D.J., Jensen, C.C., Mueller, B.A. et al. (2010). Pediatric sleep apnea and craniofacial anomalies: A population-based case-control study. *Laryngoscope* 120(10): 2098–2105.

Langvatn, E.A., Frič, R., Due-Tønnessen, B.J. et al. (2019). Intracranial volume versus static and pulsatile intracranial pressure values in children with craniosynostosis. *Journal of Neurosurgery: Pediatrics* 24(1): 66–74.

Leslie, E.J., and Marazita, M.L. (2013). Genetics of cleft lip and cleft palate. *Americal Journal of Medical Genetics Part C – Seminars in Medical Genetics* 63C(4): 246–258.

Longaker, M.T., and Siebert, J.W. (1995). Microvascular free flap correction of hemifacial atrophy. *Plastic and Reconstructive Surgery* 96: 800–809.

Loukas, M., Shayota, B.J., Oelhafen, K. et al. (2011). Associated disorders of Chiari type I malformations: A review. *Neurosurgical Focus* 31: E3.

Maarse, W., Bergé, S.J., Pistorius, L. et al. (2010). Diagnostic accuracy of transabdominal ultrasound in detecting prenatal cleft lip and palate: A systematic review. *Ultrasound in Obstetrics and Gynecology* 35: 495–502.

Maarse, W., Boonacker, C.W.B., Swanenburg de Veye, H.F.N. et al. (2018). Parental attitude toward the prenatal diagnosis of oral cleft: A prospective cohort study. *Cleft Palate-Craniofacial Journal* Jan 1. doi: 10.1177/1055665618763337.

Mak, A.S.L., and Leung, K.Y. (2019). Prenatal ultrasonography of craniofacial abnormalities. *Ultrasonography* 38(1): 13–24.

Marazita, M.L. (2012). The evolution of human genetic studies of cleft lip and cleft palate. *Annual Review of Genomics and Human Genetics* 13(1): 263–283.

Marques, I.L., de Sousa, T.V., Carneiro, A.F. et al. (2001). Clinical experience with infants with Robin sequence: A prospective study. *Cleft Palate-Craniofacial Journal* 38(2): 171–178.

Mathijssen, I.M.J and Working Group Guideline Craniosynostosis. (2021). Updated guideline on treatment and management of craniosynostosis. *Journal of Craniofacial Surgery* 32(1): 371–450. doi: 10.1097/SCS.0000000000007035. PMID: 33156164; PMCID: PMC7769187.

Mazzoni, S., Badiali, G., Lancellotti, L. et al. (2010). Simulation-guided navigation: A new approach to improve intraoperative

three-dimensional reproducibility during orthognathic surgery. *Journal of Craniofacial Surgery* 21: 1698–1705.

McCarthy, J.G. (1997). Craniofacial microsomia: A primary and secondary surgical treatment plan. *Clinics in Plastic Surgery* 24: 459–474.

McCarthy, J.G. (2007). Craniofacial microsomia. In: C.H. Thorne (ed.), *Grabb & Smith's Plastic Surgery*, 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins, pp. 248–255.

McCarthy, J.G. (2009). Development of craniofacial orthodontics as a subspecialty at New York University Medical Center. *Seminars in Orthodontics* 15: 221–224.

McCarthy, J.G., LaTrenta, G.S., Breitbart, A.S. et al. (1990). The Le Fort III advancement osteotomy in the child under 7 years of age. *Plastic and Reconstructive Surgery* 86: 633–646.

McCarthy, J.G., Schreiber, J.S., Karp, N.S. et al. (1992). Lengthening of the human mandible by gradual distraction. *Plastic and Reconstructive Surgery* 89: 1–10.

Meazzini, M.C., Mazzoleni, F., Bozzetti, A. et al. (2008). Does functional appliance treatment truly improve stability of mandibular vertical distraction osteogenesis in hemifacial microsomia? *Journal of Cranio-Maxillofacial Surgery* 36: 384–389.

Meazzini, M.C., Mazzoleni, F., Bozzetti, A. et al. (2012). Comparison of mandibular vertical growth in hemifacial microsomia patients treated with early distraction or not treated: Follow up till the completion of growth. *Journal of Cranio-Maxillofacial Surgery* 40: 105–111.

Meurman, Y. (1957). Congenital microtia and meatal atresia. *AMA Archives of Otolaryngology* 66: 443–463.

Meyer, A.C., Lidsky, M.E., Sampson, D.E. et al. (2008). Airway interventions in children with Pierre Robin sequence. *Otolaryngology – Head and Neck Surgery* 138(6): 782–787.

Miller, K.A., Twigg, S.R.F., McGowan, S.J. et al. (2017). Diagnostic value of exome and whole genome sequencing in craniosynostosis. *Journal of Medical Genetics* 54: 260–268.

Munro, I.R., and Lauritzen, C.G. (1985). Classification and treatment of hemifacial microsomia. In: E.P. Caronni (ed.), *Craniofacial Surgery*. Boston, MA: Little, Brown, pp. 391–400.

Nagy, K., Kuijpers-Jagtman, A.M., and Mommaerts, M.Y. (2009). No evidence for long-term effectiveness of early osteodistraction in hemifacial microsomia. *Plastic and Reconstructive Surgery* 124: 2061–2071.

Nargozian, C. (2004). The airway in patients with craniofacial abnormalities. *Paediatric Anaesthesia* 14(1): 53–59.

Nout, E., Cesteleyn, L.L.M., van der Wal, K.G.H. et al. (2008). Advancement of the midface, from conventional Le Fort III osteotomy to Le Fort III distraction: Review of the literature. *International Journal of Oral and Maxillofacial Surgery* 37: 781–789.

Nurko, C., and Quinones, R. (2004). Dental and orthodontic management of patients with Apert and Crouzon syndromes. *Oral Maxillofacial Surgical Clinics of North America* 16: 541–553.

Opitz, C., Ring, P., and Stoll, C. (2004). Orthodontic and surgical treatment of patients with congenital unilateral and bilateral mandibulofacial dysostosis. *Journal of Orofacial Orthopedics* 65: 150–163.

Ortiz-Monasterio, F., delCampo, A.F., and Carillo, A. (1978). Advancements of the orbits and the mid-face in one piece, combined with frontal repositioning for the correction of Crouzon's deformities. *Plastic and Reconstructive Surgery* 61: 507–516.

Ortiz-Monasterio, F., Molina, K., Andrade, L. et al. (1997). Simultaneous mandibular and maxillary distraction in hemifacial microsomia in adults: Avoiding occlusal disasters. *Plastic and Reconstructive Surgery* 100: 852–861.

Paliga, J.T., Tahiri, Y., Silvestre, J. et al. (2014). Screening for obstructive sleep apnea in children treated at a major craniofacial center. *Journal of Craniofacial Surgery* 25(5): 1762–1765.

Perkins, J.A., Sie, K.C., Milczuk, H. et al. (1997). Airway management in children with craniofacial anomalies. *Cleft Palate-Craniofacial Journal* 34(2): 135–140.

Peterson-Falzone, S.J., Pruzansky, S., Parris, P.J. et al. (1981). Nasopharyngeal dysmorphology in the syndromes of Apert and Crouzon. *Cleft Palate Journal* 18: 237–250.

Pijpers, M., Poels, P.J., Vaandrager, J.M. et al. (2004). Undiagnosed obstructive sleep apnea syndrome in children with syndromal craniofacial synostosis. *Journal of Craniofacial Surgery* 15: 670–674.

Plujimers, B.I., Caron, C.J.J.M., Dunaway, D.J. et al. (2014). Mandibular reconstruction in the growing patient with unilateral craniofacial microsomia: A systematic review. *International Journal of Oral and Maxillofacial Surgery* 43: 286–295.

Plomp, R.G., Bredero-Boelhouwer, H.H., Joosten, K.F. et al. (2012). Obstructive sleep apnoea in Treacher Collins syndrome: Prevalence, severity and cause. *International Journal of Oral and Maxillofacial Surgery* 41: 696–701.

Plomp, R.G., van Lieshout, M.J.S., Joosten, K.F.M. et al. (2016). Treacher Collins syndrome: A systematic review of evidence based treatment and recommendations. *Plastic and Reconstructive Surgery* 137(1): 191–204.

Plomp, R.G., Versnel, S.L., van Lieshout, M.J. et al. (2013). Long-term assessment of facial features and functions needing more attention in treatment of Treacher Collins syndrome. *Journal of Plastic Reconstructive and Aesthetic Surgery* 66: e217–e226.

Polley, J.W., and Figueroa, A.A. (1997). Management of severe maxillary deficiency in childhood and adolescence through distraction osteogenesis with an external adjustable, rigid distraction device. *Journal of Craniofacial Surgery* 8: 181–185.

Polley, J.W., Figueroa, A.A., Charbel, F.T. et al. (1995). Monobloc craniomaxillofacial distraction osteogenesis in a newborn with severe craniofacial synostosis: A preliminary report. *Journal of Craniofacial Surgery* 6: 421–423.

Polley, J.W., Figueroa, A.A., Liou, E.J. et al. (1997). Longitudinal analysis of mandibular asymmetry in hemifacial microsomia. *Plastic and Reconstructive Surgery* 99: 328–339.

Posnick, J.C. (2000). *Craniofacial and Maxillofacial Surgery in Children and Young Adults*. Philadelphia, PA: Saunders.

Poswillo, D. (1975). Hemorrhage in development of the face. *Birth Defects Original Article Series* 11: 61–81.

Pruzansky, S. (1974). Palatal anomalies in the syndromes of Apert and Crouzon. *Cleft Palate Journal* 11: 394–403.

Ramsden, J.D., Campisi, P., and Forte, V. (2009). Choanal atresia and choanal stenosis. *Otolaryngology Clinics of North America* 42(2): 339–352.

Robson, C.D., and Hudgins, P.A. (2003). Pediatric airway disease. In: P.M. Som and H.D. Curtin (eds.), *Head and Neck Imaging*, 4th ed. St. Louis, MO: Mosby, pp. 1521–1593.

Rogers, G.F., Murthy, A.S., LaBrie, R.A. et al. (2011). The GILLS score: Part I. Patient selection for tongue-lip adhesion in Robin sequence. *Plastic and Reconstructive Surgery* 128(1): 243–251.

Ross, R.B. (1975). Lateral facial dysplasia (first and second brachial arch syndrome, hemifacial microsomia). *Birth Defects* 11: 51–59.

Sant'Anna, E.F., Lau, G.W., Marquezan, M. et al. (2015). Combined maxillary and mandibular distraction osteogenesis in patients with hemifacial microsomia. *American Journal of Orthodontics and Dentofacial Orthopedics* 147(5): 566–577. Erratum in *American Journal of Orthodontics and Dentofacial Orthopedics* 148(1): 11.

Santiago, P.E., and Grayson, B.H. (2009). Role of the craniofacial orthodontist on the craniofacial and cleft lip and palate team.

Seminars in Orthodontics 15: 225–243.

Schaefer, R.B., Stadler, J.A., 3rd, and Gosain, A.K. (2004). To distract or not to distract: An algorithm for airway management in isolated Pierre Robin sequence. *Plastic and Reconstructive Surgery* 113(4): 1113–1125.

Scott, A.R., Tibesar, R.J., Lander, T.A. et al. (2011). Mandibular distraction osteogenesis in infants younger than 3 months. *Archives of Facial Plastic Surgery* 13(3): 173–179.

Sculerati, N., Gottlieb, M.D., Zimbler, M.S. et al. (1998). Airway management in children with major craniofacial anomalies. *Laryngoscope* 108(12): 1806–1812.

Sgouros, S., Kountouri, M., and Natarajan, K. (2007). Skull base growth in children with Chiari malformation type I. *Journal of Neurosurgery* 107(3): 188–192.

Shetye, P.R., Grayson, B.H., Mackool, R.J. et al. (2006). Long-term stability and growth following unilateral mandibular distraction in growing children with craniofacial microsomia. *Plastic and Reconstructive Surgery* 118: 985–995.

Silvestri, A., Natali, G., and Iannetti, G. (1996). Functional therapy in hemifacial microsomia: Therapeutic protocol for growing children. *Journal of Oral and Maxillofacial Surgery* 54: 271–278.

Solomon, L.M., Medenica, M., Pruzansky, S. et al. (1973). Apert syndrome and palatal mucopolysaccharides. *Teratology* 8: 287–291.

Soltan, H.C., and Holmes, L.B. (1986). Familial occurrence of malformations possibly attributable to vascular abnormalities. *Journal of Pediatrics* 108: 112–114.

Sreejith, V.P., Arun, V., Devarajan, A.P. et al. (2018). Psychological effect of prenatal diagnosis of cleft lip and palate: A systematic review. *Contemporary Clinical Dentistry* 9: 304–308.

Stavrou, P., Sgouros, S., Willshaw, H.E. et al. (1997). Visual failure caused by raised intracranial pressure in craniosynostosis. *Child's*

Nervous System 13: 64–67.

Steinbacher, D.M. (2015). Three-dimensional analysis and surgical planning in craniomaxillofacial surgery. *Journal of Oral and Maxillofacial Surgery* 73: S40–S56.

Steinberg, J.P., Brady, C.M., Waters, B.R. et al. (2016). Mid-term dental and nerve-related complications of infant distraction for Robin sequence. *Plastic and Reconstructive Surgery* 138: 82e–90e.

Sugawara, Y., Hirabayashi, S., Sakurai, A. et al. (1998). Gradual cranial vault expansion for the treatment of craniofacial synostosis. A preliminary report. *Annals of Plastic Surgery* 40: 554–565.

Susanu, S., Popescu, M., Trandafir, L.M. et al. (2018). Multidisciplinary approach for optimal growth and development in children with craniofacial and mandibular anomalies. *Romanian Journal of Oral Rehabilitation* 10(4): 102–108.

Swanson, J.W., Xu, W., Ying, G.S. et al. (2020). Intracranial pressure patterns in children with craniosynostosis utilizing optical coherence tomography. *Child's Nervous System* 36(3): 535–544.

Takashima, M., Kitai, N., Mori, Y. et al. (2003). Mandibular distraction osteogenesis using an intraoral device and bite plate for a case of hemifacial microsomia. *Cleft Palate-Craniofacial Journal* 40(4): 437–445.

Tay, T., Martin, F., Rowe, N. et al. (2006). Prevalence and causes of visual impairment in craniosynostotic syndromes. *Clinical and Experimental Ophthalmology* 34: 434–440.

Tessier, P. (1971a). Vertical and oblique facial clefts (orbitofacial fissures). In: I.C. Mustarde (ed.), *Plastic Surgery in Infancy and Childhood*. Philadelphia, PA: W.B. Saunders, p. 94.

Tessier, P. (1971b). The definitive surgical treatment of the severe facial deformities of craniofacial dysostosis. Crouzon's and Apert's diseases. *Plastic and Reconstructive Surgery* 48: 419–442.

Thompson, D.N.P., Malcolm, G.P., Jones, B.M. et al. (1995). Intracranial pressure in single suture craniosynostosis. *Pediatric Neurosurgery* 22: 235–275.

Trainor, P.A., Dixon, J., and Dixon, M.J. (2009). Treacher Collins syndrome: Etiology, pathogenesis and prevention. *European Journal of Human Genetics* 17: 275–283.

Tuite, G.F., Chong, W., Evanson, J. et al. (1996). The effectiveness of papilledema as an indicator of raised intracranial pressure in children with craniosynostosis. *Neurosurgery* 38(2): 272–278.

Tulsane, I.F., and Tessier, P.L. (1986). Results of the Tessier integral procedure for correction of Treacher Collins syndrome. *Cleft Palate Journal* 23: 40–49.

Twigg, S.R.F., and Wilkie, A.O.M. (2015). New insights into craniofacial malformations. *Human Molecular Genetics* 24: R50–R59.

Vallino-Napoli, L.D. (2002). A profile of the features and speech in patients with mandibulofacial dysostosis. *Cleft Palate and Craniofacial Journal* 39: 623–634.

van der Meulen, J.C., Mazzola, R., Vermey-Keers, C. et al. (1983). A morphogenetic classification of craniofacial malformations. *Plastic and Reconstructive Surgery* 71: 560–572.

van Vierzen, P.B., Joosten, F.B.M., Marres, H.A.M. et al. (1995). Mandibulofacial dysostosis: CT findings of the temporal bones. *European Journal of Radiology* 21: 53–57.

Vento, A.R., LaBrie, R.A., and Mulliken, J.B. (1991). The O.M.E.N.S. classification of hemifacial microsomia. *Cleft Palate-Craniofacial Journal* 28: 68–76.

Wan, D.C., Taub, P.J., Allam, K.A. et al. (2011). Distraction osteogenesis of costocartilaginous rib grafts and treatment algorithm for severely hypoplastic mandibles. *Plastic and Reconstructive Surgery* 127(5): 2005–2013.

Wang, R.R., and Andres, C.J. (1999). Hemifacial microsomia and treatment options for auricular replacement: A review of the literature. *Journal of Prosthetic Dentistry* 82: 197–204.

Wang, R.Y., Earl, D.L, Ruder, R.O. et al. (2001). Syndromic ear anomalies and renal ultrasounds. *Pediatrics* 108: e32.

Whitaker, L.A., and Bartlett, S.P. (1990). Craniofacial anomalies. In: M.J. Jurkiewicz, T.J. Krizek, S.J. Mathes et al. (eds.), *Plastic Surgery Principles and Practice*, vol. 1. St. Louis, MO: Mosby, pp. 99–136.

Wiechers, C., Thjen, T., Koos, B. et al. (2021). Treatment of infants with craniofacial malformations. *Archives of Diseases in Childhood. Fetal and Neonatal Edition* 106(1): 104–109.

Woods, R.H., Ul-Haq, E., Wilkie, A.O.M. et al. (2009). Reoperation for intracranial hypertension in TWIST1-confirmed Saethre-Chotzen syndrome: A 15-year review. *Plastic and Reconstructive Surgery* 123: 1801–1810.

Yamada, S., Park, Y.S., Nakagawa, I. et al. (2020). Non-invasive prediction of intracranial hypertension in patients with craniosynostosis using computed tomography. *Interdisciplinary Neurosurgery: Advanced Techniques and Case Management* 19: 100603.

Yoon, A.J., Pham, B.N., and Dipple, K.M. (2016). Genetic screening in patients with craniofacial malformations. *Journal of Pediatric Genetics* 5: 220–224.

Zim, S., Lee, J., Rubinstein, B. et al. (2017). Prevalence of renal and cervical vertebral anomalies in patients with isolated microtia and/or aural atresia, *Cleft Palate-Craniofacial Journal* 54(6): 664–667.

Zugazaga Cortazar, A., and Martín Martínez, C. (2012). Usefulness of magnetic resonance imaging in the prenatal study of malformations of the face and neck. *Radiologia* 54(5): 387–400.

Part III
Enhancing the Envelope of Orthodontic Care: The Medical Collaboration

9

What Can Orthodontists Learn from Orthopedists Engaged in Basic Research?

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Summary

The first part of this chapter focuses on the need for integration of the terminology used within bone biology into the orthodontic world. According to the appropriate biological terminology, bone modeling is defined as uncoupled resorption and formation activities that occur at different sites, while bone remodeling consists of coupled resorption and formation activities occurring on the same site in a specific sequence; that is, resorption always precedes formation. While bone modeling occurs mainly during growth, bone remodeling occurs throughout life, and plays a role both in the maintenance of phosphate–calcium homeostasis and in the repair of bone microdamages. The movement of the teeth "with" the alveolar bone obtained with orthodontic appliances is a result of bone modeling rather than bone remodeling, although orthodontists generally refer to this phenomenon as remodeling. Bone modeling can be used by the orthodontist for implant site development, by moving a tooth away from the area where new bone must be created. The bone remodeling rate in fact influences the tooth movement rate. Orthodontists may face situations where the bone metabolic rate has changed (due to disease or pharmacological treatment), or may want to accelerate the tooth movement rate by producing local bone damage. The latter case will stimulate bone healing, therefore increasing the tooth movement rate. Clinical situations with metabolic impairment are exemplified in this chapter, and related clinical suggestions are given. In the light of the latest morphological and finite element analysis, the pressure–tension theory is no longer valid in explanations about bone modeling reactions to orthodontic force. This chapter suggests a new paradigm, founded on the assumption that bone cells can react to deformation. Finally, the alveolar bone reaction to skeletal temporary anchorage devices is described, and a potential role for them in bone width maintenance is suggested.

A common language

As correctly indicated by the editors of this book, the face is a part of the whole body. Therefore, there is no reason to believe that the stomatognathic system would not follow general physiopathological rules that apply to the entire body. Basic research carried out by orthopedists can therefore be utilized by orthodontists. However, a precondition for a learning process is a common language.

Modeling

Regarding the biological reaction occurring as a result of orthodontic force systems, there is no lexical consistency between orthodontists and orthopedists, the former describing it as remodeling, the latter as modeling. In bone-biological terms, bone remodeling and modelling are two distinctly separate processes, with different physiological roles.

Modeling is the term applied to changes in the shape and size of bones (macro-modeling) resulting from resorption and formation activities, and is the dominant biological activity during growth. Modeling also occurs at the trabecular level, so-called mini-modeling (Frost, 1990). Resorption and formation drifts do not necessarily follow a given sequence; that is, they are biologically uncoupled. In adult life the physiological mesial drift of the alveolar socket is a result of modeling. Bone modeling reflects the structural adaptation of bone mass and shape to varying demands. It is thus largely controlled by functional and applied loads, and less by systemic metabolic requests. Formation drifts may occur in both lamellar and woven bone. Woven bone is a result of larger strain values than lamellar bone, and usually appears after fracture healing, in response to neoplasms or infections, and in reaction to large mechanical loads produced by orthodontic appliances (Frost, 1994; Figure 9.1).

Clinical implications of modelling

When teeth are moved “with bone,” modeling of the alveolar bone occurs, and thus the teeth can be moved beyond the immediate alveolar envelope while maintaining the marginal bone level. This principle underpins the treatment of partially dentate adult patients

with atrophied alveolar bone areas (Mantzikos and Shamus, 1999; Chandler and Rongey, 2005). An example of so-called tooth movement with bone is illustrated in Figure 9.2, where the tooth has been moved into an atrophic edentulous area, with “rebuilding” of the alveolar process, giving the impression that the tooth has carried the alveolus along to the new position.

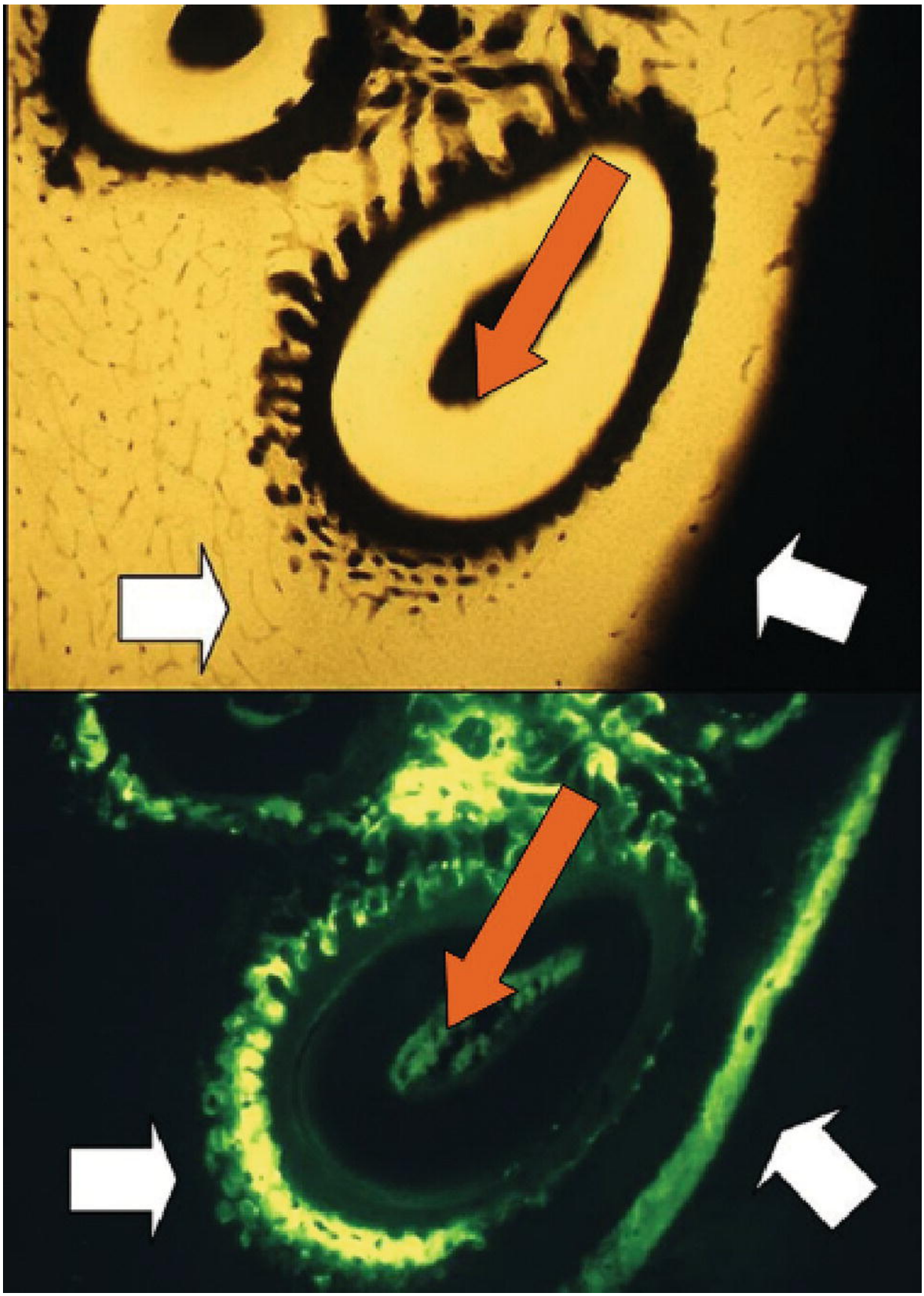


Figure 9.1 Alveolar bone modeling following the application of 25 g of force. After 14 days of treatment, the microradiographic analysis (top) shows new bone formation ahead of the tooth in the direction of the force (red arrows). On the buccal side, new periosteal bone formation is observed, as shown by the wide strips of bone markers (white arrows).

Source: Verna et al. (1999b) / with permission from ELSEVIER.

When determining the force system necessary for a planned tooth movement, the quantity and quality of the bone surrounding the tooth should be taken into consideration. High-resolution micro-computed tomography (CT) scans of alveolar bone samples show that the bone surrounding the roots is highly variable in density and that the so-called lamina dura is a nonuniform structure (Dalstra et al., 2006; Figure 9.3). Therefore, even very light forces may result in overcompression over small surfaces of the alveolar bone. This is in line with the finding that hyalinization is rarely avoidable (von Bohl et al., 2004), although the amount may vary.

Particular attention should be paid to the origin of the cells that will activate the modeling process. In the case of indirect resorption in areas dominated by dense cortical bone, for example in labial movement of lower incisors, tooth movement requires modeling of the cortical bone, and the osteoclasts should originate from the cortical bone or from the periosteum. Labial tipping of incisors in the presence of thin cortical bone increases the probability of bone fenestration (Baron, 1975). To reduce the risk of iatrogenic dehiscence, the initial force system should be directed at displacement of the apex of the root, which is usually surrounded by trabecular bone. Thereafter, the bending of the alveolar process will generate formation on the buccal side of the alveolar process. The use of controlled, uniformly distributed, low-magnitude forces is recommended and, since the modeling rate of cortical bone is slower than that of trabecular bone, adequate time should be allowed for initiation of cellular activation and subsequent bone formation at the periosteal side. An example is shown in Figure 9.4, where the system was checked monthly to adjust the line of action of the force without activation.

In sum, the drift of alveolar bone occurring following application of an orthodontic force can be described as modeling, in response to modified functional demand. Since the anatomy of the teeth differs both within an individual dental arch and between patients, modeling of the alveolar bone without bone loss can only be achieved by use of customized biomechanical systems. However, based on this premise, it is difficult, if not impossible, to agree on absolute standardization of treatments.

Remodeling

As already mentioned, orthodontists do not distinguish between modeling and remodeling. Remodeling is a phenomenon that occurs throughout life in discrete locations in the whole skeleton. It involves cycles of resorption and subsequent formation, spatially and temporally coupled. Remodeling allows bone adaptation to mechanical stresses by minimizing fatigue damage and is influenced by the action of hormones and cytokines (Burr, 1993; Mori and Burr, 1993; Frost, 1998).

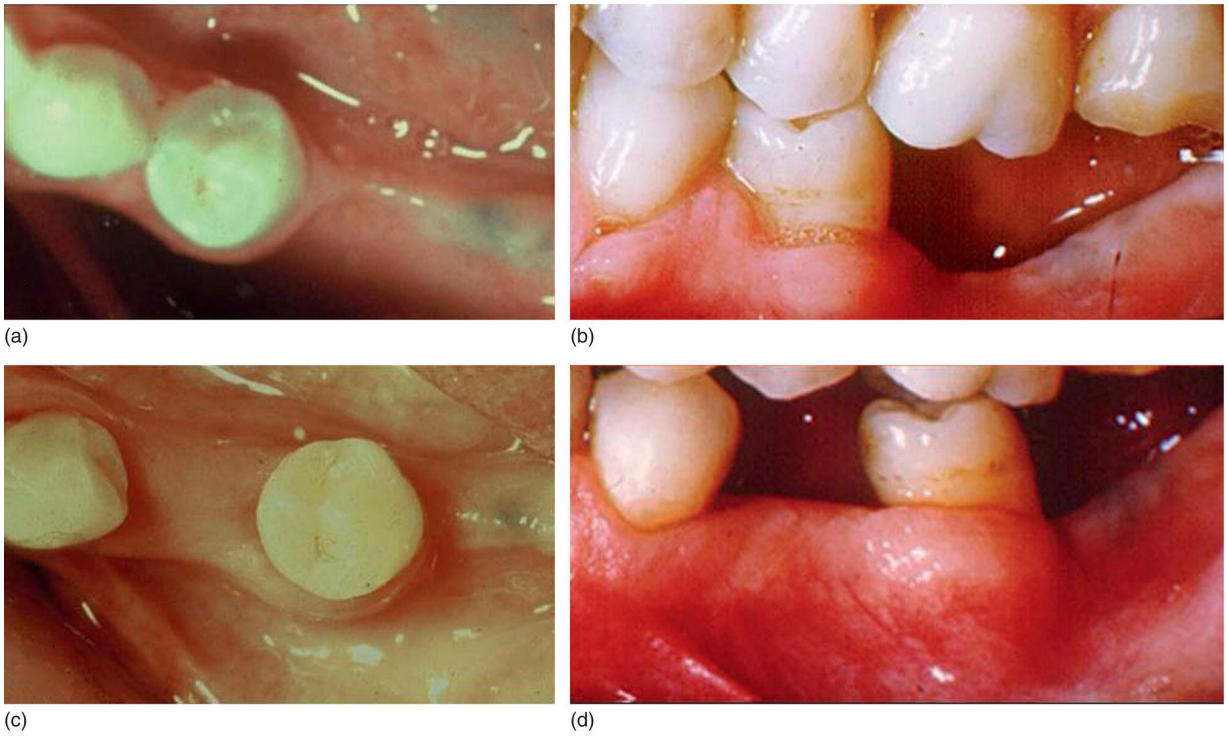


Figure 9.2 (a, b) Tooth movement with bone in an edentulous alveolar crest, where no bone is present. The alveolar drift allows for the movement of the whole alveolus (c, d), and the osteogenic potential of the periodontal ligament is fully expressed in the formation of bone.

Source: Melsen and Garbo (2004) / with permission from Quintessence Publishing Co., Inc.

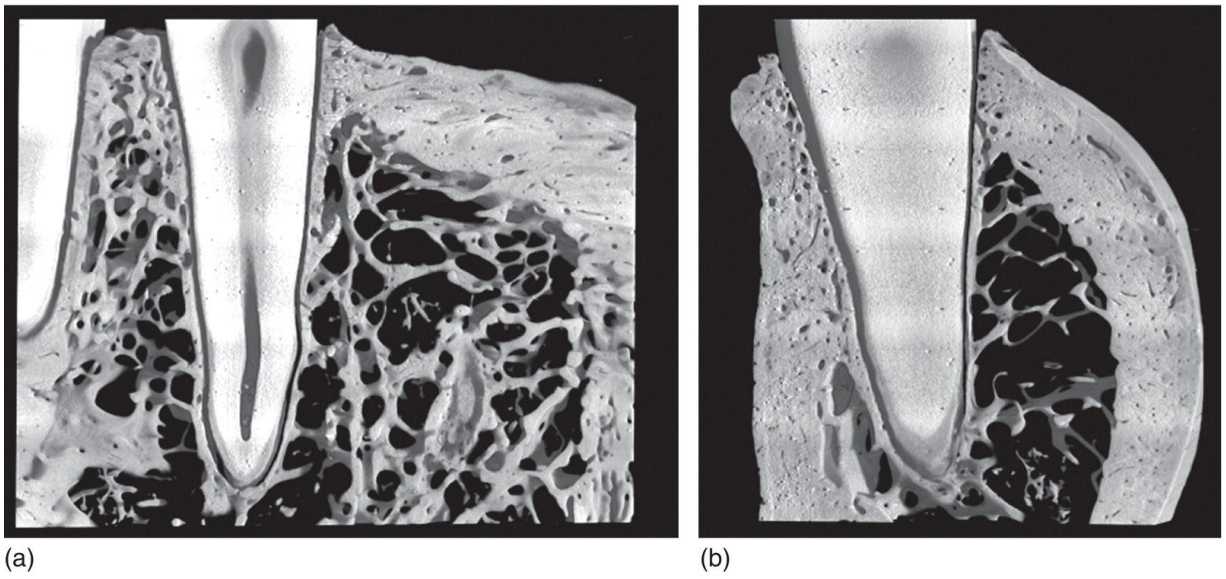
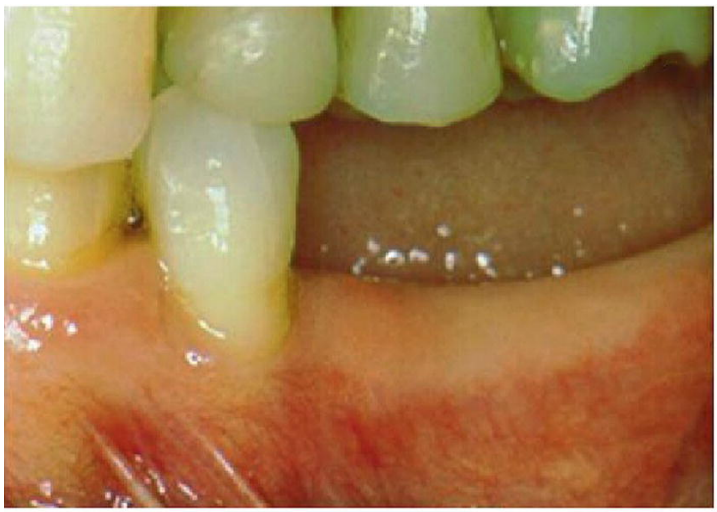


Figure 9.3 (a) Mesiodistal and (b) buccolingual views of the alveolus of the canine. Note the uneven thickness of the alveolar bone proper and the sparse trabecular support.

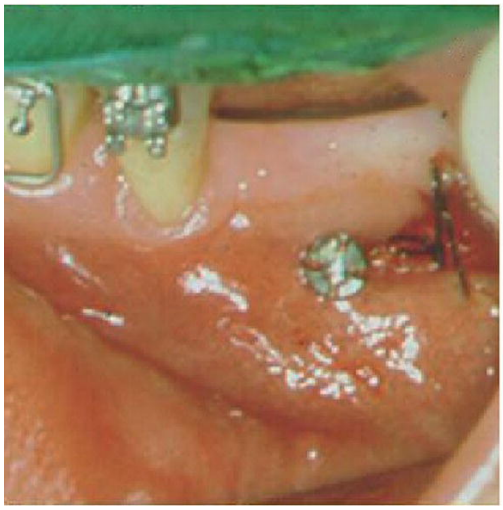
Source: Dalstra et al. (2006) / with permission from John Wiley & Sons.

The bone remodeling cycle is carried out by a team of cells called the bone multicellular unit (BMU; Frost, 1986). The cycle in humans lasts 120–160 days, and is composed of four phases: activation, resorption, reversal, and formation (Eriksen et al., 1984). Although the stimulus necessary for the initiation of a new BMU is still not fully identified, it has been shown that microcracks can initiate remodeling via the sensory input to the osteocytes. In the activation phase, the lining cells, the preosteoblasts, change to a cuboidal shape and secrete a receptor ligand, receptor activator of nuclear factor kappa B ligand (RANKL), on the cell surface. The preosteoclasts within the bone marrow present receptors for RANKL on their cell membrane, called RANK. The interaction between RANK and RANKL determines the activation of the preosteoclasts, which then fuse and differentiate into mature multinucleated osteoclasts and resorb bone. The resorption of bone also occurs as a result of inhibitory activities directed toward osteoblasts, as in the case of the release of sclerostin (SOST), which inhibits bone formation and enhances osteoblast apoptosis (Winkler et al., 2003). The RANKL present on the cell surface of the preosteoblast is neutralized by a free-floating decoy receptor belonging to the tumor necrosis factor (TNF) family, osteoprotegerin (OPG), thus controlling further activation of the preosteoclasts via RANK. Bone resorption lasts for about two weeks, after which the osteoclasts undergo programmed cell death or apoptosis.



(a)

(b)



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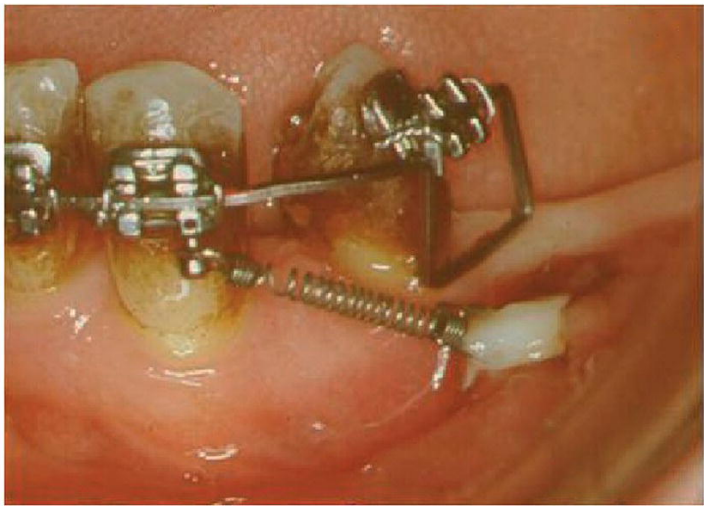

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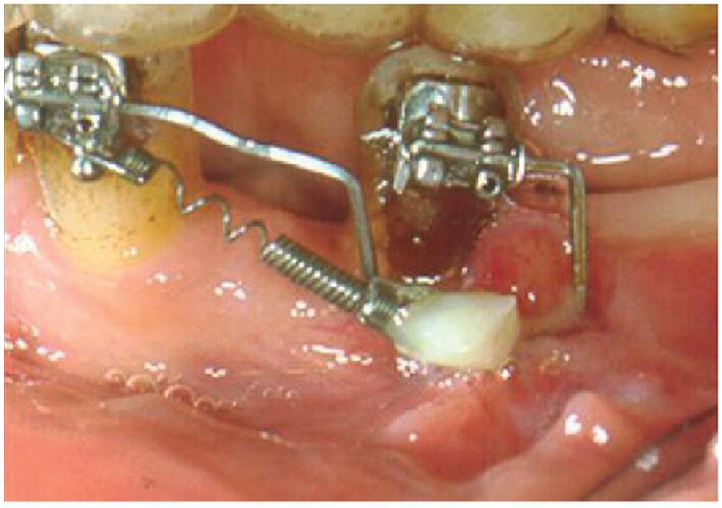


(e)

(f)

Figure 9.4 (a, b) Modeling of the alveolar bone achieved by bodily movement of a premolar in an atrophic area. (c, d) Following the insertion of a mini-implant (Aarhus® system, Medicon, Tuttlingen, Germany), the biomechanical system consisted of a box loop in titanium molybdenum in a 0.017 × 0.025 in. archwire activated to apply a distal force and uprighting moment. This enabled bodily tooth movement, with uniform distribution of the force in the periodontal ligament. Anchorage was ensured by the use of a 50 g superelastic coil spring attached to the skeletal anchorage device. (e, f) The same biomechanical system was used to achieve the final displacement, and at each appointment the appliance was adjusted to maintain the force-to-moment ratio for continuation of the translation movement.

Source: Melsen and Garbo (2004) / with permission from Quintessence Publishing Co., Inc.

Following resorption by the osteoclasts, the lacuna is deepened by mononuclear phagocyte cells (Eriksen et al., 1984). At the end of this process the reversal phase is initiated, and further preosteoblasts migrate into the resorbed cavity and differentiate into osteoblasts. The interface between the resorbed old bone and the new-formed bone is called the cement line, or reversal line, and these osteoblasts now start to form bone. The precursor preosteoblasts are probably attracted by bone-derived growth factors (such as transforming growth factor-beta, TGF-beta) and are derived from marrow stromal cells. Through a positive feedback mechanism the preosteoblasts also secrete growth factors, osteopontin, osteocalcin, and other proteins, such as insulin growth factor-1 (IGF-1), interleukin (IL)-6, bone morphogenetic proteins (BMPs), and fibroblast growth factors (FGFs), all of which enhance the osteoblast's activities. Fibroblasts also migrate toward the cement line and secrete thin collagen fibrils around which the osteoblasts start synthesizing osteoid. The osteoid is nonmineralized bone matrix that cannot be resorbed by osteoclasts. The mineralization process starts when the osteoid thickness reaches about 6 μm. After about four months the resorption cavity is filled with new bone, although not completely, with closely packed mineral crystals and subsequent increase in bone density.

It is essential for the orthodontist to understand the role of remodeling following the application of an orthodontic load. Bone formation has been observed not only in the periodontal ligament (PDL) tension side, but also in the direction of the force (Mohri et al., 1991; King et al., 1992); bone resorption has also been observed at this site (Mohri et al., 1991; Zaffe and Verna, 1995; Melsen, 1999; Figure 9.5). The presence of markers of both resorption and formation adjacent to the alveolar wall reflects the coupled activity of osteoclasts and osteoblasts that characterizes what orthopedists describe as bone remodeling. Synchronized initiation of numerous BMUs results in bone turnover on both the pressure and tension sides in the PDL (Tanne et al., 1990). The RANKL–RANK mechanism has been shown to be active in the PDL and is strengthened by a mechanical load (Ogasawara et al., 2004). Tooth movement can be accelerated by local delivery of RANKL (Kanzaki et al., 2006), whereas the delivery of OPG decreases the rate of tooth movement (Oshiro et al., 2002; Kanzaki et al., 2004). A lack of OPG has been found to be associated with a significantly higher level of bone resorption in the compression area, whereas the upregulation of RANKL induced by orthodontic forces depends on the presence of prostaglandin (PG) E2, which is released by osteoblasts and osteocytes (Kanzaki et al., 2002; Yamaguchi, 2009).

It is clear, therefore, that application of a mechanical load initiates remodeling as well as bone modeling. The variation in the quality of remodeling between patients may explain the individual variations in tissue response to orthodontic treatment.

Clinical implications of bone remodeling

Cortical anchorage was defined by Ricketts (1998) as movement of the roots toward the cortex of the alveolar bone to resist the active force of the appliance. The biological principle behind cortical anchorage is utilization of the differential turnover rates of cortical and trabecular bone, the former being 5–10 times slower than the latter (Steineche and Hauge, 2003). Teeth closer to the cortical bone need more time to be moved, but at a later stage anchorage loss will occur. Absolute anchorage can, however, only be achieved with ankylosed teeth or skeletal anchorage devices (Melsen and Costa, 2000; Melsen and Verna, 2000).

The biological reaction to an orthodontic force system interacts with the already occurring physiological bone turnover. Our knowledge of the turnover rate of bone in the alveolar process is, however, slight. The sole human histomorphometric study comparing static cortical remodeling in the mandible with that of the iliac crest, which is the most frequent site for bone biopsies, showed that the levels of remodeling parameters were lower in the basal part of the mandible than in bone samples harvested from load-bearing areas, confirming that remodeling is maintained by function (Verna et al., 1999a). Recently, the site specificity of bone remodeling has been confirmed by Deguchi et al. (2008), who demonstrated faster bone remodeling and faster tooth movement in a dog's maxilla than in the mandible. This is due not only to a different ratio between cortical and trabecular bone in the two anatomical sites, but also to differences in remodeling rates. At the clinical level, it is advisable to start the orthodontic treatment in the lower jaw to avoid unnecessary prolongation of the treatment time.

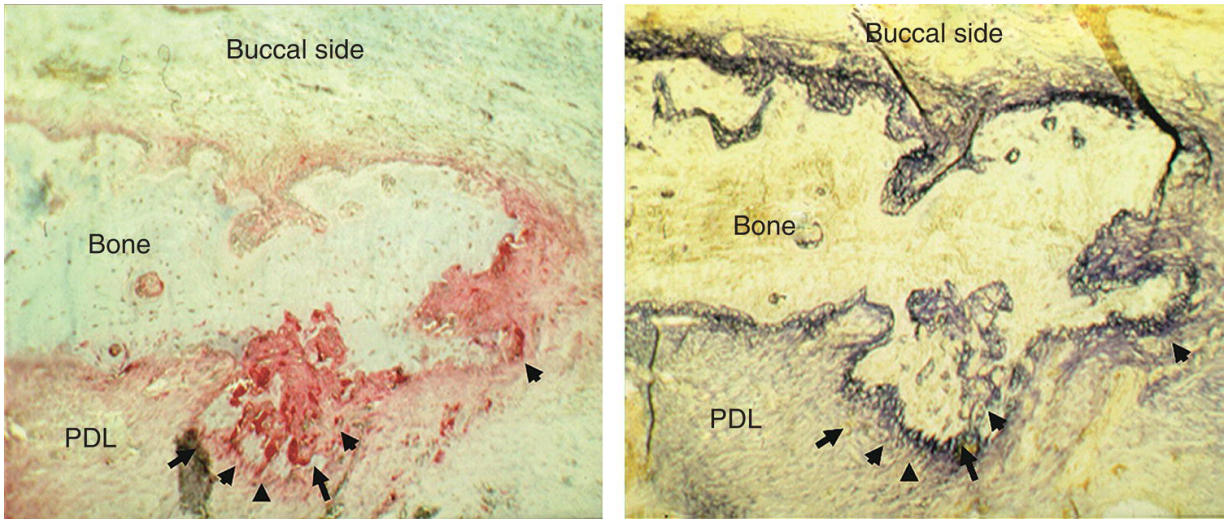


Figure 9.5 Alveolar bone on the buccal side of a rat's tooth after 14 days of orthodontic treatment. On the side facing the periodontal ligament (PDL; arrows), there is staining for alkaline phosphatase (dark blue, right panel) and for acid phosphatase (red, left panel), confirming bone remodeling activities.

Source: Verna and Melsen [2002] / with permission from Libra Ortodonzia.

The rate of tooth movement is influenced by the rate of bone remodeling. Any substance able to interfere with bone remodeling

may, in principle, influence the rate of tooth movement. Different substances have been tried experimentally and clinically to increase/decrease the rate of tooth movement, but their use is not recommended in the routine clinical setting. On the other hand, as clinicians we need to know whether substances that may interfere with orthodontic treatment are being taken by our patients. Nonsteroidal anti-inflammatory drugs, vitamin D, estrogen, and doxycycline are known to interfere with bone remodeling and to decrease the tooth movement rate (Krishnan and Davidovitch, 2006; Bartzela et al., 2009). However, acetaminophen (paracetamol) is an analgesic that does not interfere with tooth movement (Arias and Marquez-Orozco, 2006). Patients should therefore be instructed preferably to take acetaminophen for relief of pain, so that overall treatment time remains unaffected.

Corticosteroid treatment has an inhibitory effect on bone turnover that subsequently leads to secondary hyperparathyroidism. The effect on tooth movement will therefore depend on the duration of the drug treatment, and is enhanced in patients undergoing long-term corticosteroid treatment (Kalia et al., 2004). Where treatment is short, the rate of tooth movement may not be affected, but at a tissue level the remodeling process seems to be delayed. In clinical terms, if a patient is under active orthodontic treatment and has to undergo short-term steroid treatment, such as hay fever therapy, minimal adjustments should be made to the appliance during this period and the interval between appointments may be longer. In treatments of longer duration (about 12 months), the tooth movement rate is increased and the appliance should be checked as usual or more frequently. The effect of steroid treatment on root resorption has also been investigated, with higher rates of root resorption reported in rats administered steroids for a short amount of time (Verna et al., 2006). This is not surprising, since the slower turnover rate will lead to relatively larger amounts of bone covered by osteoid. Since osteoid cannot be resorbed by osteoclasts, the clastic activities are diverted toward the mineralized root surfaces. Once again, in such situations activation of the appliance will not help. On the contrary, less frequent activation will protect against further root damage. In patients with a history of allergy who are undergoing steroid treatment for a short time, it is advisable to

postpone treatment until the patient has completed his or her pharmacological treatment and to follow the earlier suggestions in case of a sudden need for steroids during orthodontic treatment. The effect of corticosteroid treatment on tooth movement is also dose dependent, since high dosages induce osteoporosis, which means there is less bone available for resorption, and therefore the rate of tooth movement increases but with a higher degree of relapse (Ashcraft et al., 1992).

Tooth movement can also be accelerated by local mechanisms that increase the remodeling rate without the use of drugs, such as the regional acceleratory phenomenon (RAP) that occurs after fracture healing, as described by Frost (1994; Roblee et al., 2009). RAP is characterized by local increased resorption and formation activities with less mineralized bone formation, which is a sign of quick repair after an injury. RAP normally occurs following orthodontic tooth movement (Verna et al., 1999b) and its intensity is related to the intensity of the damage. Cortical perforations and corticotomies (with or without surgical flap) performed as part of the orthodontic treatment increase the tooth movement rate approximately twofold (Sanjideh et al., 2010) by enhancing the repair process locally, for example in tooth movement immediately following extraction.

In animal experiments the tissue reaction occurring during corticotomy-assisted tooth movement is characterized by transient bone resorption, followed by the deposition of fibrous tissue after 21 days and by bone after 60 days (Wang et al., 2009). After corticision (a transmucosal corticotomy technique) less hyalinization and more rapid removal of hyalinized tissue has been observed, together with extensive areas of resorption followed by a 3.5-fold higher accumulated mean apposition area of new bone than the control side (Kim et al., 2009). When cortical perforation is combined with alveolar augmentation, the original alveolar volume and any existing osseous dehiscences may no longer be a limitation for orthodontic tooth movement (Wilcko et al., 2009). Since bone density is decreased, the resulting dissipation of the physiological as well as orthodontic forces over the bone surface and the more effective blood supply may reduce root resorption risk. However, to date no histological studies have analyzed root status in areas with more relative osteoid formation, such as in the enhanced bone formation

phase of RAP. Future studies should consider evaluating the duration of the RAP, and thus the possibility of speeding up tooth movement. Longitudinal animal studies have shown that the tooth movement rate approximates the level of non-corticotomy-assisted treatment after about seven weeks (Sanjideh et al., 2010). It is therefore possible that procedures such as RAP will be effective in the alignment and leveling phase. Techniques aimed at reducing the stiffness of cortical bone and increasing the remodeling rate and blood supply may be promising in areas where cortical bone is particularly thick and trabecular bone is present in very small amounts, such as in mandibular molar areas.

Systemic diseases influence the bone turnover rate and thereby the rate of tooth movement. Following the application of orthodontic tipping forces in rats with experimentally induced hyperthyroidism and hypothyroidism, faster tooth movement was observed. This occurs with high rather than with low and normal bone turnover rates. In addition, changes in the quality of the bone tend to relocate the center of resistance, thus having an impact on the type of tooth movement achieved (Verna et al., 2000). Clinically, patients may have high bone turnover rates, such as in untreated hyperthyroidism. An increasing number of adolescents and young adults present signs of eating disorders, such as anorexia nervosa, which result in an osteopenic condition not dissimilar to osteoporosis. In seeing teenage patients regularly for the orthodontic check, the orthodontic team may be the first to detect such psychological distress states.

The influence of bone metabolism on orthodontic tooth movement is particularly important when dealing with adult patients. In pregnant women, orthodontic tooth movement is faster (Hellsing and Hammarström, 1991). A low-calcium diet and lactation are associated with an increased rate of tooth movement because of the decreased bone density, which is due to secondary hyperparathyroidism (Goldie and King, 1984) and consequent reversible bone loss (Karlsson et al., 2001). In patients with transient osteopenia due to an increased bone turnover rate, it is of the utmost importance to keep the force level as low as possible, and to distribute the stresses and the strains in the PDL uniformly; that is, uncontrolled tipping should be avoided. Moreover, orthodontic checks should not simply focus on reactivation of the appliance, but

rather on assessment of the proper line of action of the force to obtain the desired movement. Although faster tooth movement is an advantage, the drawback is the resulting relapse, for which reason life-long retention is recommended.

There has been an increase in the number of older people with metabolic diseases taking long-term medication. Adult patients often benefit from adjunctive orthodontic treatment as part of an interdisciplinary treatment approach, if they have adequate residual dentition and the health of the periodontium can be maintained. In such patients, bone metabolism should be regularly assessed by their physician (Roberts, 1997).

Adult patients may also have osteopenia/osteoporosis. In an ovariectomy-induced osteoporotic rat model, tooth movement was found to be faster, with an increase in bone remodeling markers (Yamashiro et al., 1994). Since osteoporosis is bone loss resulting from a negative calcium balance, additional mechanical perturbation should be carefully considered. It has been suggested that orthodontic treatment in osteoporotic patients can increase the risk of undesirable alveolar bone and root resorption (Miyajima et al., 1996). The degree of osteopenia can be determined by evaluating bone mineral density and serum levels of bone markers. In such patients, the cost versus benefits of orthodontic treatment should be discussed with the patient's physician, especially if the patient is under pharmacological treatment.

Pharmacological treatment of osteoporosis may also influence tooth movement rates. Topical (Adachi et al., 1994; Igarashi et al., 1994, 1996) as well as systemic (Karras et al., 2009) administration of bisphosphonates in rats has been shown to result in a decrease in both the rate of tooth movement and relapse. Osteoporotic patients undergoing treatment with bisphosphonates can thus be expected to exhibit delayed orthodontic tooth movement. These findings, together with the osteonecrosis of the jaws found in a small percentage of patients undergoing bisphosphonate treatment for osteoporosis (Yoneda et al., 2010), indicate that orthodontic treatment in such patients should be performed cautiously. It has recently been suggested that the appropriateness of a "drug holiday" should be discussed with the patient's physician to minimize adverse

effects and optimize orthodontic treatment (Zahrowski, 2009). However, due to the extremely long duration of storage of bisphosphonates in bone, the usefulness of this approach in reducing the risk of potential complications is questionable.

Besides the rate of tooth movement, the risk of root resorption is influenced by the general status of the skeleton. Osteoclasts resorb only mineralized surfaces. In diseases in which there is an increase in the relative amount of osteoid-covered surfaces, such as in Paget's disease, it is more likely that osteoclasts/odontoclasts will resorb the nearest mineralized areas instead; that is, the root surface. This has been confirmed by the finding that rats with low bone remodeling rates show an increased amount of root resorption compared with those with high and normal turnover rates. However, application of an orthodontic force can cancel out these baseline differences (Verna et al., 2003). The presence of osteoid is also relatively increased in cases of fracture healing, and thus the callus requires an increase in the activation frequency of BMUs. It is not surprising that root resorption has been demonstrated in beagle dogs when teeth are actively moved into the regenerate immediately after distraction osteogenesis (Nakamoto et al., 2002). Therefore, it is advisable not to commence orthodontic tooth movement straight after the active phase of rapid palatal expansion.

The impact of general bone turnover on the local tissue reaction to orthodontic forces emphasizes the importance of taking a thorough general history at the patient's first visit. In patients with a history of bone metabolic problems, the patient's physician should be contacted to evaluate the degree of medical control of the condition. These patients are mostly under medical control but, depending on the specific pathology, sufficient diagnostic data, such as serum or urine bone markers and bone mineral density, should be acquired from the physician. However, as previously mentioned, bone remodeling seems to be site specific, and general whole-body data may not reflect the local condition in the jaws. In the case of osteoporosis, a clear association between systemic osteoporosis and bone loss in the jaws has not been established, probably due to individual variations in loading, jaw anatomy, dental health status, and methodological differences among studies (Ejiri et al., 2008). Recently, cortical erosion and/or thickness noted at the inferior

mandibular border on dental panoramic radiographs has been shown to be associated with low vertebral bone mineral density or osteoporosis (Taguchi et al., 2008). Dental practitioners could therefore be able to screen for osteoporosis at no additional expense.

Basic research in bone biology is increasingly focusing on the genetic markers that characterize the clinically observed individual variability. The field of orthodontics is also taking advantage of recent findings in attempts to identify individuals who will react differently to identical biomechanical systems, or to identify patients at risk for developing root resorption. The presence of one or more copies of allele 2 of IL1-beta, collected from human cheek-wipe samples, has been associated with faster tooth movement (Iwasaki et al., 2009). The presence of allele 2 allows for greater production of IL1-beta and for increased bone resorption, and therefore faster rates of tooth movement. The increase in bone resorption decreases the risk of root resorption in these patients (Al Qawasmi et al., 2003). According to Hartsfield (2009), around one-half to two-thirds of the variation observed among orthodontic patients with external apical root resorption is related to genetic factors.

Pressure and tension

Another lexical inconsistency in the description of the mechanical reaction to orthodontic force involves the terms pressure and tension. According to orthopedists, the change in shape observed after loading in long bones is a result of apposition on the compressed side and resorption on the side on which tension prevails (Casagrande and Frost, 1953), as loading leads to a positive bone balance, as is well known. It therefore seems contentious that orthodontists associate compression with resorption, as postulated in the traditional pressure–tension theory. However, since the mechanical load is transferred to the alveolar bone through the PDL, it is not appropriate to extrapolate the effects of the tensile and compressive strains in long bones to those occurring in the PDL.

A finite element (FE) study has also demonstrated that the transfer mechanism of orthodontic loads through the alveolar supporting structures cannot be explained in terms of compression and tension. Based on the low forces used in orthodontic tooth movement and

nonlinear properties of the PDL, the FE model revealed that tension is far more predominant than compression. On the “pressure” side, the fibers of the PDL become curled up and practically no stresses are transferred onto the alveolar wall (Cattaneo et al., 2005; Figure 9.6). Within the alveolar wall, the tensile stresses generated by pulling the PDL fibers are transformed into compressive hoop stresses like in a Roman arch, and tensile and compressive stresses coexist. Considering the findings of state-of-the-art research, orthodontists should avoid using the terms pressure and tension and relate the tissue reaction to the stress/strain distribution instead. This is, furthermore, in line with the biological fact that cells detect changes in load due to deformation and cannot distinguish between pressure and tension. The word pressure is probably still pertinent in cases of high concentration of forces over small surfaces, where the blood pressure is overcome and the root surface is separated from alveolar bone only by hyalinized areas.

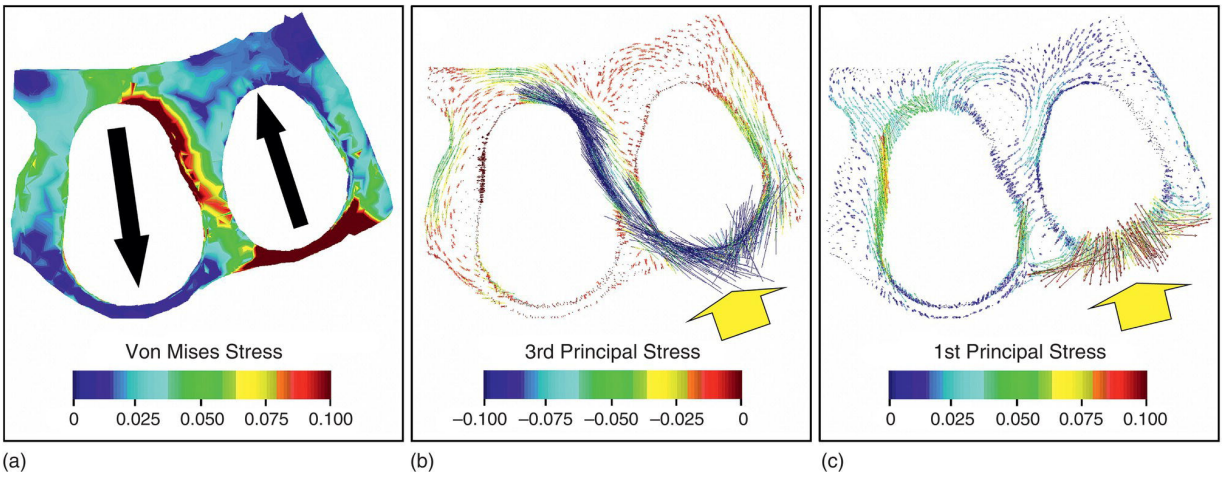


Figure 9.6 A finite element study of a canine and a premolar showing a coronal section of the alveolar bone when a tipping movement is simulated in the direction of the arrow, with material properties assumed to be nonlinear. (a) Stress concentration, described by von Mises stresses, show the lowest values in the direction of the force, while the contrary is observed on the opposite side. Compressive stresses are the lowest in the direction of the force (b), and tensile stresses (c) show an opposite trend. Note that compressive and tensile stresses are simultaneously present in the same area (yellow arrow).

Source: Cattaneo et al. (2005) / with permission from SAGE.

Bone adaptation to mechanical deformation and orthodontic tooth movement

A mechanical load induces a deformation, a change in shape, to which the skeleton must adapt. The bone cells in charge of sensing the change in mechanical loading – that is, the deformation – are the osteocytes. According to the osteocyte plasticity hypothesis, the osteocyte is capable of "normalizing" its local mechanical environment by modulating its cytoskeletal architecture, attachment to the matrix, configuration of the periosteocytic space, and communication channels with the surrounding cells. Macroscopic strains of about 0.2% can be amplified more than 15 times at the osteocyte lacunar level. Strain patterns are highly heterogeneous, and in some locations adjacent to osteocyte lacunae they are like those observed in relation to microdamage. Microdamage increases with fatigue load at physiological levels and is associated with bone remodeling and osteocyte apoptosis (Verborgt et al., 2000; Noble, 2003).

Targeted bone remodeling seems to be initiated as a sign of elimination of damage, to rebuild new bone that is in equilibrium with the new mechanical demand. Since the tissue reaction induced by orthodontic loads mirrors the tissue repair to damage, the question arises of whether the number of microcracks increases in the alveolar bone with orthodontic treatment. In an experimental investigation on 25 3-month-old Danish land-race pigs following a split-mouth design, the lower molars were tipped buccally at different treatment time points and the development of microdamage assessed on days 1 and 2 after the application of the force (Figure 9.7). Microcracks may therefore be the first sites of bone damage induced by orthodontic forces to be repaired by bone remodeling (Verna et al., 2004). It therefore seems likely that the generation of microcracks by an orthodontic force is induced by overloading of bone, as the surface on which the forces are distributed is characterized by many small bony spicules. Osteocyte apoptosis following orthodontic force application has been described (Hamaya et al., 2002), but at present no studies have related it to the microcracks in the alveolar bone. The role of osteocytes in mechanotransduction during orthodontic movement has been

extensively addressed in a recent review of the literature (Murshid, 2017).

Orthopedists associate bone strain with a change in cellular activities (effectiveness). The strain history of a bone is therefore the "rheostat" modulating the occurrence of resorption and formation activities. In describing the response to mechanical usage of bone, Frost (2003) defined four "windows" according to the magnitude of bone strain:

- The *acute disuse window*, where remodeling increases up to five times and no modelling or RAP activities are present, for example cases of resorption in edentulous crests.
- The *adapted window*, where BMUs equalize resorption and formation, and no modeling or RAP occurs. This mode tends to conserve bone and its strength and occurs during normal mechanical usage. In dental terms, an example may be bone loading via the teeth during mastication.
- The *mild overuse window*, where lamellar drift usually occurs with normal formation of BMUs, no RAP, and little microdamage. This is the usual mode of adaptation of bones to growth and to strain changes due to some dental implants.
- The *pathological overload window*, where microdamage occurs and BMUs increase in the repair process. Following fractures, surgical procedures, tooth extractions, implant positioning, and periodontal disease, a RAP takes place.

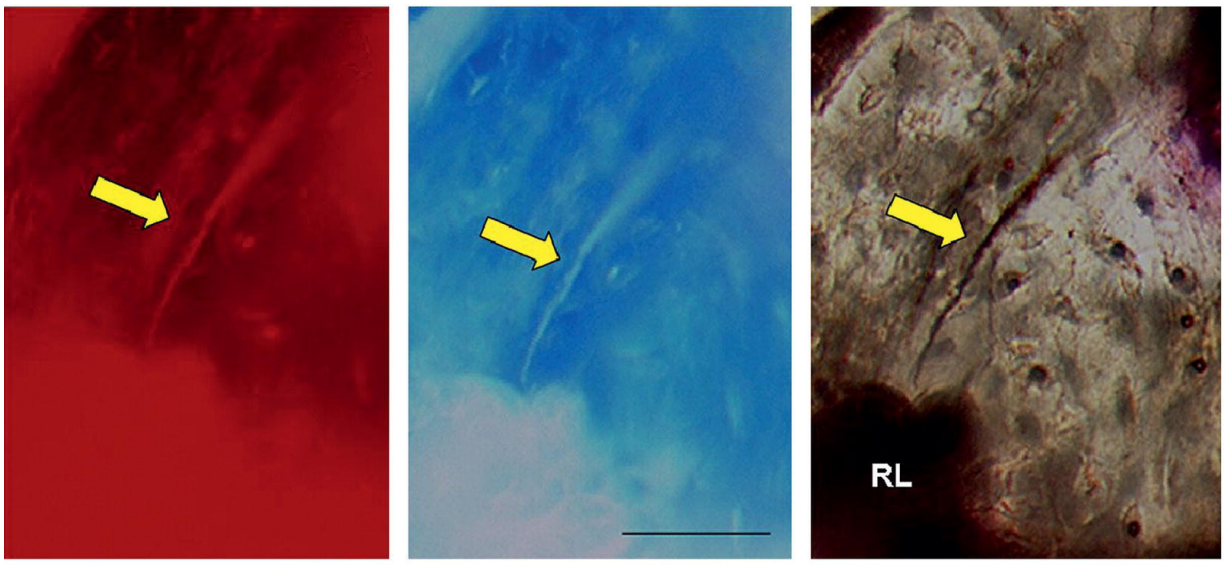


Figure 9.7 (a) A single microcrack (arrow) in the alveolar bone under green, (b) ultraviolet epifluorescence, and (c) transmitted light close to a resorption lacuna (RL) on the buccal treated side of a Danish land-race pig, at day 1. Bar = 50 μm.

Source: Verna et al. (2004) / with permission from Oxford University Press.

If we apply this hypothesis to the reaction of the alveolar bone following the application of an orthodontic force, the direct resorption can be perceived as remodeling. With the curling of PDL fibers during frontal, direct resorption, no strain will be transferred to the alveolar bone when occlusal forces are applied to the teeth and the strain will be below the minimum effective strain (MES). The alveolar wall therefore senses a decreased mechanical load, as in the acute disuse window.

Orthodontic movement "with bone" occurs when the strains are in the adapted and mild overload windows, with lamellar bone formation, and there is a balance between bone resorption and formation. The woven bone commonly observed ahead of the tooth and on the periosteal surface (Reitan, 1967; Melsen, 1999; Verna et al., 1999b) can be considered as a RAP phenomenon – that is, a healing process – occurring because of strain in the range of the overload window. Hyalinization of the PDL, ischemia-induced necrosis of the lining cells, and microdamage of the bone in the direction of the force frequently lead to increased BMU activation. In

the light of the mechanical adaptation window, orthodontic tooth movement can be perceived as a bone adaptation to mechanical deformation that will result in different biological reactions, depending on the strain induced in the alveolar bone.

Bone reaction to skeletal anchorage

In orthopedic surgery, screws are used to obtain mutual stability between different parts of a bone separated either due to a fracture or as part of a surgically planned correction. The rigid fixation allows for immediate function and thereby loading of the screws with controlled forces (Van Sickels and Richardson, 1996). The surgical screws are frequently connected by a mini-plate, whereby the loads acting on the screws are coordinated. This principle has also been applied within orthodontics, where transmucosal extensions of mini-plates fixed to the infrazygomatic crest or the basal bone of the mandible have been used as anchorage both for orthodontic tooth movement and in attempts to alter growth direction (De Clerck et al., 2002). The initial tissue reaction following the insertion of single surgical screws or temporary anchorage devices (TADs) resembles that in permanent implant cases, as the primary stability is dependent on the design of the intraosseous part of the screw and on the type and quality of the bone into which the screw is inserted.

Like surgical screws, TADs are loaded directly or indirectly immediately following insertion. The loading generates a strain in the bone of the insertion site, which is dependent not only on the local bone, the cortical thickness, and the trabecular bone density, but also on the morphology of the intraosseous part of the TAD and the applied load (Alrbata et al., 2016; Francis et al., 2017; Lakshmikantha et al., 2019). According to Frost (1994), the strain will lead to a positive or negative balance, which in the first case will lead to increased stability (so-called secondary stability) or, in the latter case, to loosening and loss of the screw. Dalstra et al. (2004) analyzed the relationship between strain values and different amounts of cortical thickness and trabecular density, and found that in the case of cortical thickness of 1 mm or more, loosening of the mini-implants should not occur if the loading is perpendicular to the long axis. These calculations are based on an FE model of a segment

of human jaw removed at autopsy and a 10 mm cylindrical implant with a 2 mm outer and a 1.2 mm inner diameter loaded with 50 cN perpendicular to the long axis (Figure 9.8). The morphology and cut of the threading do, however, have a certain influence on these results, as shown in Figure 9.9.

Surgical screws are easy to remove, but this does not mean that the screws are not osseointegrated. A certain percentage of the screw surface is in contact with bone even at magnifications of 100× (Figure 9.10). Whereas the bone-to-implant contact present immediately following insertion is the basis of the primary stability of the screw, secondary stability is a product of the strain generated adjacent to the screw. Over time the relative surface in contact with bone has been reported to be both unaltered and increased, which can be explained by differences in assessment techniques used or in data processing. When evaluating data on dogs and monkeys separately in each individual animal, Zhang et al. (2010) noted a strong tendency toward a time-related increase in osseointegration. Orthodontic loading does not seem to have an impact on the degree of osseointegration, as replacement of the bone supplying primary stability with newly formed, well-organized bone has been demonstrated in relation to both loaded and unloaded screws (Serra et al., 2010).

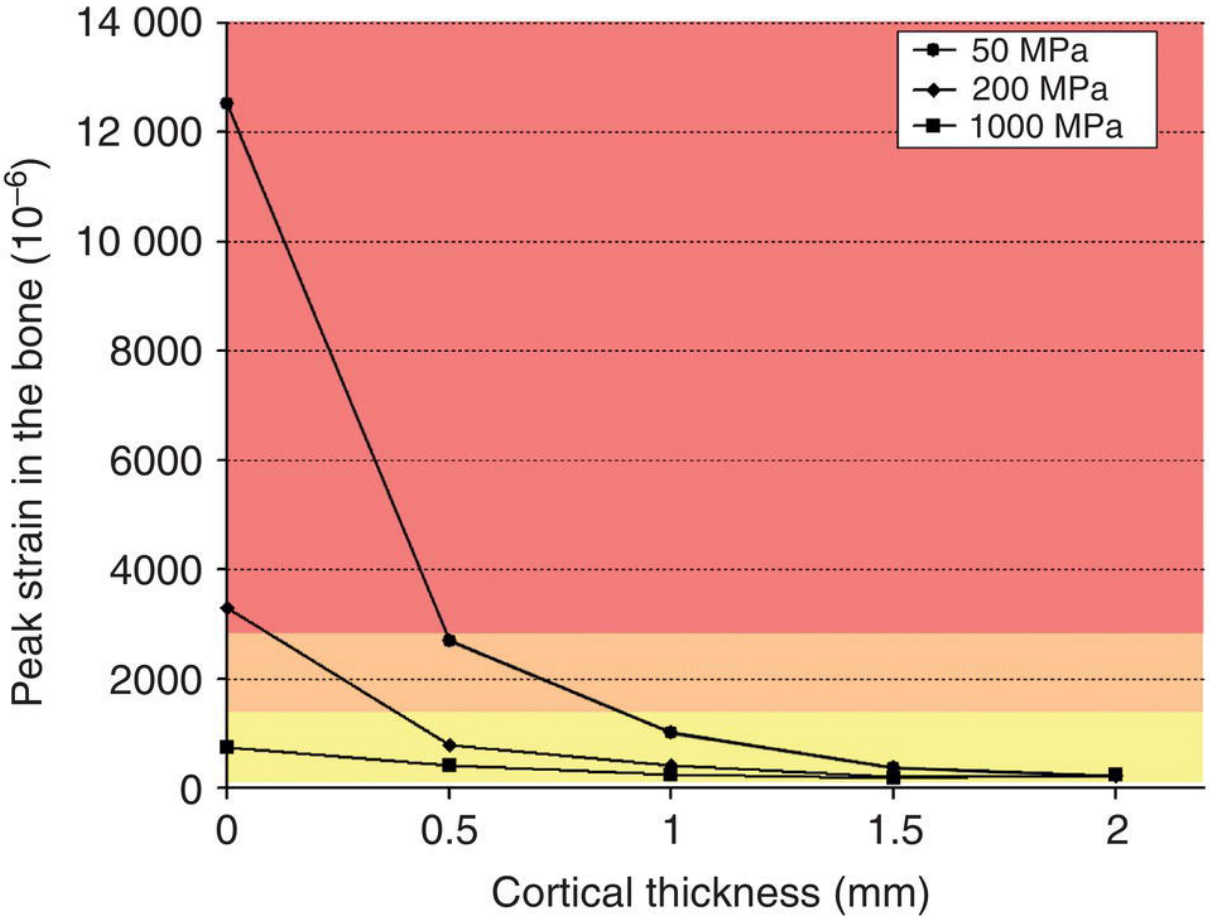


Figure 9.8 Relationship between cortical thickness, trabecular bone density expressed in megapascals, and strain values developed, when the head of the mini-implant was loaded with a 50 cN force perpendicular to the long axis.

Source: Dalstra et al. (2004) / with permission from Quintessence Publishing Co., Inc.

Surgical screws and dental implants differ regarding morphology and the preparation of the surface. Dental implants are intended to stay permanently in the alveolus and the surface treatment serves that purpose, as it increases the absolute surface and enhances the interaction of the cells and the surface (Elias and Meirelles, 2010). Surgical screws are machine polished and most frequently self-drilling. Dental implants are traditionally left unloaded during the healing phase, although research has demonstrated that controlled loading can be applied in this period (Quinlan et al., 2005). In addition to the increase in osseointegration, a time-related

significant increase in bone density was also observed during the first three months of loading (Melsen and Costa, 2000; Figure 9.11).

Histomorphometric analyses of the bone dynamics adjacent to the intraosseous parts of mini-implants have demonstrated a continuous increase in bone turnover identical to what has been described by Roberts et al. (1990) in relation to custom-made titanium implants in humans. This constant remodeling most likely reflects an adaptation of the differences in physical property of the bone and the implants. Osseointegration implies that screws cannot be used as temporary implants; they would submerge and cause periodontal damage to the adjacent teeth (Thilander et al., 2001). TADs, on the other hand, can be used to maintain the width and density of the alveolar bone while waiting for cessation of growth (Ciarlantini and Melsen, 2017; Michelogiannakis et al., 2020; Figures 9.12 and 9.13). For such purposes, it is important to place the TADs transcortically and not on top of the alveolar process, as suggested by Schefler in an interview with Cacciafesta and colleagues (Cacciafesta et al., 2009).

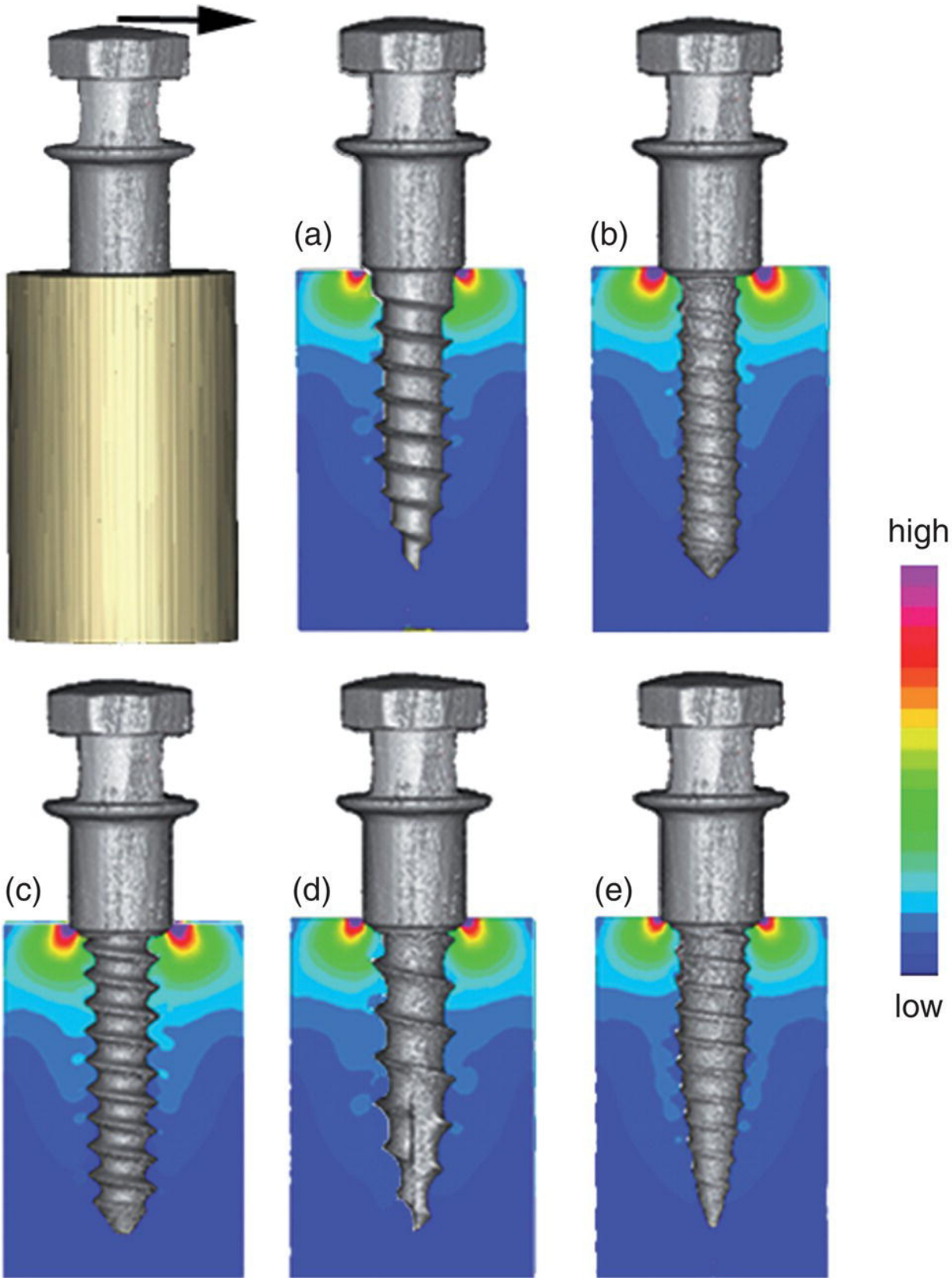

(a)
(b)
(c)
(d)
(e)
high
low

Figure 9.9 Finite element model of five different temporary anchorage devices loaded perpendicular to the long axis. Comparison of the stress intensity (von Mises stresses) distribution in the surrounding bone under force flexure loading for (a) Aarhus mini-screw (Medicon, Tuttlingen, Germany) and four hypothetical designs in which the threaded body was based on (b) Abso-Anchor® (DENTOS, Daegu, Korea), (c) Miniscrew Anchorage System® (MAS; Micerium SpA, Avegno, Italy), (d) tomas® (Dentaurum Group, Ispringen, Germany), and (e) VectorTAS® (Ormco Corporation, Brea, CA, USA) mini-screws. Peak stresses are lowest in designs (a) and (d), suggesting that these devices can withstand the highest loading.

Courtesy of M Dalstra.

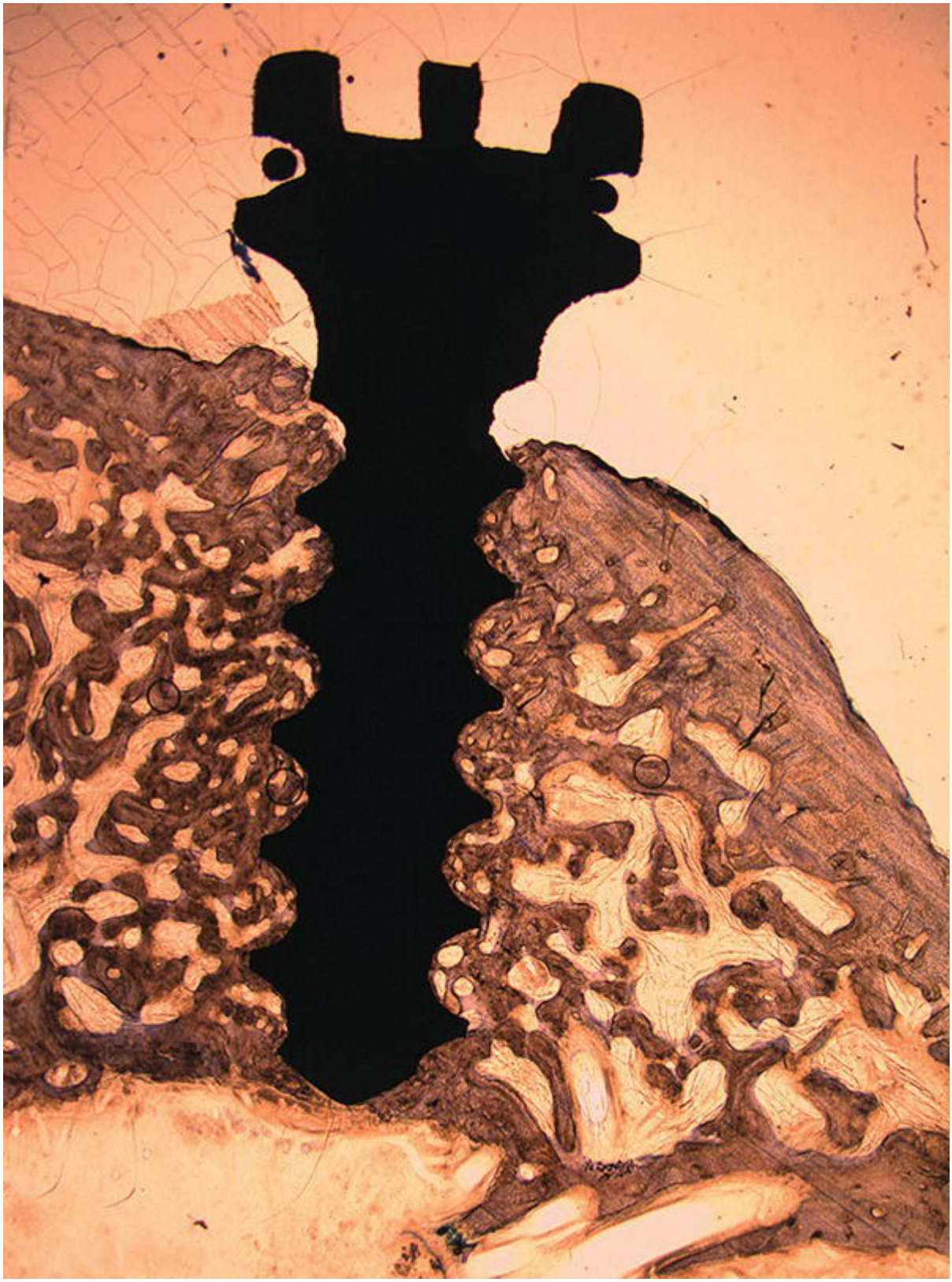
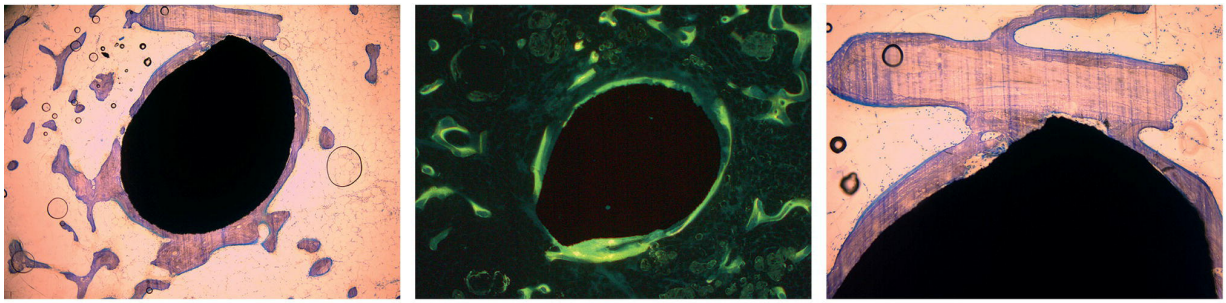


Figure 9.10 Mini-implant inserted into the infrazygomatic crest of a rhesus macaque monkey. Note the increased density of the bone three months after insertion.



(a) (b) (c)

Figure 9.11 (a) Osseointegration of an Aarhus mini-implant at 40× magnification. The bone adjacent to the mini-implant is composed of old lamellar bone and new woven bone. (b) The remodeling of the bone in contact with the mini-implant is reflected in the tetracycline labeling close to the mini-implant. (c) 100× magnification. Note the close contact between bone and implant.

(a)

(b)

(c)

Figure 9.12 (a–c) Intraoral views in a patient with agenesis of all four lower and two upper premolars. On the right side of the lower arch the transcortical mini-implant that was used as anchorage for the mesial movement of the molar was left in place. Note that the thickness and height of the alveolar bone have been maintained.

Figure 9.13 Intraoral view of another patient with agenesis of all four lower and two upper premolars. On the right side of the lower arch a mini-implant, which was placed on the top of the alveolar process and used as anchorage for the mesial movement of the molar, was left in place. It can be seen that eruption of the molar was impeded, whereas the adjacent teeth continued to erupt.

Conclusion

So what can we learn from orthopedists engaged in basic research?

- The tissue reaction in the jaws mirrors that of other parts of the skeleton when submitted to a variety of orthodontic forces.
- The modeling induced by tooth movement permits the generation of alveolar bone, thereby changing the outline of the alveolar process and allowing better conditions for occlusal rehabilitation.
- The general status of bone metabolism influences the rate and quality of tooth movement. The general health of the patient must be taken into consideration.
- As bone remodeling is patient and site related, the rate of tooth movement may differ between patients, even with the use of the same biomechanical systems.
- The strain in bone should be kept as low as possible to maintain the bone balance. The RAP phenomenon can be orthodontically induced and used to enhance bone formation.
- Skeletal anchorage units can be used as absolute anchorage and as a means for the maintenance of alveolar bone width and density.

References

Adachi, H., Igarashi, K., Mitani, H. et al. (1994). Effects of topical administration of a bisphosphonate (risedronate) on orthodontic tooth movements in rats. *Journal of Dental Research* 73: 1478–1486.

Al Qawasmi, R.A., Hartsfield, J.K., Jr., Everett, E.T. et al. (2003). Genetic predisposition to external apical root resorption in orthodontic patients: Linkage of chromosome-18 marker. *Journal of Dental Research* 82: 356–360.

Alrbata, R.H., Momani, M.Q., Al-Tarawneh, A.M. et al. (2016). Optimal force magnitude loaded to orthodontic microimplants: A finite element analysis. *Angle Orthodontist* 86(2): 221–226.

Arias, O.R., and Marquez-Orozco, M.C. (2006). Aspirin, acetaminophen, and ibuprofen: Their effects on orthodontic tooth

movement. *American Journal of Orthodontics and Dentofacial Orthopedics* 130: 364–370.

Ashcraft, M.B., Southard, K.A., and Tolley, E.A. (1992). The effect of corticosteroid-induced osteoporosis on orthodontic tooth movement. *American Journal of Orthodontics and Dentofacial Orthopedics* 102: 310–319.

Baron, R. (1975). Histophysiologie des reaction tissulaires au cours du deplacement orthodontique. In: M. Chateau (ed.), *Orthopedie dento-faciale. bases fondamentales*. Paris: J. Prelat, pp. 328–364.

Bartzela, T., Turp, J.C., Motschall, E. et al. (2009). Medication effects on the rate of orthodontic tooth movement: A systematic literature review. *American Journal of Orthodontics and Dentofacial Orthopedics* 135: 16–26.

Burr, D.B. (1993). Remodeling and the repair of fatigue damage. *Calcified Tissue International* 53(Suppl 1): S75–S80.

Cacciafesta, V., Bumann, A., Cho, H.J. et al. (2009). JCO Roundtable. Skeletal anchorage, part 2. *Journal of Clinical Orthodontics* 43: 365–378.

Casagrande, P.A., and Frost, H.M. (1953). *Fundamental of Clinical Orthopaedics*. New York: Grune and Stratton.

Cattaneo, P.M., Dalstra, M., and Melsen, B. (2005). The finite element method: A tool to study orthodontic tooth movement. *Journal of Dental Research* 84: 428–433.

Chandler, K.B., and Rongey, W.F. (2005). Forced eruption: Review and case reports. *General Dentistry* 53: 274–277.

Ciarlantini, R., and Melsen, B. (2017). Semipermanent replacement of missing maxillary lateral incisors by mini-implant retained pontics: A follow-up study. *American Journal of Orthodontics and Dentofacial Orthopedics* 151(5): 989–994.

Dalstra, M., Cattaneo, P.M., and Beckmann, F. (2006). Synchrotron radiation-based microtomography of alveolar support tissues. *Orthodontics and Craniofacial Research* 9: 199–205.

Dalstra, M., Cattaneo, P.M., and Melsen, B. (2004). Load transfer of miniscrews for orthodontic anchorage. *Orthodontics* 1: 53–62.

De Clerck, H., Geerinckx, V., and Siciliano, S. (2002). The zygoma anchorage system. *Journal of Clinical Orthodontics* 36: 455–459.

Deguchi, T., Takano-Yamamoto, T., Yabuuchi, T. et al. (2008). Histomorphometric evaluation of alveolar bone turnover between the maxilla and the mandible during experimental tooth movement in dogs. *American Journal of Orthodontics and Dentofacial Orthopedics* 133: 889–897.

Ejiri, S., Tanaka, M., Watanabe, N. et al. (2008). Estrogen deficiency and its effect on the jaw bones. *Journal of Bone and Mineral Metabolism* 26: 409–415.

Elias, C.N., and Meirelles, L. (2010). Improving osseointegration of dental implants. *Expert Review of Medical Devices* 7: 241–256.

Eriksen, E.F., Gundersen, H.J., Melsen, F. et al. (1984). Reconstruction of the formative site in iliac trabecular bone in 20 normal individuals employing a kinetic model for matrix and mineral apposition. *Metabolic Bone Diseases and Related Research* 5: 243–252.

Francis, J.C., Oz, U., Cunningham, L.L. et al. (2017). Screw-type device diameter and orthodontic loading influence adjacent bone remodeling. *Angle Orthodontist* 87(3): 466–472.

Frost, H.M. (1986). *Intermediary Organization of the Skeleton*, vols. I, II. Boca Raton, FL: CRC Press.

Frost, H.M. (1990). Skeletal structural adaptations to mechanical usage (SATMU): 1. Redefining Wolff's law: The bone modeling problem. *Anatomical Records* 226: 403–413.

Frost, H.M. (1994). Wolff's law and bone's structural adaptations to mechanical usage: An overview for clinicians. *Angle Orthodontist* 64: 175–188.

Frost, H.M. (1998). A brief review for orthopedic surgeons: Fatigue damage (microdamage) in bone (its determinants and clinical

implications). *Journal of Orthopaedic Science* 3: 272–281.

Frost, H.M. (2003). Bone's mechanostat: A 2003 update. *Anatomical Record. Part A, Discoveries in Molecular, Cellular, and Evolutionary Biology* 275: 1081–1101.

Goldie, R.S., and King, G.J. (1984). Root resorption and tooth movement in orthodontically treated, calcium-deficient, and lactating rats. *American Journal of Orthodontics* 85: 424–430.

Hamaya, M., Mizoguchi, I., Sakakura, Y. et al. (2002). Cell death of osteocytes occurs in rat alveolar bone during experimental tooth movement. *Calcified Tissue International* 70: 117–126.

Hartsfield, J.K., Jr. (2009). Pathways in external apical root resorption associated with orthodontia. *Orthodontics and Craniofacial Research* 12: 236–242.

Hellsing, E., and Hammarström, L. (1991). The effects of pregnancy and fluoride on orthodontic tooth movements in rats. *European Journal of Orthodontics* 13: 223–230.

Igarashi, K., Adachi, H., Mitani, H. et al. (1996). Inhibitory effect of the topical administration of a bisphosphonate (risedronate) on root resorption incident to orthodontic tooth movement in rats. *Journal of Dental Research* 75: 1644–1649.

Igarashi, K., Mitani, H., Adachi, H. et al. (1994). Anchorage and retentive effects of a bisphosphonate (AHBuBP) on tooth movements in rats. *American Journal of Orthodontics and Dentofacial Orthopedics* 106: 279–289.

Iwasaki, L.R., Chandler, J.R., Marx, D.B. et al. (2009). IL-1 gene polymorphisms, secretion in gingival crevicular fluid, and speed of human orthodontic tooth movement. *Orthodontics and Craniofacial Research* 12: 129–140.

Kalia, S., Melsen, B., and Verna, C. (2004). Tissue reaction to orthodontic tooth movement in acute and chronic corticosteroid treatment. *Orthodontics and Craniofacial Research* 7: 26–34.

Kanzaki, H., Chiba, M., Arai, K. et al. (2006). Local RANKL gene transfer to the periodontal tissue accelerates orthodontic tooth movement. *Gene Therapy* 13: 678–685.

Kanzaki, H., Chiba, M., Shimizu, Y. et al. (2002). Periodontal ligament cells under mechanical stress induce osteoclastogenesis by receptor activator of nuclear factor kappaB ligand up-regulation via prostaglandin E2 synthesis. *Journal of Bone and Mineral Research* 17: 210–220.

Kanzaki, H., Chiba, M., Takahashi, I. et al. (2004). Local OPG gene transfer to periodontal tissue inhibits orthodontic tooth movement. *Journal of Dental Research* 83: 920–925.

Karlsson, C., Obrant, K.J., and Karlsson, M. (2001). Pregnancy and lactation confer reversible bone loss in humans. *Osteoporosis International* 12: 828–834.

Karras, J.C., Miller, J.R., Hodges, J.S. et al. (2009). Effect of alendronate on orthodontic tooth movement in rats. *American Journal of Orthodontics and Dentofacial Orthopedics* 136: 843–847.

Kim, S.J., Park, Y.G., and Kang, S.G. (2009). Effects of corticision on paradental remodeling in orthodontic tooth movement. *Angle Orthodontist* 79: 284–291.

King, G.J., Keeling, S.D., and Wronski, T.J. (1992). Histomorphological and chemical study of alveolar bone turnover in response to orthodontic tipping. In: D.S. Carlson and S.A. Goldstein (eds.), *Bone Biodynamics in Orthodontic and Orthopedic Treatment*. Ann Arbor, MI: Center for Human Growth and Development, pp. 281–297.

Krishnan, V., and Davidovitch, Z. (2006). The effect of drugs on orthodontic tooth movement. *Orthodontics and Craniofacial Research* 9: 163–171.

Lakshmikantha, H.T., Ravichandran, N.K., Jeon, M. et al. (2019). 3-Dimensional characterization of cortical bone microdamage

following placement of orthodontic microimplants using optical coherence tomography. *Scientific Reports* 9(1): 1–13.

Mantzikos, T., and Shamus, I. (1999). Forced eruption and implant site development: An osteophysiologic response. *American Journal of Orthodontics and Dentofacial Orthopedics* 115: 583–591.

Melsen, B. (1999). Biological reaction of alveolar bone to orthodontic tooth movement. *Angle Orthodontist* 69: 131–138.

Melsen, B., and Costa, A. (2000). Immediate loading of implants used for orthodontic anchorage. *Clinical Orthodontics and Research* 3: 23–28.

Melsen, B., and Garbo, D. (2004). Treating the "impossible case" with the use of the Aarhus Anchorage System. *Journal of Orthodontics* 1: 13–20.

Melsen, B., and Verna, C. (2000). A rational approach to orthodontic anchorage. *Progress in Orthodontics* 1: 10–22.

Michelogiannakis, D., Javed, F., and Vastardis, H. (2020). Mini-screw implant-supported pontics for the transitional management of missing permanent maxillary lateral incisors in children and adolescents: A review of currently available evidence. *European Archives of Paediatric Dentistry* 21(3): 285–293.

Miyajima, K., Nagahara, K., and Iizuka, T. (1996). Orthodontic treatment for a patient after menopause. *Angle Orthodontist* 66: 173–178.

Mohri, T., Hanada, K., and Osawa, H. (1991). Coupling of resorption and formation on bone remodeling sequence in orthodontic tooth movement: A histochemical study. *Journal of Bone and Mineral Metabolism* 9: 57–69.

Mori, S., and Burr, D.B. (1993). Increased intracortical remodeling following fatigue damage. *Bone* 14: 103–109.

Murshid, S.A. (2017). The role of osteocytes during experimental orthodontic tooth movement: A review. *Archives of Oral Biology*

73: 25–33.

Nakamoto, N., Nagasaka, H., Daimaruya, T. et al. (2002). Experimental tooth movement through mature and immature bone regenerates after distraction osteogenesis in dogs. *American Journal of Orthodontics and Dentofacial Orthopedics* 121: 385–395.

Noble, B. (2003). Bone microdamage and cell apoptosis. *European Cells and Materials* 6: 46–55.

Ogasawara, T., Yoshimine, Y., Kiyoshima, T. et al. (2004). In situ expression of RANKL, RANK, osteoprotegerin and cytokines in osteoclasts of rat periodontal tissue. *Journal of Periodontal Research* 39: 42–49.

Oshiro, T., Shiotani, A., Shibasaki, Y. et al. (2002). Osteoclast induction in periodontal tissue during experimental movement of incisors in osteoprotegerin-deficient mice. *Anatomical Records* 266: 218–225.

Quinlan, P., Nummikoski, P., Schenk, R. et al. (2005). Immediate and early loading of SLA ITI single-tooth implants: An in vivo study. *International Journal of Oral and Maxillofacial Implants* 20: 360–370.

Reitan, K. (1967). Clinical and histologic observations on tooth movement during and after orthodontic treatment. *American Journal of Orthodontics* 53: 721–745.

Ricketts, R.M. (1998). The wisdom of the bioprogressive philosophy. *Seminars in Orthodontics* 4: 201–209.

Roberts, W.E. (1997). Adjunctive orthodontic therapy in adults over 50 years of age. Clinical management of compensated, partially edentulous malocclusion. *Journal of the Indiana Dental Association* 76: 33–40.

Roberts, W.E., Helm, F.R., Marshall, K.J. et al. (1990). Rigid endosseous implants for orthodontic and orthopaedic anchorage. *Angle Orthodontist* 59: 247–256.

Roblee, R.D., Bolding, S.L., and Landers, J.M. (2009). Surgically facilitated orthodontic therapy: A new tool for optimal interdisciplinary results. *Compendium of Continuing Education in Dentistry* 30: 264–275.

Sanjideh, P.A., Rossouw, P.E., Campbell, P.M. et al. (2010). Tooth movements in foxhounds after one or two alveolar corticotomies. *European Journal of Orthodontics* 32: 106–113.

Serra, G., Morais, L.S., Elias, C.N. et al. (2010). Sequential bone healing of immediately loaded mini-implants: Histomorphometric and fluorescence analysis. *American Journal of Orthodontics and Dentofacial Orthopedics* 137: 80–90.

Steineche, T., and Hauge, E. (2003). Normal structure and function of bone. In: H.A. Yuehuei and M.L. Kylie (eds.), *Handbook of Histology Methods for Bone and Cartilage*. Totowa: Humana Press, pp. 59–72.

Taguchi, A., Asano, A., Ohtsuka, M. et al. (2008). Observer performance in diagnosing osteoporosis by dental panoramic radiographs: Results from the osteoporosis screening project in dentistry (OSPD). *Bone* 43: 209–213.

Tanne, K., Nagataki, T., Matsubara, S. et al. (1990). Association between mechanical stress and bone remodeling. *Journal of the Osaka University Dental School* 30: 64–71.

Thilander, B., Odman, J., and Lekholm, U. (2001). Orthodontic aspects of the use of oral implants in adolescents: A 10-year follow-up study. *European Journal of Orthodontics* 23: 715–731.

Van Sickels, J.E., and Richardson, D.A. (1996). Stability of orthognathic surgery: A review of rigid fixation. *British Journal of Maxillofacial Surgery* 34: 279–285.

Verborgt, O., Gibson, G.J., and Schaffler, M.B. (2000). Loss of osteocyte integrity in association with microdamage and bone remodeling after fatigue in vivo. *Journal of Bone and Mineral Research* 15: 60–67.

Verna, C., Dalstra, M., and Melsen, B. (2000). The rate and the type of orthodontic tooth movement is influenced by bone turnover in a rat model. *European Journal of Orthodontics* 22: 343–352.

Verna, C., Dalstra, M., and Melsen, B. (2003). Bone turnover rate in rats does not influence root resorption induced by orthodontic treatment. *European Journal of Orthodontics* 25: 359–363.

Verna, C., Dalstra, M., Lee, T.C. et al. (2004). Microcracks in the alveolar bone following orthodontic tooth movement: A morphological and morphometric study. *European Journal of Orthodontics* 26: 459–467.

Verna, C., Hartig, L., Kalia, S. et al. (2006). Influence of steroid drugs on orthodontically induced root resorption. *Orthodontics and Craniofacial Research* 9: 57–62.

Verna, C., and Melsen, B. (2002). The biology of tooth movement. In: G. Fiorelli and B. Melsen (eds.), *Biomechanics in Orthodontics – Rel. 1 on CD ROM*. Arezzo: Libra Ortodonzia.

Verna, C., Melsen, B., and Melsen, F. (1999a). Differences in static cortical bone remodeling parameters in human mandible and iliac crest. *Bone* 25: 577–583.

Verna, C., Zaffe, D., and Siciliani, G. (1999b). Histomorphometric study of bone reactions during orthodontic tooth movement in rats. *Bone* 24: 371–379.

von Bohl, M., Maltha, J.C., Von Den Hoff, J.W. et al. (2004). Focal hyalinization during experimental tooth movement in beagle dogs. *American Journal of Orthodontics and Dentofacial Orthopedics* 125: 615–623.

Wang, L., Lee, W., Lei, D.L. et al. (2009). Tissue responses in corticotomy- and osteotomy-assisted tooth movements in rats: Histology and immunostaining. *American Journal of Orthodontics and Dentofacial Orthopedics* 136: 770–771.

Wilcko, M.T., Wilcko, W.M., Pulver, J.J. et al. (2009). Accelerated osteogenic orthodontics technique: A 1-stage surgically facilitated

rapid orthodontic technique with alveolar augmentation. *Journal of Oral and Maxillofacial Surgery* 67: 2149–2159.

Winkler, D.G., Sutherland, M.K., Geoghegan, J.C. et al. (2003). Osteocyte control of bone formation via sclerostin, a novel BMP antagonist. *EMBO Journal* 22: 6267–6276.

Yamaguchi, M. (2009). RANK/RANKL/OPG during orthodontic tooth movement. *Orthodontics and Craniofacial Research* 12: 113–119.

Yamashiro, T., Sakuda, M., and Takano-Yamamoto, T. (1994). Experimental tooth movement in ovariectomozed rats. *Journal of Dental Research* 73: 148.

Yoneda, T., Hagino, H., Sugimoto, T. et al. (2010). Bisphosphonate-related osteonecrosis of the jaw: Position paper from the Allied Task Force Committee of Japanese Society for Bone and Mineral Research, Japan Osteoporosis Society, Japanese Society of Periodontology, Japanese Society for Oral and Maxillofacial Radiology, and Japanese Society of Oral and Maxillofacial Surgeons. *Journal of Bone and Mineral Metabolism* 28: 365–383.

Zaffe, D., and Verna, C. (1995). Acid and alkaline phosphatase activities in rat's alveolar bone experimentally loaded by orthodontic forces. *Italian Journal of Mineral and Electrolyte Metabolism* 9(Suppl 1): 11.

Zahrowski, J.J. (2009). Optimizing orthodontic treatment in patients taking bisphosphonates for osteoporosis. *American Journal of Orthodontics and Dentofacial Orthopedics* 135: 361–374.

Zhang, L., Zhao, Z., Li, Y. et al. (2010). Osseointegration of orthodontic microscrews after immediate and early loading. *Angle Orthodontist* 80: 354–360.

10
Acute and Chronic Infections Affecting the Oral Cavity: Orthodontic Implications

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Summary

Infectious diseases occur worldwide, posing multilevel challenges to orthodontists everywhere. Each new patient must be examined thoroughly to uncover the possible presence of infections that could be potentially dangerous for others. Recognition of pathological conditions in a patient's orofacial region before or during treatment requires a precise diagnostic technique to eliminate all potential health risks to other patients and staff in the orthodontic clinic. In those cases where patients have such infections, it is advisable to promptly interact with pertinent medical specialists to obtain confirmation of the disease identity, its treatment, and any bearing of the disease and medications on the orthodontic treatment plan and projected outcome. Both infectious diseases and the medications taken for their treatment may affect the tissue remodeling response to orthodontic forces. This chapter discusses the features of infectious diseases, both acute and chronic, that may profoundly affect the diagnosis, course, and outcome of orthodontic treatment. These infectious diseases are caused by bacteria, viruses, fungi, and parasites, and some may be potentially lethal. The goal of this chapter is to stress the importance of identifying these diseases during the diagnostic phase of orthodontic therapy and of seeking advice from medical specialists to prevent the spread of disease and achieve optimal orthodontic outcomes.

Orthodontics, a specialty based on solid scientific foundations, is being practiced predominantly as a mechanical art, due, at least in part, to its close association with dentofacial esthetic dogmas. Orthodontists are keen to correct facial and dental disfigurements, but often little attention is paid to the general health status of patients, as if the dentofacial region exists in isolation from the rest of the body. This approach can be termed "regional diagnosis," where an emphasis is placed on the face and oral cavity while ignoring the overwhelming evidence on an intimate association between dentofacial events and a multitude of pathophysiological developments throughout the

rest of the body (Moore, 1939). Such a narrow approach to orthodontic diagnosis and treatment planning, which overlooks basic biological principles, may jeopardize not only treatment outcomes but also the well-being of patients. Thus, it is essential to shift the paradigm of orthodontic patient evaluation to encompassing all aspects, both medical and dental, in the diagnostic data sheet, with due consideration of all health-related issues.

Orthodontic tooth movement results from profound remodeling activities of all dental and paradental tissues in response to the application of mechanical forces to the crowns of the teeth. These remodeling activities are performed by various cells, including cells of the nervous, immune, endocrine, and skeletal systems, providing tooth movement with a noticeable systemic involvement. Therefore, orthodontics should be considered as an integral part of medicine, and as aiming to treat and correct malocclusions while weighing the possible effects of each patient's systemic condition on his or her orthodontic diagnosis and treatment plan. This definition introduces biological factors into orthodontic practice, and increases the probability of attaining pleasing and durable results (Childs, 1933).

The close relationship that an orthodontist should maintain with other medical and dental specialists depends on the extent of his or her knowledge base, on which depends the ability to identify conditions requiring and/or justifying patient referral to appropriate medical professionals (Weinberger, 1938). An orthodontic practice might encounter patients with oral manifestations of a variety of diseases. Recognizing these signs and symptoms should prompt the practitioner to perform specific laboratory tests to facilitate making the correct diagnosis, identifying the course of the disease process, and assessing its effects on the treatment plan and the course of treatment. Such a routine could include differentiation between infectious and noninfectious diseases, and aid in deciding whether orthodontic treatment can be provided without further delay, or if a referral to a medical specialist for consultation is deemed necessary prior to formulating a comprehensive diagnosis. Lack of adequate knowledge of infectious diseases can cause unnecessary delays in instituting appropriate therapy, and at the same time lead to failure in implementing proper safety measures for prevention of disease transmission to the orthodontic office personnel. This chapter will concentrate on nonodontogenic infections and their possible orthodontic implications (odontogenic infections are discussed in subsequent chapters of this book). Systemic infectious diseases with oral manifestations and with a high degree of microbiological specificity are discussed here, providing a clear guide to distinguish between bacterial, viral, fungal, and parasitic infections.

In many systemic infectious diseases, the salient causative organisms have been identified and characterized as bacteria, viruses, fungi, or parasites. The infectious nature of these diseases requires the implementation of strict hygiene procedures and disinfection, to avoid any chance of contamination and transmission of the disease in the orthodontic office. To achieve this goal, it is imperative to identify at the first appointment patients who may be carriers of such diseases, prior to proceeding with any clinical activities. However, in addition to efforts to eliminate the risk of spreading an infectious disease to other people in the orthodontic office, orthodontists should realize that infectious diseases, with no exception, modify the immune system of each infected person. Such modifications may have profound effects on the paradental cellular and tissue response to orthodontic forces. Inflammation is a major part of this

response, intimately involved in every step of the tissue remodeling process that facilitates tooth movement. Signaling molecules produced by migratory primed inflammatory cells reaching the mechanically stressed periodontal ligament (PDL) are capable of both accelerating and inhibiting the rate of tooth movement, depending on the nature of the specific molecules involved. Moreover, patients who have been diagnosed as having acute or chronic infectious diseases are usually being treated with medications that may markedly alter the course and outcome of orthodontic therapy, primarily by affecting the patient's immune system and the paradental inflammatory process. All these facets of infectious diseases dictate that a consultation with a physician specializing in treating patients with these diseases is imperative prior to the onset of any orthodontic treatment. This communication between the orthodontist and the physician must continue throughout the course of treatment in the event of any change in the health status of the infected patient during this period.

Bacterial infections

The resident and transient microflora of the oral cavity consist of more than 700 bacterial species or phylotypes, providing a useful defense mechanism against the establishment of more pathogenic species (Aas et al., 2005). The resident oral flora can be divided into the indigenous flora – that is, those are found in almost all humans irrespective of environmental conditions (e.g. species of *Streptococcus*, *Actinomyces*, *Haemophilus*, *Neisseria*, *Fusobacterium*, and *Prevotella*) – and the supplemental flora, which have specific requirements for adhesion, nutrition, redox potential, and pH levels (Dahlèn, 2009). The species of transient flora do not permanently colonize the oral cavity, have low virulence, and live in harmony with the hosts. This might include some opportunistic pathogens, such as *Staphylococcus aureus*, pneumococci, enterococci, enteric rods, and yeasts. If the host's immunity becomes impaired, these bacteria might initiate an infectious process (Kononen, 2000). Moreover, impairment of the host immune response destroys microbial homeostasis, which allows some pathogens to grow in greater numbers and cause an infection characterized by increased pathogen load and inflammation.

Mucosal lesions of uncertain microbiological basis

Mucositis

Mucositis is a form of mucosal barrier injury, characterized clinically by oral erythema, ulceration, and pain (Figure 10.1). It is a common complication of therapeutic procedures involving chemotherapy, radiotherapy, or both, and in patients receiving bone marrow transplants, which are damaging to the epithelial cells (Scully et al., 2003). Published evidence points toward the activated innate immune responses with reactive oxygen species (ROS)–mediated inflammatory cascade and dysbiotic relationship of oral microflora playing the central role in pathogenesis oral mucositis (Chen et al., 2020). Commonly, the oral manifestation of cancer therapy is a generalized stomatitis whose association with the primary underlying infection is more obvious (for further details, see "Oral mucosal bacterial infections" later in this chapter). Secondary bacterial infections may also arise in bite wounds, and in viral stomatitis and aphthous ulcerations, and lead to streptococcal bacteremia in any area

of the mouth, such as the tongue, buccal mucosa, floor of the mouth, palate, and gingiva.

Figure 10.1 Oral mucositis.

Courtesy of Dr. Nathaniel S. Treister.

In addition, there is increased occurrence of opportunistic pathogens such as aerobic Gram-negative bacilli (AGNB), including enterics (*Escherichia coli*, *Enterobacter* spp.) and pseudomonads, as well as yeasts (*Candida* spp.), in mucositic lesions. If xerostomia prevails, oral health can be seriously compromised (Sonis, 2007). Xerostomia can lead to decreased clearance of oral microorganisms, along with decreased pH, resulting in increased colonization by lactobacilli, *Candida albicans*, and other opportunistic microorganisms, such as *Staphylococcus aureus*, enterococci, and enteric rods (Pajukoski et al., 2001). The simple ways to help alleviate and prevent the symptoms of xerostomia include drinking water to hydrate tissues and cleanse the mouth just as saliva does; using oral mouthwashes, gels, sprays, and artificial saliva; use of oral care products specifically formulated for dry mouth (containing no detergents, with a mild taste and containing antimicrobial proteins); sugarless chewing gum and hard candies; as well as some commercially available lozenges and sprays. Vitamin C tablets have also been recommended to stimulate salivary flow as it acts as a reducing agent, breaking disulfide bonds between cysteine residues in proteins, leading

to a decrease in saliva viscosity. Alcohol, caffeine, and smoking should be avoided as they can further irritate and dry out the mucosa (Ristevska et al., 2015).

Recurrent aphthous stomatitis

Otherwise known as canker sore, this is the most common nontraumatic type of oral ulcer (Figure 10.2). The sore is often mistaken for a virus infection (herpes simplex), and is differentiated by appearance only in the nonkeratinized mucosa, such as the labial mucosa, buccal mucosa, ventral tongue, and vestibule (Ship et al., 2000). Based on their clinical appearance, aphthous ulcers can be classified as minor (<1 cm in diameter), major (>1 cm diameter), and herpetiform, in which multiple minute ulcers might coalesce to form plaques (Woo and Sonis, 1996). Most aphthae are of the minor variety and heal within 10 days. Factors predisposing to this condition include stress, poor nutrition, infection, hormonal fluctuation, and trauma (McCullough et al., 2007). The disease is usually self–limiting, and nutritional supplementation, alleviation of stress, and warm saline rinses have been found to help in its management. Orthodontic attachments are considered to be one among the main reasons for triggering its appearance. AlDahash et al. (2020) reported that more than half of the orthodontic patients (out of 196 patients in the study) developed oral ulcers, which mainly develop due to trauma. If the ulcers appear following orthodontic bonding, the irritating attachment can be either covered with orthodontic wax or removed to prevent further irritation aggravating the process. The patient should be well instructed in what to do in such instances before leaving the office. It is suggested that primary care practitioners should be educated to provide adequate supportive management for oral ulceration caused by orthodontic fixed appliances.

Figure 10.2 Major aphthous ulceration.

Burning mouth syndrome

Scala et al. (2003) defined burning mouth syndrome as a chronic pain syndrome that mainly affects middle-aged/older women with hormonal changes or psychological disorders. This disorder reduces the quality of life, especially with large psychological implications. Although the etiology of the syndrome remains unclear, the presence of salivary gland dysfunction or systemic diseases, such as diabetes, makes a patient

prone to it. In addition, patients with chronic pulmonary diseases, asthma, and rheumatic fever can develop epithelial atrophia, glossitis, xerostomia, and burning mouth syndrome. All these symptoms are due to superimposing fungal and bacterial infections that follow adverse reactions to immunosuppressive medications and reduced salivary flow. Chemotherapeutic agents also have the potential to induce changes in the oral epithelium, leading to superinfection (Lopez-Jornet et al., 2010).

Reducing the chronic pain is still a quest. In a recent network meta-analysis, four pain-relieving strategies were investigated: photobiomodulation therapy, alpha-lipoic acid, phytotherapics, and anxiolytics/antidepressants (Alvarenga-Brant et al., 2023). Only the anxiolytic clonazepam seemed to relieve pain. Pain-relief measures such as cold beverages, ice chips, and avoidance of irritants such as tobacco, spicy or acidic foods, and alcohol are considered home remedies for burning mouth syndrome.

Oral mucosal bacterial infections

Acute mucosal infections of the oral cavity may appear locally or as generalized stomatitis, and can be asymptomatic or accompanied by mild discomfort or severe pain (Dahlèn, 2009). Patients often neglect these conditions unless they become bothersome. The most common symptoms are burning sensations, followed by clinical signs of redness and epithelial atrophy or desquamation. Helovuo et al. (1993) observed an increased prevalence of *E. coli*, *Enterobacter* spp., and *Staph. aureus* after treatment with penicillin and erythromycin. Patients with conditions causing immunocompromise, such as leukemia and other malignancies, are at high risk of developing oral mucosal ulcerations due to drug consumption and development of granulocytopenia. Similar conditions have been found in patients with organ transplants and rheumatic fever (Dahlèn, 2009). As a result of decreasing general health and increased medication intake, older people are more prone to develop oral mucosal lesions (Sweeney et al., 1994). Dahlèn et al. (2009) confirmed that bacterial mucosal infections are more prevalent than fungal infections in the oral cavity. They also observed a marked decline in the levels of normal mucosal bacteria, such as viridians streptococci (alpha-streptococci), *Neisseria*, and *Haemophilus* spp.

Dentists, more specifically orthodontists, frequently ignore such conditions and/or leave them underdiagnosed. Infections associated with the oral cavity have a unique microbiological base, often a mixed one, making it difficult to identify a specific, salient microorganism. The best diagnostic approach starts with comprehensive history taking, which should be followed by a thorough physical examination. Microbiological laboratory investigations and antibiotic susceptibility tests should be conducted routinely on orthodontic patients with oral lesions, so that the conditions can be effectively and properly managed. An orthodontist accepting patients in this category should emphasize the importance of maintaining impeccable oral hygiene to postpone or minimize the development of oral mucosal ulcerations. It is also highly recommended to refer any patient with an oral microbiological infection that might be contagious to a physician for consultation. The infections arising in the oral cavity are listed in Table 10.1.

Aerobic infections of the oral cavity

Microorganisms causing oral mucosal infection have a predominantly aerobic character, and the majority comprise staphylococci, enterococci, AGNB, and yeasts. They are all categorized as classic opportunists and are commonly associated with immunocompromise (Dahlèn et al., 2009), although they have been noted in healthy individuals. These aerobic infections are difficult to treat due to a pronounced resistance against common antibiotics by these microorganisms and a low response if the compromised condition prevails. A microbiological diagnosis is strongly recommended, since the treatment strategy may be quite different depending on the identity of the involved microorganisms. Treatment of these infections is also sometimes challenging due to a combination of infections caused by two or more opportunists. A brief description of bacteria commonly producing oral mucosal infections is provided here. Yeasts involved in the process are discussed later in the chapter.

Staphylococcus aureus

Staph. aureus is a relevant pathogen in symptomatic oral mucosal lesions. Until then, if isolated, it was considered to be a part of a transient microbial flora that seems to increase with advanced age. This bacterium is frequently isolated from infections of the facial skin and lips (Faergemann and Dahlèn, 2009). Angular cheilitis is commonly secondarily infected by *Staph. aureus* (Figure 10.3), with a particular predilection in young individuals and those with dry skin. If a healthy individual harbors high numbers of salivary *Staph. aureus* (>100,000 colony-forming units/mL) over an extended period, they are considered to be healthy carriers (Dahlèn, 2009). Infected medical and dental professionals pose a risk of transmitting the pathogen to other individuals visiting them. A serious concern in this regard is the infection caused by methicillin-resistant *Staph. aureus*. Treatment of infection with *Staph. aureus* typically includes penicillinase-stable penicillins, such as cloxacillin, dicloxacillin, or flucloxacillin, because of the risk of developing resistant strains (Dahlèn, 2009).

Enterococci

Enterococci, particularly *Enterococcus faecalis*, are commonly involved in oral mucosal infections. These infections occur sporadically in the oral mucosa and around the teeth in healthy individuals, but enterococci are a typical opportunist in immunocompromised patients, often in combination with other opportunists such as enterics and yeasts (Dahlén, 2009).

Table 10.1 Bacterial infections of the oral cavity.

Type of infection **Bacterial infections of the oral cavity and its environment**	Main causative agent	Prevalence in the disease[a]	Prevalence in the resident flora of the oral cavity[b]	Treatment
Oral mucosal infections (including bacterial associated lesions)	*Staphylococcus aureus* *Streptococcus pyogenes*[c] *Enterococcus faecalis* Aerobic Gram-negative bacilli Yeasts[d]	++ + ++ +++ +++	+ (+) + + ++	Cloxacillin, clindamycin, vancomycin Penicillin V Amoxicillin/ampicillin Multiresistance drugs (ciprofloxacin) Mucostatins, amphotericin, azoles
Acute necrotizing ulcerative gingivitis	*Treponema* spp. Anaerobes (*Fusobacterium* spp., *Prevotella* spp.)	+++ ++	+ +++	Penicillin V
Peritonsillar abscess	*Strep. pyogenes*[c]	+++	(+)	Penicillin V
Lemierre disease	Anaerobes (*Fusobacterium* spp., *Prevotella* spp.) *F. necrophorum*	+ +++	+++ (+)	Metronidazole Metronidazole, surgery
Suppurative parotitis	*Staph. aureus* Anaerobes	+ +	+ +++	Cloxacillin, clindamycin Penicillin V
Noninfectious rhinitis	Allergy	+++	?	–
Rhinitis and sinusitis	Primary infection – viral Secondary infection – facultative bacteria (*Strep. pneumoniae, Haemophilus influenzae*) and less commonly facultative	++ + +++	+ +++ +++ (nostrils)	Penicillin V, amoxicillin Penicillin V, macrolides Cloxacillin, clindamycin

Type of infection **Bacterial infections of the oral cavity and its environment**	Main causative agent	Prevalence in the disease[a]	Prevalence in the resident flora of the oral cavity[b]	Treatment
	bacteria (*Staph. aureus, Strep. pyogenes*) Third-phase infection – anaerobes			
Chronic rhinitis	*Staph. aureus*			
Epiglottitis	*H. influenzae*	+++	+	Amoxicillin, ceftriaxone, penicillin V, ampicillin, chloramphenicol
Chronic infections with oral manifestations				
Actinomycosis	*Actinomycosis israelii*	+++	+	Penicillin V (long time, high doses)
Gonorrhea	*Neisseria gonorrhea*	+++	–	Penicillin V
Mycobacterial infections	*Mycobacterium tuberculosis* *M. leprae*	+++ +	– –	Rifampicin
Syphilis	*Treponema pallidum*	+	–	Penicillin V

[a] Prevalence: + <10%, ++ <30%, +++ >30%.

[b] Not isolated, (+) sporadically present in low numbers, + present in <10% and in low numbers, ++ commonly present <30% sparsely or in moderately heavy growth, +++ usually present and in the predominant flora.

[c] Group A hemolytic streptococci.

[d] *Candida* spp.

Enterococci were known as streptococci for a long time, and were classified as Lancefield group D. However, owing to their survival in harsh environments (temperature, dryness, salts, dyes, antiseptics, and antibiotics), they were classified as a new genus, which normally resides in a significant part of the upper intestine and is resistant to bile salts. It is spread to the oral cavity by vomiting and fecal

contamination. Enterococci are commonly used in food processing, for instance in cheese, and their spread through food cannot be excluded (Templer et al., 2008). It is resistant to penicillin V and clindamycin, and broad-spectrum penicillins such as ampicillin and amoxicillin remain the drugs of choice (Dahlén et al., 2009).

Figure 10.3 Angular cheilitis with *Staphylococcus aureus*.

Courtesy of Dr. Maria Westin.

Enterococci are of particular interest to dentists due to their persistence even after treatment of endodontically involved teeth. Studies have elucidated the presence of *Enterococcus faecalis* in root-filled teeth with persistent lesions, and confirmed its ability to invade dentinal tubules and to survive for a prolonged period under adverse conditions such as starvation, high pH of calcium hydroxide medication, and adhesion of *E. faecalis* to collagen (Ørstavik and Haapasalo, 1990; Evans et al, 2002). A study has confirmed that demineralization and apical resorption at root cementum play a significant role in penetration of *E. faecalis* into root cementum. The severity of infection is directly proportional to the depth of penetration of *E. faecalis* into root cementum (Halkai et al., 2014).

AGNB, including *E. coli*, *Enterobacter* spp., *Klebsiella* spp., *Proteus* spp., and more, are typically involved in human opportunistic infections, including oral mucosal infections. AGNB are part of the normal resident intestinal flora, frequent participants in nosocomial infections, and cause the classic opportunistic infections affecting the

oral cavity. Transmission of these bacteria to the oral cavity can occur through poor personal hygiene, or through food and drinking water. They are frequently associated with periodontitis and peri-implantitis. They rapidly become drug resistant, and the drug to be used should be selected only after a susceptibility test, although the choices are more or less exhausted. Quinolones (ciprofloxacin, norfloxacin) are the drugs of choice for the infections with AGNB, but should be prescribed only under proper medical supervision. Empirically, it has been observed that it is difficult to harm the bacteria and to heal the infection as long as the patient is in a compromised state (Dahlèn et al., 2009).

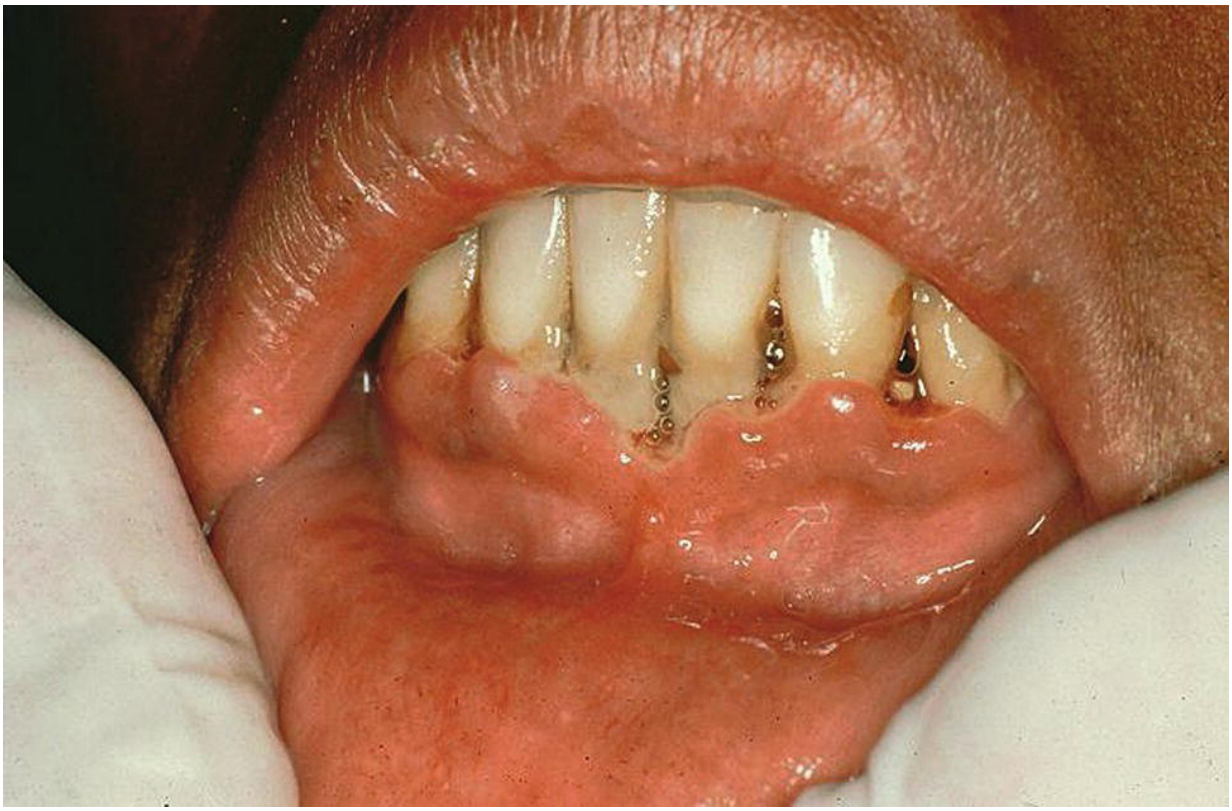

Figure 10.4 Acute necrotizing ulcerative gingivitis.

Courtesy of Dr. Martin S Spiller.

Acute necrotizing ulcerative gingivitis

Acute necrotizing ulcerative gingivitis (ANUG) is an infectious disease of the gingiva (Figure 10.4) caused by a mixed flora consisting of spirochetes, fusobacteria, *Prevotella intermedia*, *Veillonella* spp., and streptococci (Rivera-Hidalgo and Stanford, 1999; Dufty et al., 2017). This disease often results in gingival bleeding, ulceration, and episodes of severe pain. Factors predisposing to the condition include stress, smoking, malnutrition, and poor oral hygiene (Horning and Cohen, 1995). ANUG is common in patients with human immunodeficiency virus (HIV) infection and in undernourished children (Aaron and DeBlois, 2022). If it is associated with rapid alveolar bone loss, it is categorized as necrotizing ulcerative periodontitis, in which severe deep, aching pain is a characteristic feature (Murayama et al., 1994).

The treatment of this condition is directed toward debridement of affected soft tissues and teeth, along with antibiotic therapy (Rivera-Hidalgo and Stanford, 1999). A referral to a competent periodontist, if an orthodontist encounters such a condition, can be of great value in its management.

Acute pharyngitis

Acute pharyngitis, otherwise known as a sore throat, can have either viral or bacterial etiology. The most common bacterium involved is *Streptococcus pyogenes* (beta-hemolytic streptococci or group A streptococci [GAS]; Peterson and Thomson, 1999). During the acute phase of the disease, these microorganisms can be detected in the saliva. It is among the 20 most common diseases that occur without any age, sex, or racial predilection. The exotoxins produced in this infection by the beta-hemolytic streptococci act as superantigens that upregulate the T lymphocytes, prompting the release of proinflammatory cytotoxins, and have synergistic effects along with the lipopolysaccharides of the extracellular matrix. The superantigens then evade the pharyngeal immune response, resulting in proliferation of *Strep. pyogenes*. The most common symptoms of acute pharyngitis are sore throat, odynophagia, headache, nausea, vomiting, and abdominal pain. On physical examination, the patient may have fever, tonsillopharyngeal erythema, exudates, beefy red swollen uvula, anterior cervical tender lymph nodes, petechiae on the palate, and scarlatiniform rash. The gold standard diagnostic test for acute pharyngitis is throat culture, but unfortunately this test takes 24–48 hours to be completed (Buensalido and Nepomuceno, 2022). Instead, rapid antigen detection tests (RADTs) with commercial kits or nucleic acid amplification (via polymerase chain reaction, PCR) for group A *Streptococcus* (GAS) are available, but these are relatively expensive. Samples for throat culture or RADTs should be obtained from the posterior pharynx or the tonsils. Imaging studies have no role in the diagnosis of this disease.

Oral penicillin V, 1.2M IU orally (PO) every 12 hours for 8–10 days, is the drug of choice for this disease. Amoxicillin remains a better alternative, but tetracyclines or sulfamethoxazole should not be used due to the high resistance rate. In the case of penicillin allergy, cephalosporins, which contain a beta-lactam ring, can be used with caution. In rare cases, the pharyngitis spreads to adjacent areas, forming abscesses requiring surgical drainage. Surgery is an option, especially if the history reveals recurrent tonsillitis (Brook, 2009). The patient should be allowed to eat a normal diet and drink warm liquids that provide symptomatic relief (Buensalido and Nepomuceno, 2022). An otorhinolaryngologist should be consulted for local suppurative complications such as peritonsillar abscess and mastoiditis. An infectious disease expert should be consulted for patients with immunocompromising conditions, or when HIV infection is suspected.

A rare but often underdiagnosed form of an oropharyngeal infection is the Lemierre syndrome, an infection caused by *Fusobacterium necrophorum* (Karkos et al., 2009), which occurs in adolescents and young adults as a complication of tonsillitis (“sore throat”), especially in recurrent forms (Klug et al., 2009). It is life-threatening if neglected and is characterized by acute venous thrombosis of the vena jugularis interna and septic emboli to the lungs (Pleming et al., 2022). It should be treated aggressively with antibiotics (metronidazole) and/or surgery (Ridgway et al., 2010).

Peritonsillar abscess

Peritonsillar abscess (PTA) is a localized accumulation of pus in the peritonsillar tissues, which forms as a result of suppurative tonsillitis (Figure 10.5). The peritonsillar space is bounded by the tonsillar pillars antero-posteriorly, the piriform fossa inferiorly, and the hard palate superiorly. The area can be infected with both aerobic (*S. pyogenes*) and anaerobic (*Prevotella* and *Peptostreptococcus* spp.) bacteria. The infection begins superficially, progresses into deep tissues, and has no age, sex, or racial predilection. The symptoms include sore throat, dysphagia, and change in the voice, headache, malaise, fever, neck pain, otalgia, and odynophagia. Physical examination reveals mild to moderate discomfort, fever, tachycardia, dehydration, drooling of saliva, trismus, cervical lymphadenitis, asymmetrical tonsillar hypertrophy, inferior and medial displacement of a tonsil, contralateral deviation of the uvula, and erythema and exudates from the tonsils. Complete blood count (CBC) and electrolytes, heterophile antibody test (to rule out suspicion of infectious mononucleosis), pus culture sensitivity from needle aspirate of the abscess, and C-reactive protein blood culture might be required in patients presenting with features of sepsis (Gupta and McDowell, 2022). Patients are often managed in the outpatient department, unless they show signs of airway obstruction, sepsis, toxicity, or other complications. Along with incision and drainage, analgesics, and throat wash, antibiotics are typically prescribed for complete resolution of PTA. A combination therapy of penicillin and metronidazole is generally preferred. Clindamycin is a good choice in people with penicillin allergy. Consultation with an otorhinolaryngologist should be sought whenever a PTA is recognized, before, during, or after the onset of orthodontic treatment, for proper management of these patients. Help from an anesthetist might sometimes be required if the patient develops difficulty in maintaining airway patency (Flores et al., 2022).

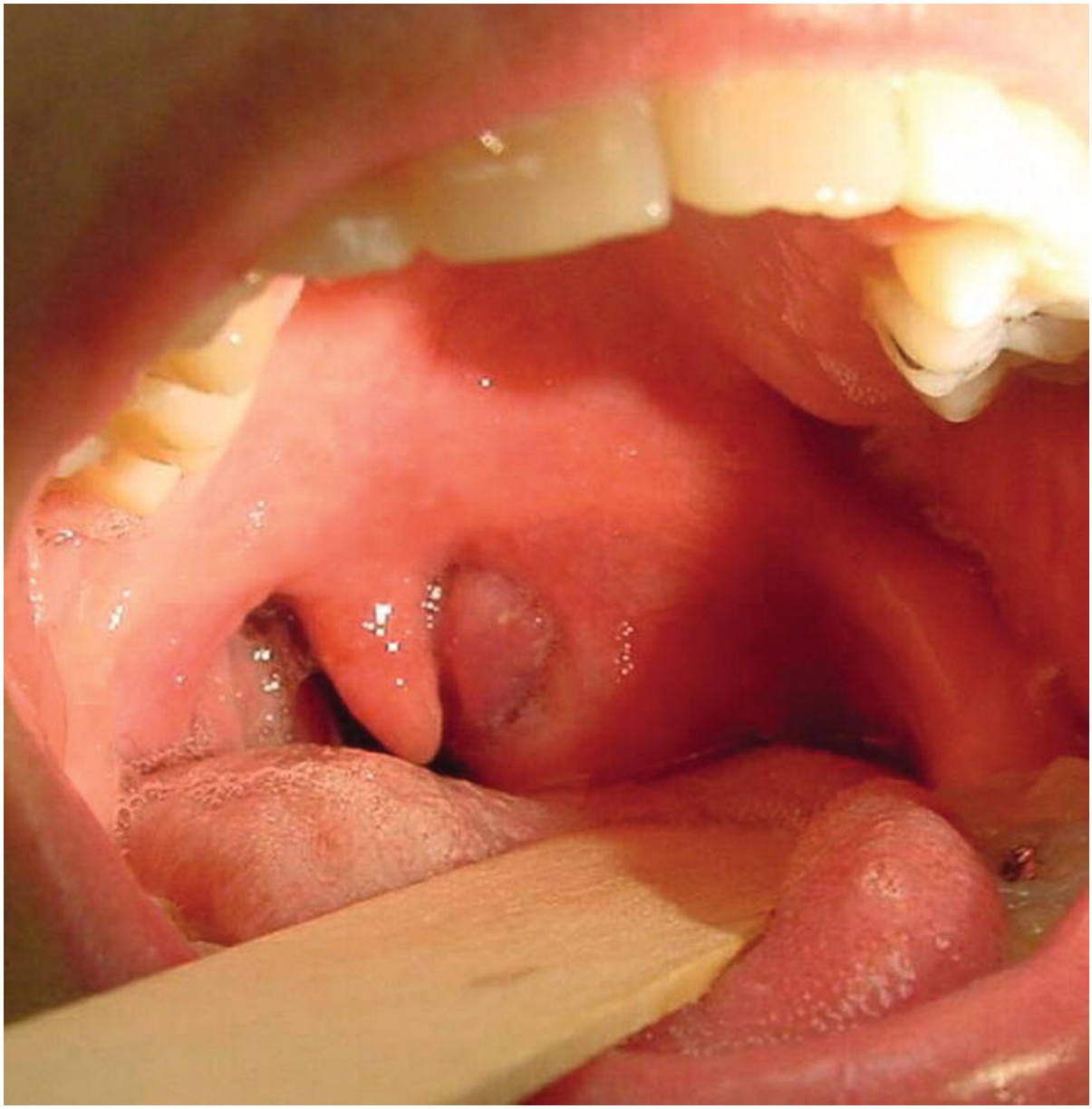

Figure 10.5 Peritonsillar abscess.

Suppurative parotitis/sialadenitis

Acute suppurative parotitis (ASP) is an infectious process of the parotid gland, usually seen in elderly people who are dehydrated, malnourished, or recovering from surgery (Raad et al., 1990). Although the infection is usually confined to the parotid capsule, it can occasionally spread to cervical fascial planes. Immunosuppression states such as diabetes, alcoholism, HIV infection, autoimmune disorders (e.g. Sjögren syndrome), poor oral hygiene, decreased salivary flow, postsurgical dehydration, sialolithiasis, tumors, or foreign bodies in the duct can increase the risk for ASP. The most common clinical manifestation of ASP is an indurated, erythematous, warm swelling of the cheek. The patient will also have mild fever along with pain. Intraorally, the orifice of Stensen's duct will be red, and pus may be expelled while palpating it (Brook, 2009). In

rare instances, facial nerve dysfunction may be the end result (Noorizan et al., 2009). Diagnosis can be established by a thorough clinical examination, along with CBC and chemistry, and culture and sensitivity. Radiological evaluation should include computed tomographic (CT) scanning with an intravenous contrast medium, ultrasound scanning for detection of abscesses, and also sialography.

Traditionally, the main causative agent of ASP is thought to be *Staph. aureus*. However, Brook et al. (1991) isolated strict anaerobes such as *Peptostreptococcus* spp. and Gram-negative anaerobic rods from ASP lesions. The key treatment for ASP is rehydration and supportive treatment, which should include intravenous (IV) fluids, nutritional support, a warm compress, sialogogs, good oral hygiene, and antibiotic therapy. The drugs of choice in ASP are penicillin, first-generation cephalosporins, or clindamycin; however, more important is the selection of the drug in relation to the causative agent. Intraductal injections of antibiotics usually lead to improvement in the condition. If there is lack of improvement after 3–5 days of antibiotic treatment, and if there is facial nerve involvement or involvement of adjacent vital structures, surgical opinion must be sought; usually incision and drainage via a standard parotidectomy incision will be the preferred treatment. Proper follow-up, repeated clinical examinations, fine needle biopsy, and imaging should be performed on a regular basis to ensure the absence of any neoplastic changes in the gland (Brook, 2009).

Rhinitis and sinusitis

Rhinitis implies a heterogeneous group of nasal disorders, characterized by sneezing, nasal itching, rhinorrhea, and nasal congestion, which can be allergic, nonallergic, infectious, occupational, or hormonal in nature. Dykewicz and Hamilos (2010) suggested that in 44–87% of patients with rhinitis, the condition is either allergic or nonallergic in nature. Common allergens causing the problem include proteins and glycoproteins in airborne dust, mite fecal particles, cockroach residues, animal dander, molds, and pollens. Within minutes of inhalation, these allergens are recognized by immunoglobulin (Ig)E antibody bound to mast cells and basophils, causing degranulation and release of preformed mediators, such as histamine and tryptase, and inflammatory mediators, such as leukotrienes and prostaglandin D2. These mediators cause plasma extravasation from blood vessels, with consequent edema, pooling of blood in cavernous sinusoids, and occlusion of nasal passages. These developments are accompanied by active secretion of mucus from glandular and goblet cells, and release of histamine, which manifests as itching, rhinorrhea, and sneezing. In late stages a prominent nasal congestion develops (Rosenwasser, 2007). Rhinitis is often accompanied by nonnasal symptoms, such as allergic conjunctivitis, and it is frequently associated with allergic asthma, pathophysiologically and epidemiologically.

Diagnosis should include evaluation of all specific symptoms and the pattern of occurrence of the symptoms (infrequent/intermittent, seasonal and perennial) along with identification of predisposing factors, previous responses to medication, and coexisting diseases. A handheld otoscope or head lamp with nasal speculum permits viewing of the anterior third of the nasal airway, including the anterior tip of the inferior turbinates. Determination of specific antibody involvement can be made through skin testing, which has high sensitivity, and at the same time is simple, easy, and can be rapidly performed (Wallace et al., 2008). The main treatment for rhinitis is directed toward avoidance of the inciting factors, such as allergens and irritants. A

multitude of drugs are available for the management of this disease, including antihistamines, corticosteroids, oral and nasal decongestants, and leukotriene receptor antagonists. For the orthodontist, making a referral to an otorhinolaryngologist is an important step in managing the condition. The specialist will determine an individualized treatment approach for each patient, based on their responses, preferences, and the cost-effectiveness of the treatment options (Dykewicz and Hamilos, 2010).

Sinusitis or rhinosinusitis is defined as inflammation of the nose and the paranasal sinuses, and is usually infectious in nature (Meltzer et al., 2004). Typically, from a microbiological point of view sinusitis follows a characteristic pattern, starting as a viral infection, followed by superinfection with facultative bacteria after a couple of days, and after one week showing anaerobes as the predominant organisms (Brook, 2009). Acute rhinosinusitis is diagnosed when there is purulent nasal drainage of up to four weeks, accompanied by nasal obstruction, facial pain, pressure, fullness, or both. The pain is usually described as being dull, or felt as pressure in the upper cheeks, between the eyes, or in the forehead. The most common bacteria isolated from sites of acute rhinosinusitis are *H. influenzae, Strept. pneumoniae*, *Moraxella catarrhalis*, and sometimes *Staph. aureus*. Disturbances in the sense of smell, which occur in sinusitis, can be either partial (hyposmia) or complete (anosmia), and are usually associated with mucosal thickening or opacification in the anterior ethmoid sinuses, which can be seen as hyperdense areas in an orthopantomograph and CT images (Dykewicz and Hamilos, 2010; Figure 10.6). An initial period of watchful waiting without initiation of antibiotics is the best treatment for acute rhinosinusitis.

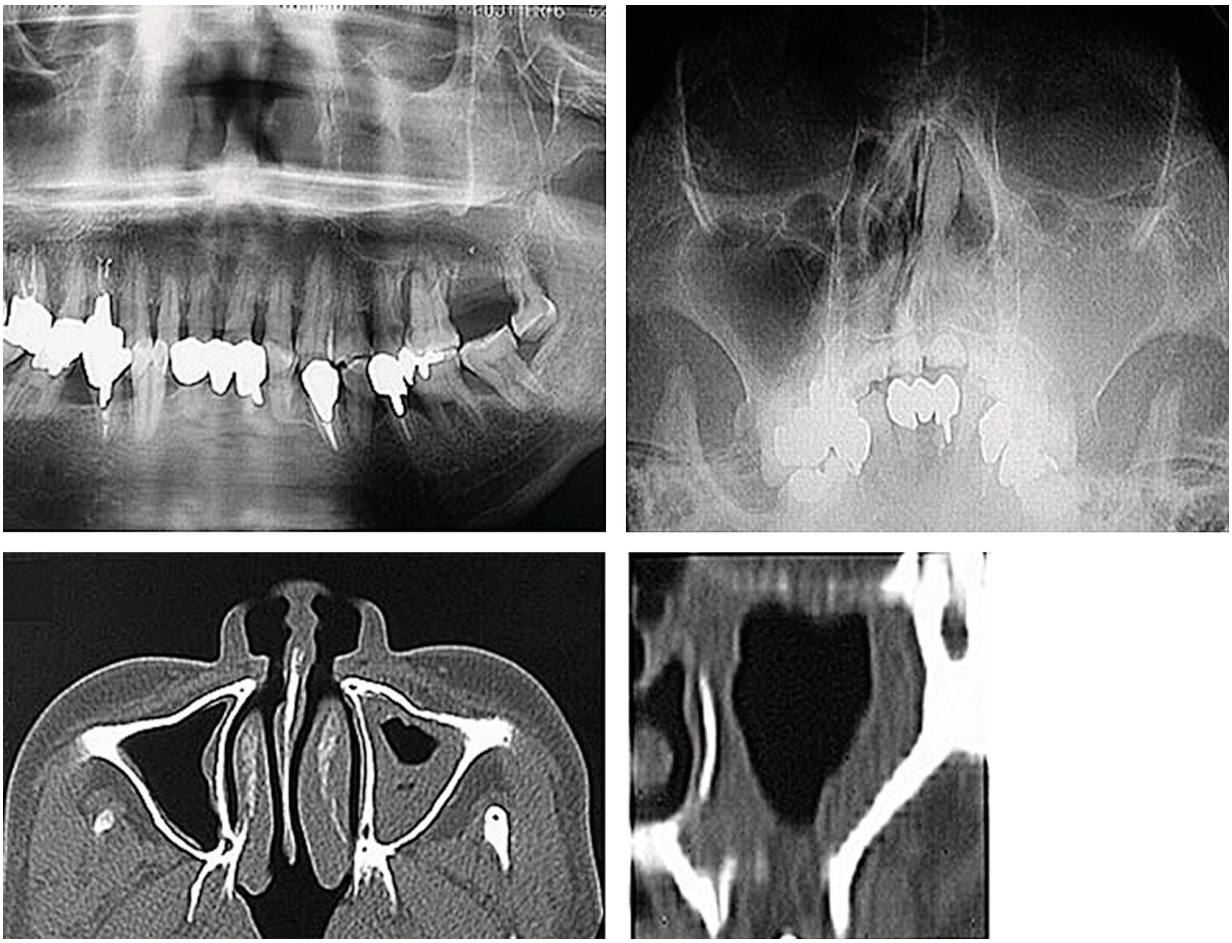

Figure 10.6 Radiological appearances of sinusitis in various radiographs.

Courtesy of Akitoshi Kawamata.

An important aspect of the diagnosis of sinusitis is to differentiate between bacterial and viral causes, as only bacterial infections respond to antibiotic therapy. Clinical signs suggestive of bacterial infection include symptoms that last for more than seven days. Patients with more severe forms of the disease can be treated with antibiotics, and if this approach is decided on, amoxicillin is the drug of choice. If the patient is allergic to penicillin, a combination of trimethoprim and sulfamethoxazole (not used in Scandinavian countries) or macrolide antibiotics can be considered. Intranasal decongestants can be prescribed, but for no more than three days, to avoid rebound decongestions (Brook, 2010). In contrast to acute rhinosinusitis, chronic rhinosinusitis (CRS) is defined as an inflammatory condition involving the paranasal sinuses and nasal passages over a minimum duration of 8–12 weeks, despite attempts at medical management (Meltzer et al., 2004). Superimposed bacterial infections further complicate the process. The four major symptoms of CRS are anterior, posterior, or mucopurulent drainage; nasal obstruction or blockage; facial pain, pressure, or fullness; and decreased sense of smell (Meltzer et al., 2004). The bacteria can also form a biofilm over the sinus epithelium. Sequestration of bacteria within biofilms allows the bacteria to resist antibiotic treatment and persist as a low-grade infection within the sinus mucosa. Topical corticosteroid nasal sprays are preferred for all forms of CRS, along with antihistamines for underlying allergic causes, and antibiotics

(penicillin V, amoxicillin, or cloxacillin) are prescribed when nasal purulence is present (Dykewicz and Hamilos, 2010). Functional endoscopic sinus surgery (FESS) is the management of choice of chronic refractory rhinosinusitis.

Epiglottitis

Epiglottitis, or inflammation of the epiglottis, is a medical emergency, as it can lead to airway obstruction and death. It follows oral infection with *H. influenzae* (Peterson and Thomson, 1999). This microorganism is abundant in the oral mucosal surfaces and in dental plaque. However, certain capsulated strains are considerably more virulent and are thought to be a major pathogen in the respiratory tract, causing otitis, sinusitis, and pharyngitis. Other agents such as *Streptococcus pyogenes*, *S. pneumoniae*, and *S. aureus* have been implicated. In immunocompromised patients, *Pseudomonas aeruginosa* and *Candida* have been named. The signs of epiglottitis, often referred to as the four Ds, include dysphagia, dystonia, drooling, and distress, and it is often associated with fever (38 °C/100.4 °F or higher) as well.

An oropharyngeal exam is usually not performed to evaluate a suspected case of epiglottitis because manipulation of the oral cavity may lead to disaster, such as respiratory arrest. This diagnosis is primarily one of clinical suspicion. A lateral neck radiograph will show swelling of the epiglottis, also referred to as the "thumb sign." A flexible fiberoptic laryngoscopy can theoretically be performed (which will show cherry-red and swollen epiglottis and arytenoids; Jenkins and Saunders, 2009), but only in a very controlled setting such as the operating room due to the risk of inducing laryngospasm. This is almost never done. If clinical suspicion for acute epiglottitis exists, the patient should be taken urgently to the operating room for airway examination under the most optimal conditions possible. Ultrasonography has been mentioned as another way to evaluate these patients, revealing an "alphabet P sign" in a longitudinal view. A CBC with differential, a blood culture, and an epiglottal culture should only be obtained in patients with a secured endotracheal tube. CT scan of the neck is rarely needed and can precipitate disaster. The chest x-ray may reveal concomitant pneumonia in 10–15% of patients (Guerra and Waseem, 2021).

This condition requires immediate medical attention, with urgent endotracheal intubation, to protect the airway. This procedure should be performed by a competent anesthetist, with the help of a respiratory therapist and otorhinolaryngologist (D'Agostino, 2010). In addition, the patient should be given antibiotics, such as ceftriaxone or chloramphenicol, either alone or in combination with penicillin or ampicillin, for streptococcal coverage.

Chronic infections with oral manifestations

Actinomycosis

Actinomycosis is a chronic disease characterized by the formation of abscesses, fibrosis, and draining sinuses (Figure 10.7). The causative agent is the non-spore-forming anaerobic or microaerophilic bacterial species of the genus *Actinomyces* (most commonly *A. israelii*), which are normal inhabitants of cervicofacial, thoracic, and abdominal areas (Rivera-Hidalgo and Stanford, 1999). A similar infection, nocardiosis, is caused by the related facultative *Nocardia* spp. Cervicofacial actinomycosis is the

most common form of the disease (Laskaris, 1996). Actinomyces get access to the host tissues when there is an interruption in the mucosal barrier, caused by procedures such as tooth extraction and endodontic infection and treatment. Following this initial superficial invasion, the infection spreads deep into the tissues and a hard, slow-growing, relatively tender swelling may form with multiple drainage areas or sinus tracts. The discharge from these tracts typically contains the visible yellowish colonies of the microorganisms and are termed “sulfur granules.” If left untreated, osteomyelitis with extensive bone destruction will result (Feder, 1990; Brook, 2008).

Figure 10.7 Oral actinomycosis.

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Diagnosis can be confirmed by isolation of *Actinomyces* species from clinical specimens. Indirect immunofluorescence can also be utilized for this purpose (Gohean et al., 1990). The gold standard test for diagnosis is tissue biopsy culture with anaerobic pus cultures. Swabs from the infected sites should be avoided. Cultures can be falsely negative; Gram stain may demonstrate the presence of branched, beaded, Gram-positive filamentous rods with sulfur granules, which helps in making a preliminary diagnosis (Sharma and Hashmi, 2022). *Actinomyces* species are susceptible to several antibiotics such as penicillins, tetracyclines, erythromycin, clindamycin, and ciprofloxacin. Antibiotics need to be given at high doses for long periods (2–6 weeks) for a complete cure. Surgery might be required in some cases to aspirate or surgically drain the abscesses (Brook, 2008). Consultation with an oral medicine specialist and with an otorhinolaryngologist will be of great help in managing these patients.

Gonorrhea

Gonorrhea is the most frequently encountered sexually transmitted disease, caused by *Neisseria gonorrhea*, a nonmotile spherical oval coccus. The organism is aerobic, Gram negative, and cannot penetrate an intact stratified squamous epithelium, such as that of the skin and oral mucous membrane (Rivera-Hidalgo and Stanford, 1999). However, it can directly invade the urethra, cervix, pharynx, and conjunctiva, because of the presence of columnar and transitional epithelium in these areas. From these sites, infection may spread readily along mucosal surfaces, or systemically, resulting in disseminated disease (Guinta and Fiumara, 1986). Humans are the only known hosts for *N. gonorrhea,* and the organism has been cultured from saliva of infected individuals. There is oral, pharyngeal, and tonsillar involvement in 20% of patients with gonorrhea. The tonsils are red and swollen, with grayish exudates. Lesions in the oral mucosa may appear fiery red and edematous, and occasionally there may be painful ulcerations. Diagnosis is established by culture and identification of *N. gonorrhoeae* (Laskaris, 1996; Bruce and Rogers, 2004). Sugar fermentation tests aid in species differentiation, and fluorescent antibody techniques have been used for rapid identification of gonococci. Penicillin is the drug of choice for this infection, and in drug-resistant patients ceftriaxone and ciprofloxacin have been used successfully (Chue, 1975).

Mycobacterial infections

The most common mycobacterial infections are tuberculosis, caused by the air-borne tubercle bacilli *Mycobacterium tuberculosis*, and leprosy, caused by *M. leprae*. There are also numerous nontuberculous mycobacteria, such as *M. kansasii, M. chelonei*, and *M. avium* intercellular complex (Weg, 1976; Rivera-Hidalgo and Stanford, 1999), which cause most of the medical infections. These infections are noncommunicable from person to person, and do not require long-term systemic medication as in the case of tuberculosis (Rivera-Hidalgo and Stanford, 1999).

Tuberculosis

Tuberculosis is a chronic infectious disease and spreads almost exclusively via droplets from a person with active disease. Tuberculosis is still among the most life-threatening infectious diseases in humans and one-third of the world's population comes into contact with the disease at some stage in their life (Kakisi et al., 2010). It commonly affects the lungs, but can occur in any part of the body, and is characterized by formation of granulomas with caseation necrosis caused by cell-mediated response. Primary tuberculosis is seen in patients who have had no previous exposure to the disease and initially is predominantly subclinical. Secondary tuberculosis is seen in previously sensitized patients (Phalen et al., 1996). Oral lesions are rare (0.1–5%; Kakisi et al., 2010), but if they occur they appear as chronic, painless, irregular ulcers, with a vegetative surface covered by grayish or yellow exudates. The dorsal surface of the tongue is a common site of secondary tuberculous infection, followed by the palate, gingiva, buccal mucosa, and lips (Hale and Tucker, 2008). The Mantoux reaction following the injection of a dose of purified protein derivative (PPD) is the traditional screening test for exposure to tuberculosis. Diagnosis is reached based on the medical history, identification of acid-fast mycobacteria in clinical specimens, a positive

delayed hypersensitivity skin reaction to PPD, and chest radiograph findings, which include infiltrates or consolidations and/or cavities in the upper lungs with or without mediastinal or hilar lymphadenopathy (Ellner et al., 1988). A chest x-ray is indicated to rule out or rule in the presence of active disease in all screening test–positive cases. Other diagnostic evaluation methods include acid-fast staining–Ziehl-Neelsen, culture, and the new generation of nuclear amplification and gene-based tests, which enable identification of the bacteria or bacteria particles making use of DNA-based molecular techniques.

Combination therapy is always indicated, and monotherapy should never be used for tuberculosis. A four-drug regimen (usually including isoniazid, rifampicin, ethambutol, and pyrazinamide) for two or six months, along with vitamin B6 to prevent neural damage (neuropathies) caused by isoniazid, is the first-line treatment for tuberculosis (Adigun and Singh, 2022).

If a patient has tuberculosis, all orthodontic procedures should be carried out under strict medical or pulmonologist supervision, in order to prevent the spread of the disease as well as its aggravation.

Leprosy

Leprosy, otherwise known as Hansen disease, is a chronic disease and is characterized by damage to the nerves and skin, resulting in deformities and disability. *M. leprae* is a Gram-positive, acid-fast, nonspore-forming, nonmotile, pleomorphic bacillus, which causes four types of leprosy: indeterminate, tuberculoid, borderline, and lepromatous (Rivera-Hidalgo and Stanford, 1999). Oral lesions have been demonstrated in tuberculoid, borderline, and lepromatous leprosy. The lesions present as nodules/lepromas that progress to necrosis and ulcerations. The ulcers may heal with scarring or progress to produce further tissue destruction. Lepromas are filled with *M. leprae*, and might occur in the palate, dorsum of the tongue, uvula, and lips. When left untreated, these lesions can cause extensive destruction of the oral tissues (Ghosh et al., 2009). The diagnosis is based on clinical signs such as anesthetic skin lesions and enlarged peripheral nerves, and laboratory techniques such as histopathological analysis using skin biopsies and PCR to detect *M. leprae* and *M. lepromatosis* DNA in tissue.

General treatment of leprosy usually involves multiple-drug therapy (MDT) to ensure no microbial resistance. The treatment depends on the type of disease – for tuberculoid disease dapsone (100 mg daily) with rifampicin (600 mg daily) for 12 months; and for lepromatous disease dapsone, rifampicin, and clofazimine (50 mg daily) for 24 months (Bhandari et al., 2021).

Syphilis

Syphilis caused by the spirochete *Treponema pallidum* is a venereal disease, with a decreasing prevalence rate. Syphilis can be either congenital (when the fetus becomes infected *in utero*) or acquired (contracted by sexual contact, direct inoculation, or transfusion with fresh human blood). Early congenital syphilis may manifest itself as papulosquamous lesions of the skin and the oral mucous membranes. The lesions at the commissures of the lips, angle of the nose, and eyes heal with radiating scars called rhagades (Rivera-Hidalgo and Stanford, 1999). Oral manifestations of late congenital

syphilis include Hutchinson's triad of deafness, interstitial keratitis, and malformed incisors, along with other dental anomalies such as hypoplastic molars with poorly developed cusps, called mulberry molars.

Acquired syphilis has three classic phases. Primary syphilis is characterized by chancre, a centrally ulcerated granulomatous lesion with a raised, indurated border; the lesion is painless and resolves within 2–8 weeks. Secondary syphilis is the systemic or disseminated phase and may occur 2–12 weeks after contact. Signs and symptoms consist of fever, headache, malaise, a symmetrical rash, and mucous patches in the oral cavity. The oral lesions appear as grayish-white, glistening patches on the soft palate, tongue, and buccal mucosa, but rarely on the gingiva. After this the patient enters a latent stage and 30–40% of untreated patients develop tertiary syphilis, which includes multiorgan involvement. Gumma is the characteristic lesion in this phase and is seen in the hard palate. This phase is not infectious (Little, 2005).

Clinical examination and serological tests aid in the diagnosis of syphilis. Dark field microscopy can sometimes be useful when serological test results are negative but there is a high index of suspicion (Seigel, 1996). The serological tests are classified as nontreponemal and treponemal. The nontreponemal tests – venereal disease research laboratory test (VDRL) and rapid plasma reagin test (RPR) – are screening tests that detect antibodies to cardiolipin in blood and are therefore not specific for syphilis. Positive nontreponemal tests must be confirmed with a treponemal test – fluorescent treponemal antibody absorption assay (FTA-ABS) or *T. pallidum* particle agglutination assay (TP-PA – that detects specific serum antibodies to *T. pallidum*. Primary, secondary, or early latent syphilis is treated with a single dose of intramuscular (IM) benzathine penicillin G 2.4 million units. Neurosyphilis is treated with IV penicillin G aqueous 18–24 million units daily for 14 days. An alternative regimen would be procaine penicillin G 2.4 million units IM once daily *and* probenecid 500 mg orally 4 times per day for 10–14 days. Tertiary and latent syphilis and HIV-infected patients should be treated with weekly benzathine penicillin G 2.4 million units IM for three weeks. Alternative therapies include doxycycline 100 mg PO twice daily for 14 days, or ceftriaxone 1–2 gm IM or IV daily for 10–14 days, or tetracycline 100 mg PO 4 times a day for 14 days. Azithromycin is no longer recommended due to reports of resistance. Patients need to be followed post treatment at 6, 12, and 24 months with a clinical evaluation and serial nontreponemal (VDRL and RPR) testing. In addition, re-examinations at 3 and 9 months are suggested for high-risk individuals (Tudor et al., 2022).

The three mycobacterial infections, tuberculosis, leprosy, and syphilis, are highly contagious, posing a serious danger to all the people in the orthodontic office, including the orthodontist, staff, and patients. It is therefore essential to identify suspected carriers of these diseases, and refer them promptly to a physician for a definitive diagnosis. Failure to recognize and appropriately refer potential carriers and proceeding to address only their malocclusion may endanger all personnel and patients visiting an orthodontic office.

Viral infections

Oral diseases and infections of viral etiology are common in dental as well as orthodontic practices, and awareness of them can effectively prevent their spread.

Viruses contain one type of nucleic acid alone, either DNA or RNA. They often require a host, who provides them with ribosomes, which they need to multiply to produce disease conditions. Nearly all viruses are icosahedral and possess a protein shell or nucleocapsid; protein spikes project from the surface of the viral nucleocapsids. The proteins are usually glycoproteins, participating in viral attachment and infection of the host. Viral infections have two stages: attachment and penetration. Viruses attach to their host cells by the way of cellular receptors, and after getting enveloped they fuse with the host cell membrane. Receptor-mediated endocytosis is the process through which enveloped and naked viruses gain entry into host cells.

The outcome of viral infection depends on the viral state. If the virus is in a lytic stage, the host cell is destroyed. In lysogeny, the virus enters and integrates with the host cell, and is reactivated at a later date to become lytic in nature. In a latent stage, a form of lysogeny, the viral genome stays in the host cell but is not necessarily incorporated. Once the viral gene is released, early gene transcription begins, the products of which are proteins that regulate the transcription of further genes and viral DNA replication (McCullough and Savage, 2005b). Viral diseases may be the direct result of cell destruction by a virus, or a consequence of host immune reactions against viral proteins. Viruses may encode homologs of host cytokines and decoy receptors capable of binding and neutralizing host-derived cytokines. The rapid rate of mutation in critical viral genes can help viruses to overcome adaptive host defenses (Slots, 2009).

The most common viral infections that are relevant to dentists and orthodontists are listed in Table 10.2.

Herpesvirus

This virus belongs to the family *Herpetoviridae* and consists of a double-stranded DNA molecule surrounded by an icosahedral capsid, a proteinaceous tegument, and a lipid-containing envelope with embedded viral glycoproteins (Greenberg, 1996). Around 300 different types of herpesvirus have been identified, of which eight human herpesvirus species with distinct biological and clinical implications have been classified in three groups (Slots, 2009):

Table 10.2 Viral infections of relevance for the dentist and orthodontist.

Adapted from Sällberg (2009) and Slots (2009).

Virus family	Virus name	Viral disease	General clinical or oral appearance	Treatment
Herpes viruses				
Alfa group	Herpes simplex (HSV-1 and -2) Varicella zoster (VZ or herpes virus 3)	Primary infection: gingivostomatitis	Swollen and red gingiva, sometimes with ulcers, multiple vesicles in mucosa	Aciclovir
		Recurrent infection: herpes labialis and intraoral herpes	Lesions on lips (usually unilateral), perioral skin, intraoral ulcer lesions, trigeminal neuralgia	Aciclovir
		Shingles	"Belt of roses" rash and neuralgia with pain commonly from the trigeminal nerve (15%), on one or sometimes both sides of the face	Palliative
Beta group	Cytomegalovirus (CMV or herpesvirus 5)	CMV infection	May infect fetus during pregnancy	Ganciclovir
Gamma group	Epstein–Barr virus (EBV or herpesvirus 4)	Infectious mononucleosis	Tonsillitis	Palliative
Morbilli virus	Morbilli virus	Measles	Cough, conjunctivitis, fever, photophobia, rhinitis, Koplik spots, skin rash	Vaccine
Paramyxoma	Mumps virus	Mumps (parotitis)	Glandular infection especially of salivary glands, which become swollen and painful – unilaterally or bilaterally	Vaccine
Papovavirus	Human papillomavirus (HPV)	Papilloma	Squamous cell papilloma – cauliflower-like lesions, narrow base, pink, exophytic	Surgery

Virus family	Virus name	Viral disease	General clinical or oral appearance	Treatment
			growth Verruca vulgaris – wart-like and broader base	
Retroviruses	HIV-1, HIV-2	Acquired immune deficiency syndrome (AIDS) Acute and chronic (years)	Hairy leukoplakiaAggressive periodontitis Candidiasis and other fungal infections Kaposi sarcoma Frequently mucosal infections	Retarding medicine – highly active antiretroviral therapy (HAART)
Picorna virus	Coxsackie virus	Herpangina	Clustered petechiae in the soft palate that becomes ulcerated in a few days	Palliative
Picorna virus	Enterovirus	Hand, foot, and mouth disease	Ulcerations on the buccal mucosa and soft palate, often in conjunction with ulcers on the hands and feet	Benign and heals within 7–10 days Aciclovir
Hepatitis virus	Hepatitis B virus (HBV) Hepatitis C virus (HCV)	Liver infection	Jaundice (yellow skin and eye) HBV – acute infections and 5% develop the chronic, benign carrier state HCV – 60% develop chronic liver disease and 80% of these develop cirrhosis	HBV – vaccine HBC – no vaccine, Acyclovir

- *Alpha group*: herpes simplex virus 1 (HSV-1), herpes simplex virus 2 (HSV-2), and varicella zoster (VZ) virus.
- *Beta group*: human cytomegalovirus (CMV), human herpesvirus 6, and human herpesvirus 7.
- *Gamma group*: Epstein–Barr virus (EBV) and human herpesvirus 8.

Primary herpetic gingivostomatitis

The primary infection with herpes simplex virus, which usually occurs in infants and children, often goes unnoticed, being subclinical in nature (Scott et al., 1997). There may be a prodrome of fever, malaise, and nausea. The infection might also present as vesicles on the mucosa of the mouth and pharynx. The vesicles break down to form

clusters of small, round, or irregular superficial ulcers with yellowish base and red margins. There is a characteristic widespread inflammation of the gingivae, which appear pinkish red and swollen (Figure 10.8). The patient will experience difficulty eating and swallowing, and the condition, which is self-limiting, heals without scars in about 10 days. The lesion is always accompanied by cervical lymphadenopathy and may be more severe if it occurs in adults (Tovaru et al., 2009).

After primary infection, the virus remains dormant in the sensory and autonomic trigeminal or sacral ganglia, and is reactivated at a later stage, when host immunity is compromised. Recurrent infections are observed in 20–40% of individuals after a primary infection. The reappearance of the infection shows regional predilection, with the type 1 virus (mostly activated from trigeminal ganglia) producing oral infections, and type 2 (activated from sacral ganglia) producing genital lesions. The typical picture of the intraoral recurrent lesions is a cluster of small ulcers in the attached gingivae, which are initially discrete and painful and then coalesce at a later stage to form larger lesions that heal in 10–12 days (Arduino and Porter, 2008).

Herpes labialis (Figure 10.9) is a common recurrent herpes infection (otherwise known as cold sores). A prickling sensation precedes blister formation. These blisters enlarge, coalesce, rupture, and become crusted before healing within 7–10 days. The lesions usually appear on the lips and perioral skin, often triggered by ultraviolet radiation. In some cases, trigeminal neuralgia has been described in conjunction with episodes of herpes labialis, suggesting induction of neurosensory abnormalities (Treister and Woo, 2010). Herpetic whitlow (Figure 10.10), a herpetic infection of the fingers, is an occupational hazard as far as dental professionals are concerned, consisting of severely painful localized lesions, but can spread following surgical intervention (Wu and Schwartz, 2007).

Figure 10.8 Acute herpetic gingivostomatitis.

Courtesy of Professor Mats Jontell.

Figure 10.9 Herpes labialis.

Clinical features are usually sufficient for diagnosis of herpes infection, the major differential diagnosis of which is recurrent aphthous ulceration. The gold standard for diagnosing HSV-1 infection is HSV-1 serology (antibody detection via western blot). The most sensitive and specific mechanism is viral PCR. However, while serology remains the gold standard, viral culture, direct fluorescent antibody (DFA) assay, and Tzanck smear are alternative methods of diagnosis (Saleh et al., 2022).

For the treatment of orolabial herpes, the current recommendation is oral valacyclovir (2 g twice daily for 1 day). If the patient has frequent outbreaks, chronic suppression is warranted. For chronic suppression of immunocompetent patients, oral valacyclovir 500 mg daily (for patients with <10 outbreaks per year) or oral valacyclovir 1 g daily (for patients with >10 outbreaks a year) is recommended. For the treatment of eczema herpeticum, it is recommended to use 10–14 days of either acyclovir (15 mg/kg with a 400 mg maximum) 3–5 times daily or valacyclovir 1 g PO twice a day (Saleh et al., 2022).

Figure 10.10 Herpetic whitlow affecting the fingers.

It is to be remembered that all the drugs indicated for treating herpes infection should be prescribed only under strict medical guidance. They should be supplemented with bed rest, fluids, and a soft diet, along with antipyretics for fever reduction (Wilson et al., 2009). Patients should be discouraged from touching the lesions, in order to reduce the risk of spreading the infection.

Varicella zoster infection

The primary infection from varicella virus is chicken pox, which occurs mainly in children. The virus remains in a latent state in dorsal root ganglia, and is reactivated when host immunity is compromised at a later stage to produce herpes zoster or shingles. Varicella is a highly infectious disease, transmitted by inhalation of infective droplets and by direct contact with the lesions. The pruritic skin rash progresses through macules, papules, vesicles, drying vesicles, and scabs, with healing occurring over 2–3 weeks. Intraoral vesicles are commonly seen on the tongue, buccal mucosa, gingiva, palate (Figure 10.11), and oropharynx, and are generally not painful (Birek, 2000). Several predisposing factors can lead to recurrence of the infection in tissues supplied by sensory nerves, such as immunosuppression with cytotoxic drugs, radiation, internal malignancies, malnutrition, old age, alcohol, and substance abuse. In immunocompromised patients, including those infected with HIV, the recurrence rate of herpes infection is increased (Civen et al., 2009).

Occasionally, dental manipulation can also lead to recurrence. The first signs are pain and tenderness in the dermatome corresponding to the sensory ganglion, following which vesicles appear on one side of the face or along the distribution area of one branch of the trigeminal nerve. The unilateral vesicles form clusters with areas of surrounding erythema, ending abruptly in the midline. The lesions often heal with scarring, and areas of hypo/hyperpigmentation may be seen. When the facial and auditory nerves are affected, there is facial paralysis, vesicles in external ear, tinnitus, deafness, and vertigo, the combination of which is called Ramsay–Hunt syndrome (Persson et al., 2009). A residual complication of herpes zoster infection is postherpetic neuralgia, which occurs in 10% of patients and manifests as unilateral persistent pain in the affected area (Gilden et al., 2010).

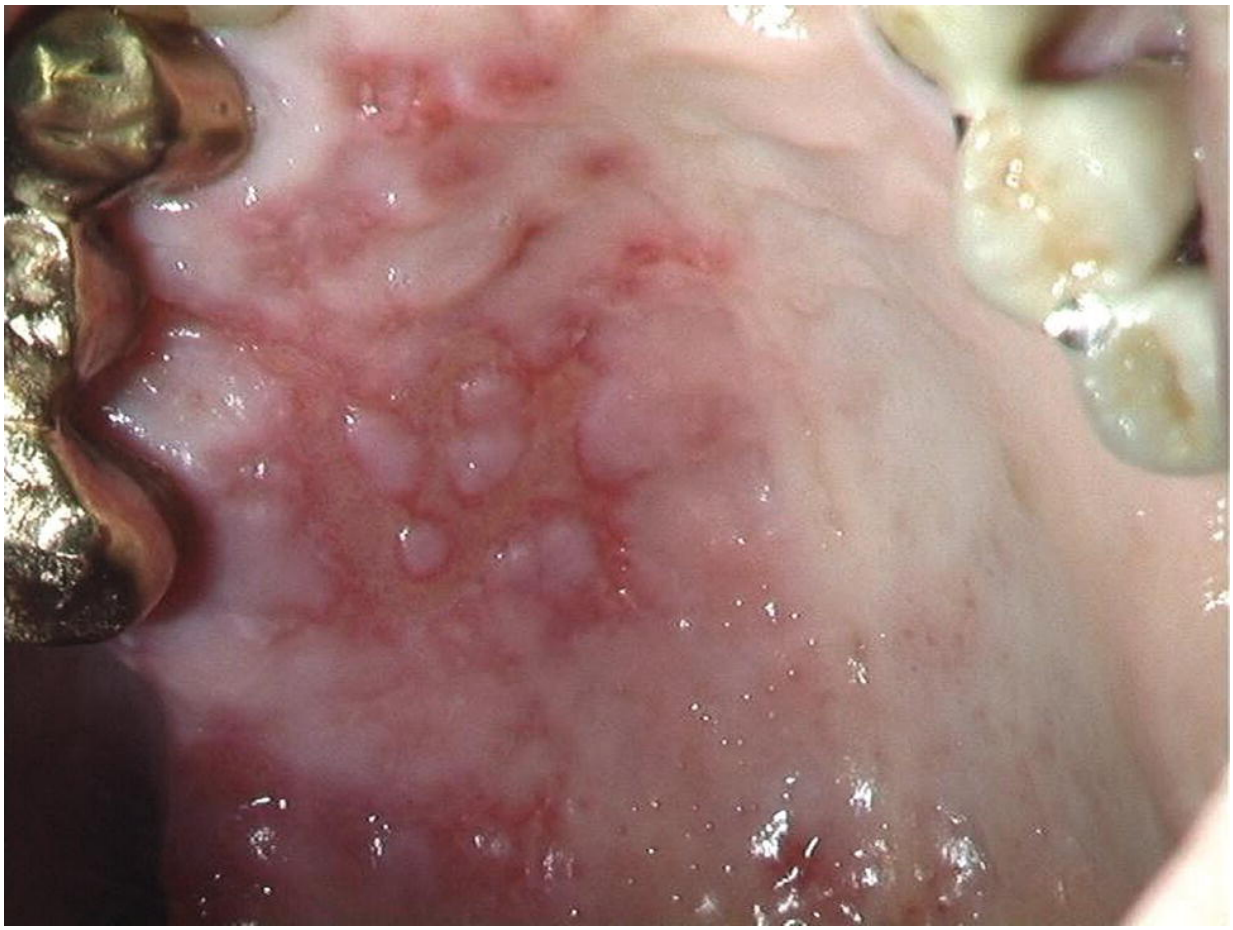

Figure 10.11 Herpes zoster.

Courtesy of Professor Mats Jontell.

Confirmation is by examination of the fluid within the vesicles, scraping of lesions that have not crusted, or by blood for evidence of an acute immunological response. PCR has the highest yield and can be utilized for nonskin samples such as bronchoalveolar lavage samples and cerebrospinal fluid.

Treatment of this infection is supportive and symptomatic. Topical calamine lotion may relieve pruritus. Daily cleansing with warm water will help avoid secondary bacterial infection. Acetaminophen may be used to reduce fever. Avoid aspirin, as it

may cause Reye syndrome. In children, acyclovir decreases symptoms by one day if taken within 24 hours of the start of the rash, but it has no effect on complication rates, and it is not recommended for individuals with normal immune function. In adults, infection tends to be more severe, and treatment with antiviral drugs (acyclovir or valacyclovir) is advised if they can be started within 24–48 hours of rash onset (Ayoade and Kumar, 2022).

Epstein–Barr virus

EBV is the causative agent in infectious mononucleosis or "kissing disease" in young adults and children, transmitted mainly through blood and saliva (Rivera-Hidalgo and Stanford, 1999). The disease manifestations include fever, lymphadenopathy, malaise, and sore throat. Oral ulcers, multiple palatal petechiae, gingival ulcerations, and enlarged tonsils (Figure 10.12) are the reported oral manifestations (Mendoza et al., 2008). This virus is also implicated in oral hairy leukoplakia, which is seen in HIV-infected patients, and in malignancies (nasopharyngeal carcinoma, Burkitt lymphoma, and oral squamous cell carcinoma) and periodontal disease (Mendoza et al., 2008; Hoelzer, 2009). EBV and CMV have been associated with multiple autoimmune disorders, such as systemic lupus erythematosus, rheumatoid arthritis, multiple sclerosis, pemphigus vulgaris, Sjögren syndrome, Wegener granulomatosis, and polyarteritis nodosa (Barzilai et al., 2007).

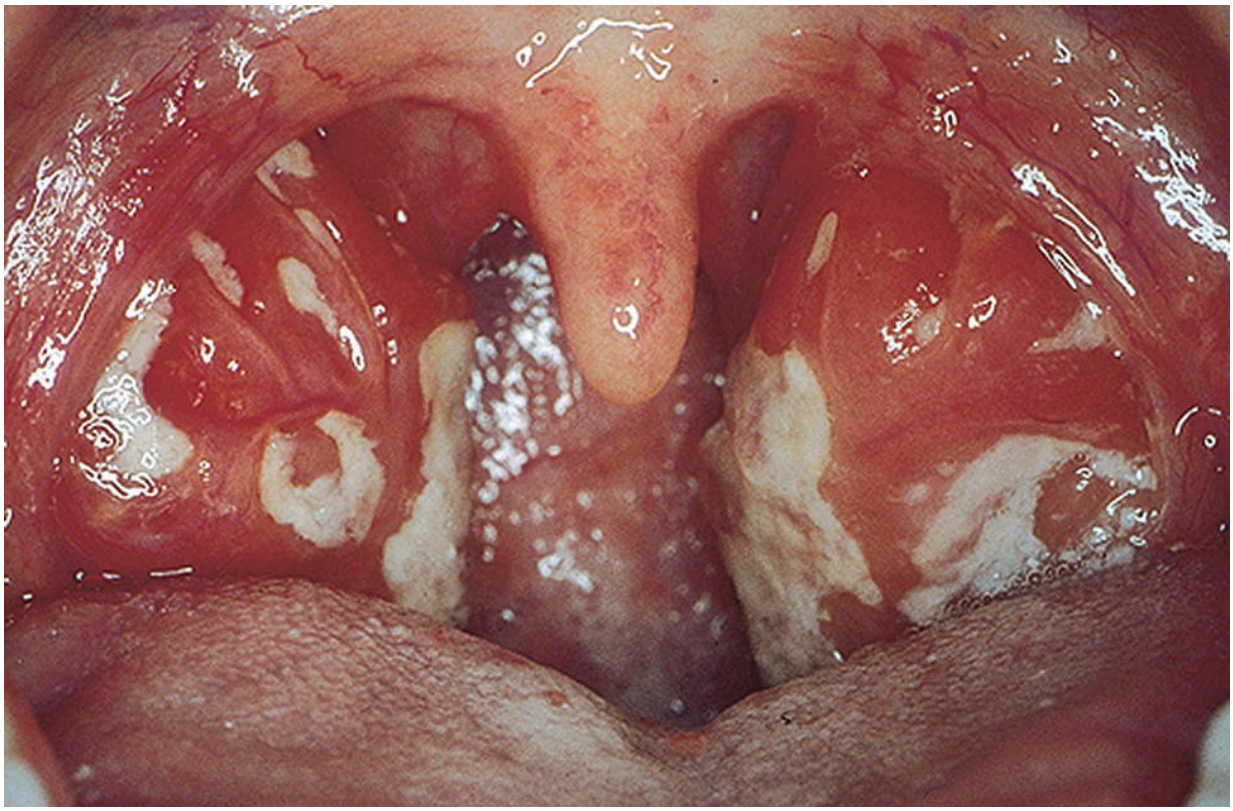

Figure 10.12 Infectious mononucleosis.

Determining whether a patient has an infection due to EBV is usually most effectively done through serological testing. Atypical-appearing lymphocytosis is most commonly

present on peripheral smear. Heterophile antibody tests identify IgM antibodies against EBV. Viral capsid antigen (VCA) IgM and IgG can be used to confirm the diagnosis. Elevated levels of VCA IgM antibodies detect an acute infection, while increased VCA IgG antibody levels indicate prior or chronic infection.

EBV is treated symptomatically with medications that can reduce fever and pain. Some studies using antiviral medications for EBV treatment did show a decrease in the amount of virus shed in the oral cavity, but there was no improvement in overall symptoms (Hoover and Higginbotham, 2022).

Cytomegalovirus infection

CMV, along with the herpes 6, 7, and 8 viral infections, is the least common of the herpes viral infections. Human CMV infection presents as mainly three syndromes: perinatal and human cytomegalovirus inclusion disease, acute acquired human cytomegalovirus infection, and human cytomegalovirus disease in immunocompromised hosts (Rivera-Hidalgo and Stanford, 1999). Oral manifestations are observed in the latter two syndromes, which are together called heterophil-negative infectious mononucleosis. Infection often arises after blood transfusion or sexual contact (Miller, 1996). Sahin et al. (2009) identified the saliva of patients with chronic periodontitis as the source for human cytomegalovirus and EBV, from where the reactivation process can start. These viruses become very active in immunocompromised patients and are often associated with malignancies such as oral squamous cell carcinoma and cervical carcinoma (Miller, 1996).

The diagnosis of CMV cannot be made solely based on clinical examination. Laboratory viral identification is the preferred initial test in patients who have suspected CMV infection. Although a histopathological diagnosis is the gold standard for diagnosis (by identification of CMV inclusion bodies), quantitative PCR assays are the preferred method for viral detection. Immunocompetent patients present with minimal or no symptoms, are self-limiting, and do not require specific therapy other than symptomatic management. But for severe cases, several antiviral agents have been approved for the treatment of CMV: cidofovir, foscarnet, ganciclovir, and valganciclovir (Gupta and Shorman, 2022).

Measles

An enveloped virus belonging to the family *Morbillivirus* causes measles, otherwise known as rubeola. This is a highly communicable disease, transmitted by inhalation of infective droplets, with an incubation period of 10–14 days. It is an acute systemic condition, the prodrome of which consists of cough, conjunctivitis, fever, malaise, photophobia, rhinitis, and Koplik spots, which appear on the mucosa next to the molars as bluish-gray specks on a red base. The spots start to appear 48 hours before the development of the irregular red-brick maculopapular rash characteristic of measles, and may last four days (Steichen and Dautheville, 2009). Shedding of measles virus starts in the prodromal stage and continues through the acute stage.

The diagnosis of measles is based on three elements: clinical manifestations, epidemiology, and laboratory testing. Serological tests with specific IgG and IgM measurements, molecular biological techniques with reverse transcription-PCR application, and viral isolation are available for diagnostic confirmation.

Measles remains a major cause of childhood mortality in developing countries (Rivera-Hidalgo and Stanford, 1999). However, vaccination can prevent its occurrence. For children, vaccination begins with the first dose between the ages of 12 and 15 months, followed by a second dose at 4–6 years of age, though it can be administered as early as 28 days after the first dose if the patient is above 12 months of age (Krawiec and Hinson, 2022).

Mumps

Mumps, or epidemic parotiditis, is caused by the mumps virus, which belongs to the single-stranded RNA paramyxovirus virus genus. The parotid salivary gland infection may appear either unilaterally or bilaterally, and viremia can lead to complications such as orchitis in males, oophoritis in females, pancreatitis, deafness, and aseptic meningitis and encephalitis. Affected salivary glands will appear swollen, and will be accompanied by swelling of Stensen's duct, erythema, and pain. It is a highly communicable disease, transmitted by inhalation of infective droplets, with an incubation period of 14–21 days.

Clinical diagnosis is based on the classic parotid swelling, while laboratory diagnosis is based on isolation of the virus, detection of viral nucleic acid, or serological confirmation with the presence of IgM mumps antibodies. Vaccination can prevent mumps; one dose of vaccine is about 80% effective against the disease (Hviid et al., 2008).

Orthodontic treatment should not be carried out during the infectious stages of the disease, as interpersonnel transfer occurs rapidly. If the orthodontist is unaware of the disease process, its clinical signs and symptoms, especially the initial oral manifestations, he or she might contract the infection and become a carrier. Thus for ethical reasons, an orthodontist, as part of the healthcare system, should be aware of the signs and symptoms of the disease along with the methods of identification and management/referral strategies, to protect not only him- or herself but also office staff and patients from contacting it.

Human papillomavirus infections

Human papillomavirus is composed of more than 60 serological types, and produces lesions in many areas of the body, such as the trachea, esophagus, genitalia, nasal cavity, larynx, and mouth (Dhariwal et al., 1995). The classic oral lesions associated with papillomavirus infection are squamous cell papilloma, condyloma acuminatum, verruca vulgaris, and focal epithelial hyperplasia (Chaudhary et al., 2009). Squamous cell papilloma is a slow-growing, solitary, painless, exophytic, cauliflower-like, small, pink mucosal lesion with a narrow base. It can occur at any age, but is most commonly seen between 30 and 50 years of age, with a predilection for the tongue, lip, and soft palate (Carneiro et al., 2009). Verruca vulgaris or the common wart is a narrow exophytic growth with a wider base, which is sessile and firm. Oral lesions arise through autoinoculation, with the labial mucosa, tongue, and gingiva the preferred sites. The most common site is the buccal mucosa, and the infection is strongly associated with oral habits such as areca quid chewing and cigarette smoking (Wang et al., 2009). Condyloma acuminatum is usually found in the genitalia, with occasional occurrence in the oral cavity. Oral infections are predominantly transmitted through

oral–genital sexual contact, and consist of multiple cauliflower-like lesions; the labial mucosa, lingual frenulum, and soft palate are the sites of preferred invasion. Kui et al. (2003) traced the occurrence of condyloma acuminatum to infection by human papillomavirus, and suggested sexual abuse as the most common route of transmission. Focal epithelial hyperplasia, or Heck disease, usually presents as multiple plaque-like lesions, which are the same color as the mucosa and have a smooth surface. Individual lesions tend to be small (0.3–1 cm), but they coalesce and cluster, giving the mucosa a cobblestone or fissured surface. Lesions occur exclusively in the oral mucosa, and often present as asymptomatic papules (Bennett and Hinshaw, 2009). Other lesions such as erythroplakia, proliferative verrucous leukoplakia, candidal leukoplakia, squamous cell carcinoma, and lichen planus have also been associated with papillomavirus infection (Rivera-Hidalgo and Stanford, 1999).

Individuals with cutaneous warts have numerous treatment options available, including surgical removal, cryotherapy (freezing the infected tissue), irritant or immunomodulating medications, and laser removal.

Retroviral infections

Retroviral species, which inhabit almost all vertebrates, have seven established genera. HIV and T-lymphocytic viruses are the human pathogens in this group. The name retrovirus has its origin in its unique mode of replication. After entering a cell, the viral RNA is transcribed by viral reverse transcriptase into a DNA molecule, which is integrated as a provirus into the host chromosomal DNA. The provirus DNA serves as a template for the formation of viral RNA and the proteins used in the assembly of new virions. The ability of a provirus to remain transcriptionally inactive enables retroviruses to maintain persistent infection despite a functional host immune system (Slots, 2009).

HIV belongs to the Lentivirus genus, and HIV-1 and HIV-2 are its two subspecies. HIV-1 is the most virulent type and is responsible for the majority of HIV infections globally. The most common mode of spread is through the sexual route, followed by blood or blood products infusion and mother-to-child transmission *in utero*. HIV uses the CD4 receptor and chemokine co-receptor (CCR5) for entry into susceptible cells, and results in selective depletion of CD4+ T lymphocytes by apoptosis or necrosis. This process leads to progressive loss of cell-mediated immunity (Sällberg, 2009). The course of infection can be primary, acute, or chronic, finally culminating in acquired immune deficiency syndrome (AIDS). In the early stages, there is development of oral and vaginal candidiasis along with pneumococcal infections, tuberculosis, and reactivation of herpes simplex and varicella infections. Later stages involve infections caused by *Candida*, *Pneumocystis jiroveci, Histoplasma*, *Toxoplasma*, and *Cryptococcus* spp. (Reichart, 2003; Slots, 2009). Malignancies in HIV patients are often viral related, and EBV lymphomas, human herpesvirus, Kaposi sarcoma, and papillomavirus sarcomas predominate (Slots, 2009).

Oral hairy leukoplakia presents as a white, vertically corrugated, nonremovable lesion on the lateral or ventral margin of the tongue. The lesion is caused by EBV and has no premalignant potential (McCullough and Savage, 2005b; Gonzalez et al., 2010). Kaposi sarcoma is characterized by erythematous or violaceous plaque-like lesions that develop into tumorous growths over time. Large lesions may get ulcerated and become

painful and interfere with function. Hairy leukoplakia is predominantly seen in the palate or in the attached gingiva (Van Heerden, 2006). Other HIV-related oral lesions include pseudomembranous candidiasis, non-Hodgkin lymphoma, linear gingival erythema, necrotizing ulcerative periodontitis, and necrotizing ulcerative gingivitis (Leao et al., 2009). In HIV-positive children until 18 years of age the most common manifestation is oral candidiasis, with a prevalence of 50–80%, next to gingivitis (Lauritano et al., 2020). HIV infection can remain undetected for years. However, they are several tests to diagnose it: fourth-generation assay to detect specific antibodies and P24 HIV antigens, rapid test using blood or saliva to detect an HIV infection within hours, and PCR to analyze the viral load.

Current therapy for HIV infection is called HAART, or highly active antiretroviral therapy, and it includes at least two classes of antiretroviral agents. These may be a combination of two nucleoside analog inhibitors of reverse transcriptase, together with a protease inhibitor or a nonnucleoside reverse transcriptase inhibitor. If immune reconstitution has not happened there may be a rebound of symptoms, such as oral candidiasis and parotid gland enlargement (Ortega et al., 2008). If the patient is resistant to antiretroviral agents, the newer classes of drugs such as CCR5 antagonists can be prescribed (Slots, 2009). The HIV Workgroup of the National Institutes of Health (NIH) in the USA regularly updates the guidelines for the use of antiretroviral agents in adults and adolescents living with HIV (NIH Office of AIDS Research, 2021).

If an orthodontist fails to identify this highly contagious, globally prevalent viral infection, for which no effective cure has yet been developed, this will be considered highly negligent and dangerous. There is every chance that infected individuals will request correction of their malocclusion, but treating them without taking proper precautionary measures may lead to transmission of the infection. It is therefore imperative to obtain a detailed medical history and perform a thorough orofacial examination, in both young and adult candidates for orthodontic treatment, in order to detect those who may have symptoms suggestive of viral infection. Provision of orthodontic care for patients with viral diseases requires close and continuous interaction with the physicians treating them.

Herpangina

Herpangina is an acute febrile illness of sudden onset, characterized by the presence of ulcerations, vesicles, and diffuse erythema of the soft palate (Figure 10.13), fauces, and tonsillar areas. It commonly occurs in children, mainly during the summer, with a sudden onset of malaise, fever, and sore throat. The absence of oral lesions on the hard palate, and the acute onset and short period of morbidity, help to differentiate herpangina from other infectious processes. It is more frequently caused by the Coxsackie group A serotypes (Figure 10.14), and less frequently by group B serotypes, echovirus, and enterovirus. Usually the disease is self-limiting (Rivera-Hidalgo and Stanford, 1999; McCullough and Savage, 2005b; Van Heerden, 2006; Slots, 2009).

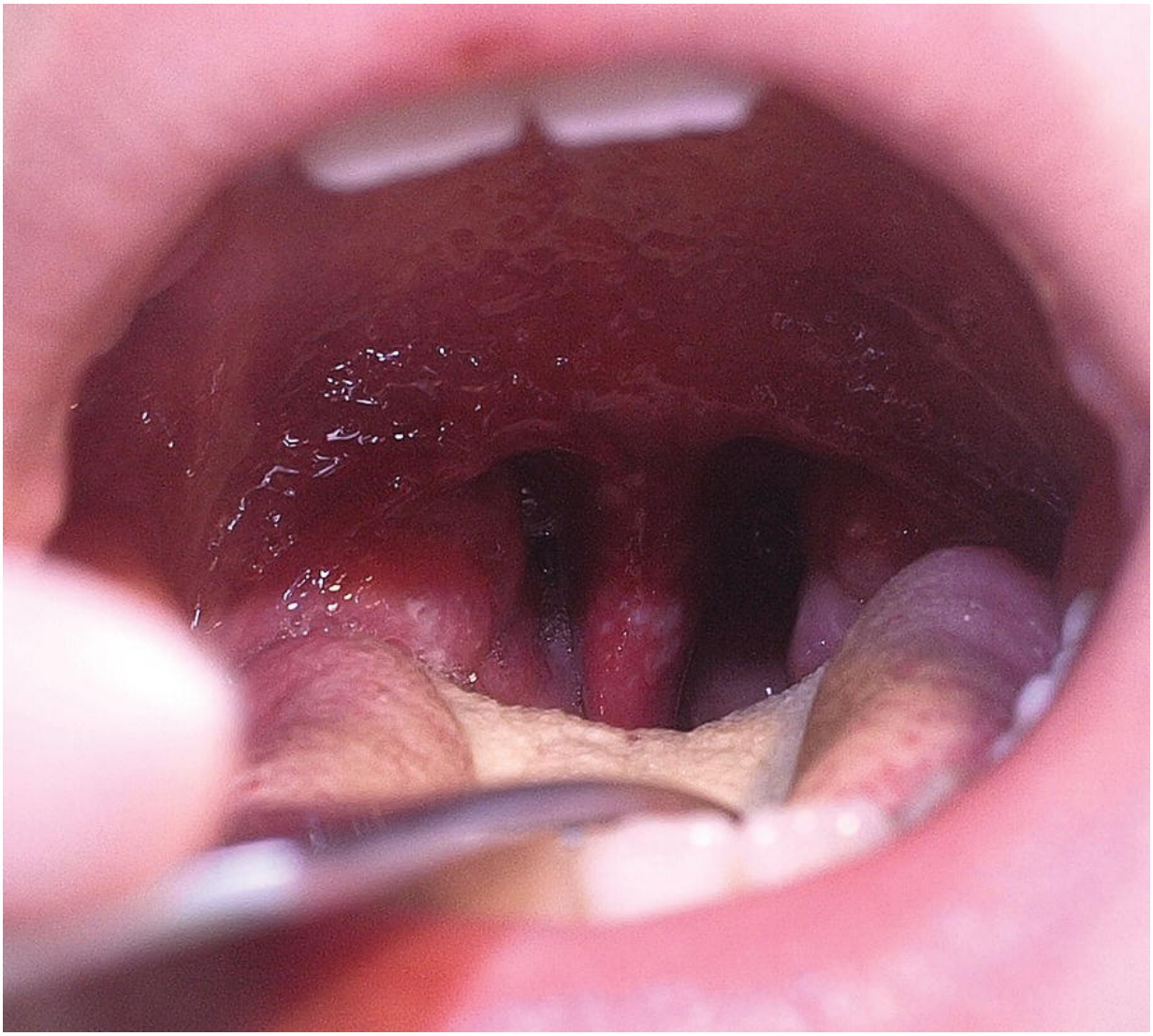

Figure 10.13 Herpangina.

Courtesy of Dr. Peter Johansson.

Figure 10.14 Coxsackievirus infection of the gingiva.

Courtesy of Professor Mats Jontell.

Hand, foot, and mouth disease

Hand, foot, and mouth disease (HFMD) is a mild exanthematous lesion, most commonly seen in children aged 1–5 years, but older children and young adults are not spared. Several enteroviruses are thought to be causative, and the most important ones are human enterovirus-71 and Coxsackievirus serotype (Kushner and Caldwell, 1996). The typical feature is exanthematous illness with vesicular lesions, 2–10 mm in diameter, of the hands, feet, and mouth. The cutaneous vesicles can resemble chicken pox (Slots, 2009). Oral lesions appear as ulcerations in the buccal mucosa (square blisters) and soft palate.

The diagnosis of HFMD is usually made clinically. The virus can be detected in the stool for about six weeks after infection; however, shedding from the oropharynx is generally less than four weeks. Light microscopy of biopsies or scrapings of vesicles will differentiate HFMD from varicella zoster virus and herpes simplex virus.

HFMD is a mild clinical syndrome and will resolve within 7–10 days. Treatment is primarily supportive. Pain and fever can be managed with NSAIDs and acetaminophen. Making sure the patient remains well hydrated is important. Additionally, a mixture of liquid ibuprofen and liquid diphenhydramine can be used to gargle, which helps coat the ulcers, easing the pain (Rivera-Hidalgo and Stanford, 1999; McCullough and Savage, 2005b; Van Heerden, 2006; Slots, 2009; Guerra et al., 2022).

Viral hepatitis

Viral hepatitis does not have any oral manifestations, but is important because it can spread through the oral route. Dentists and orthodontists treating patients with this disease should be aware of its signs and symptoms, so that they can prevent the spread of the infection to themselves and to their patients and clinical staff.

Infection with hepatitis B virus has three distinct phases: the first phase is acute, and is either subclinical or shows the classic signs of liver disease. This phase is seen mainly in adults. Children show the other two stages: chronic infection, in which there is a high rate of viral replication, and later on a latent phase, where the virus maintains a lower replication rate. During the infectious phase, the child is highly contagious and the risk for severe liver disease is increased (Broderick and Jonas, 2003). The disease can be easily transmitted via an accidental needle stick injury, or a bite, through just 1 ml of blood, which contains 10^5–10^7 viral genomes. Dental staff should be vaccinated against hepatitis B, as once infected they can become life-long carriers. Treatment for hepatitis B infection requires a combinatorial approach, as in HIV-infected patients, and it requires drugs that attack the various stages of viral replication (Sällberg, 2009).

Hepatitis C is quite rare in childhood, but can be seen owing to vertical transmission (from mother to child) or transmission through a nosocomial route. This virus can also lead to a serious liver disorder, and children are often treated with interferon gamma and riboflavin combination regimen. No vaccine is presently available for hepatitis C (Fischler, 2007; Sällberg, 2009).

Coronavirus disease 2019

Coronavirus disease 2019 (COVID-19) is the highly contagious viral illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Like other RNA viruses, SARS-CoV-2, while adapting to its new human hosts, is prone to genetic evolution with the development of mutations over time, resulting in mutant variants that may have different characteristics than its ancestral strains. Several variants of SARS-CoV-2 have been described during the course of the pandemic that began in 2020, such as alpha, beta, gamma, delta, and omicron. The primary mode of transmission of SARS-CoV-2 is via exposure to respiratory droplets carrying the infectious virus from close contact or droplet transmission from presymptomatic, asymptomatic, or symptomatic individuals harboring the virus. Airborne transmission with aerosol-generating procedures has also been implicated in the spread of COVID-19. SARS-CoV-2 gains entry into the hosts' cells by binding the SARS-CoV-2 spike or S protein (S1) to the angiotensin-converting enzyme 2 (ACE2) receptors abundant on respiratory epithelium, such as type II alveolar epithelial cells. The viral attachment process is followed by priming the spike protein S2 subunit by the host transmembrane serine protease 2 (TMPRSS2), which facilitates cell entry and subsequent viral replication endocytosis with the assembly of virions. Although the respiratory system is the principal target for SARS-CoV-2, the virus can affect other major organ systems such as the gastrointestinal tract, hepatobiliary, cardiovascular, renal, and central nervous system. A detailed clinical history regarding the onset and duration of symptoms, travel history, exposure to people with COVID-19 infection,

underlying preexisting medical conditions, and drug history should be elicited by treating providers.

The standard diagnostic mode of testing is testing a nasopharyngeal swab for SARS-CoV-2 nucleic acid using a real-time PCR assay. An antibody test can evaluate for the presence of antibodies that occur as a result of infection and is mainly used for mass surveillance. Considering that this viral illness commonly manifests as pneumonia, radiological imaging has a fundamental role in the diagnostic process, management, and follow-up. Imaging studies may include chest x-ray, lung ultrasound, or chest CT.

Currently, a variety of therapeutic options are available that include antiviral drugs (e.g. molnupiravir, paxlovid, remdesivir), anti-SARS-CoV-2 monoclonal antibodies (e.g. bamlanivimab/etesevimab, casirivimab/imdevimab), anti-inflammatory drugs (e.g. dexamethasone), and immunomodulatory agents (e.g. baricitinib, tocilizumab), which are available under a US Food and Drug Administration (FDA)-issued Emergency Use Authorization (EUA) are being evaluated in the management of COVID-19. Besides the importance of imposing public health and infection control measures to prevent or decrease the transmission of SARS-CoV-2, the most crucial step to contain this global pandemic has been by vaccination to prevent SARS-CoV-2 infection in communities across the world (Cascella et al., 2022).

Fungal infections

The most common fungal infections affecting the oral cavity and of interest to dental surgeons, and especially orthodontists, are listed in Table 10.3.

Candidiasis

Candidiasis is the most common oral mycotic infection, and *Candida albicans* is the organism most associated with it. Other species observed in oral fungal infections are *C. tropicalis*, *C. glabrata*, *C. krusei*, and *C. dublinensis*. Clinically, candidiasis can be the cause of oral discomfort or pain, dysgeusia, and aversion to food (Samaranayake et al., 2009). Oral candidal infections are categorized as primary and secondary; primary candidiasis is confined to the oral and perioral tissues. If oral candidiasis is a manifestation of systemic disease, it is categorized as secondary candidiasis (Axell et al., 1997). Primary oral candidiasis is further subdivided into pseudomembranous, erythematous, and hyperplastic types. Pseudomembranous candidiasis (Figure 10.15), otherwise known as thrush, is characterized by white patches on the labial and buccal mucosa, tongue, and soft palate. The lesions often resemble milk curd and can be wiped off very easily with the help of a tongue blade, to reveal an erythematous, erosive base. The white mass consists of a tangled mass of fungal hyphae, bacteria, inflammatory cells, fibrin, and desquamated epithelial cells. Erythematous candidiasis (Figure 10.16) occurs as a consequence of persistent acute pseudomembranous candidiasis and is the most common form seen in HIV-infected patients. It consists of red patches, often in the mid-dorsum of the tongue, palate, and buccal mucosa. Palatal erythematous lesions, otherwise known as “kissing” lesions, are a common finding in HIV infection. Motta-Silva et al. (2010) concluded that oral erythematous candidiasis is more prevalent in patients with controlled diabetes mellitus type 2. Hyperplastic candidiasis, or candidal leukoplakia (Figures 10.17 and 10.18), is the least common

form, appearing as chronic, discrete, slightly raised lesions that vary from small palpable, translucent, whitish areas, to large, dense, opaque plaques, with hard and rough areas evident on palpation (Sitheeque and Samaranayake, 2003). There is a tendency toward malignant conversion in 15% of candidal leukoplakia (McCullough and Savage, 2005a; Samaranayake et al., 2009).

Table 10.3 Fungal infections of relevance for the dentist and orthodontist.

Adapted from Samaranayake et al. (2009).

Type of fungi	Type of fungal infection	Common species	Clinical manifestations	Treatment
Oral yeast infections	Candidiasis	*C. albicans*	Acute pseudomembranous	Mucostatin
		C. glabrata		Amphotericin
	Candida-associated lesions	*C. tropicalis*	Chronic hyperplastic or erythematous (atrophic)	Azoles
		C. krusei		
		C. dublinensis	Hyperkeratinized (white) or atrophic (red) mucosal lesions from which *Candida* can be isolated	
Systemic mycoses by molds	Aspergillosis	*A. fumigates*	Pulmonary	Amphotericin B Azoles
	Cryptococcosis	*C. neoformans*	Pulmonary	Amphotericin B Flucytosine
	Blastomycosis	*B. dermatitidis*	Pulmonary, cutaneous	Amphotericin B Azoles
	Mucormycosis	*Mucorales* spp.	Pulmonary	Amphotericin Surgery
	Histoplasmosis	*H. capsulatum*	Pulmonary, cutaneous	Amphotericin B Azoles
	Paracoccidioidomycosis	*P. brasilisensis*	Pulmonary	Amphotericin B Azoles
	Sporotrichosis	*S. schenckii*	Cutaneous	Amphotericin B

Figure 10.15 Acute pseudomembranous candidiasis.

Courtesy of Professor Mats Jontell.

Figure 10.16 Acute erythematous candidiasis.

Courtesy of Dr. Bengt Hasseus.

Other conditions caused by *Candida* spp. are chronic atrophic candidiasis or denture sore mouth, linear gingival erythema, secondary oral candidiasis, and chronic mucocutaneous candidiasis syndromes. In denture sore mouth (Figure 10.19), which can be seen in patients wearing removable orthodontic appliances, there is overgrowth of *C. albicans* on the fitting surface of a denture or a removable orthodontic appliance. The patient may complain of angular cheilitis (Figure 10.20), or an occasional burning or tingling sensation beneath the acrylic baseplate. This can be prevented by educating the patient about the importance of oral hygiene measures and cleaning and proper follow-up of inserted dentures and removable orthodontic appliances (Coelho et al., 2004).

Figure 10.17 Chronic nodular candidiasis in the buccal mucosa.

Courtesy of Professor Mats Jontell.

Figure 10.18 Chronic nodular candidiasis of the lip.

Courtesy of Dr. Per-Olov Rödström.

Figure 10.19 Denture sore mouth with secondary *Candida* infection.

Courtesy of Dr. Ranimol Sreekumar.

Linear gingival erythema is defined as nonplaque-induced gingivitis, presenting as a distinct erythematous band of at least 2 mm along the margin of the gingiva, with either diffuse or punctate erythema of the attached gingiva. The lesions may be localized to one or two teeth or can be generalized, and may or may not be accompanied by occasional bleeding and discomfort. *C. dubliniensis* has been implicated in linear gingival erythema, and is one of the common oral manifestations of HIV infection (Zhang et al., 2009). Treatment of this condition does not require antifungal medications, but rather professional periodontal scaling and debridement, along with effective plaque control at home, and twice-daily mouth rinses with 0.12% chlorhexidine gluconate for two weeks.

Secondary candidiasis occurs consequent to HIV infection, hematological malignancies, and aggressive treatment with cytotoxic agents. Chronic mucocutaneous candidiasis syndrome is a persistent candidiasis that responds poorly to topical antifungal agents (Samaranayake et al., 2009).

Diagnosis of oral candidiasis is often clinical, based on clinical examination, medical history taking, and assessment of risk factors. The diagnosis is made after finding the typical lesion's features, excluding other conditions, and assessing the lesion's response to antifungal treatment. Acute atrophic candidiasis and chronic hyperplastic candidiasis resemble premalignant or malignant lesions; therefore, a biopsy is recommended on top of the empirical treatment.

Figure 10.20 (a) Angular cheilitis due to *Candida albicans*. (b) Healing lesions in the same patient.

Courtesy of Professor Mats Jontell.

Topical antifungal therapy and oral hygiene measures are usually sufficient to resolve mild oral candidiasis. Topical antifungal drugs available include nystatin, miconazole, clotrimazole, and ketoconazole. Nystatin is a widely used topical antifungal for treating oral candidiasis, available as pastille, mouthwash, and oral suspension. Patients are indicated to rinse their mouth with 5 ml nystatin oral suspension (100,000 units/ml) four times daily for two weeks (swished for several minutes then swallowed). Its adverse effects most commonly include nausea, vomiting, and diarrhea. Another option is clotrimazole troches 10 mg orally five times daily (dissolved over 20 minutes). In the appropriate circumstances, miconazole oral gel may also be an option. The use of miconazole in the mouth is limited since it induces vomiting and diarrhea, but it is prescribed to manage angular cheilitis and denture stomatitis. Nystatin (oral rinse) and clotrimazole (troches) are high in sucrose. Therefore, triazoles – fluconazole or itraconazole – prescribed once daily can be an alternative in oral candidiasis associated with diabetes mellitus or if there is a high risk of dental caries. Topical treatment is recommended for patients with a mild presentation or first presentation of the disease (Taylor et al., 2022).

By preventing the proper performance of oral hygiene measures, orthodontic appliances, removable, fixed, or functional, can promote candidal overgrowth (Lucchese and Bondemark, 2021). Orthodontists should be equipped for management of these lesions after appropriate identification, as well as differential diagnosis to eliminate serious underlying disorders. They should be aware of the available antifungal preparations and their dosages, so that minor problems can be tackled in the orthodontic office. Major problems should be identified, followed by referral to an oral medicine specialist or a physician, so that the patient's well-being and quality of life are not compromised.

Some uncommon systemic mycoses with oral lesions

An increasing number of immunocompromised patients are attending dental as well as orthodontic offices, thus a number of uncommon mycotic lesions are now being first detected by dental surgeons and orthodontists.

Aspergillosis

Aspergillosis is the second most common opportunistic mycotic infection and affects the paranasal sinuses, the nasal cavity, and oral mucosa, as well as the facial skin. It is caused by several *Aspergillus* spp., of which *A. fumigates* is the most common. It is generally contracted through inhalation of spores, leading to both upper and lower respiratory tract infection, and to bronchopulmonary aspergillosis. Oral aspergillosis lesions are yellow or black in color, with a necrotic ulcerated base, typically seen in the posterior palate or posterior tongue (Iatta et al., 2009). The hyphae may penetrate the walls of small to medium-sized arteries and veins and cause infarction, thrombosis, and necrosis, leading to systemic spread (Sales, 2009). The fungal stain of the sputum should be done first to identify a patient with invasive aspergillosis. Serum biomarkers such as galactomannan and beta-D-glucan assays can also be helpful.

Treatment of suspected invasive aspergillosis should be initiated promptly, as the patient's condition can decline quickly over 1–2 weeks from onset to death. IV therapy for critically ill patients can include voriconazole (4 mg/kg, twice daily), posaconazole (300 mg, daily), micafungin (150 mg, daily), or amphotericin B (1 mg/kg, daily) for a 6–12-week course. Voriconazole is considered the first-line treatment. While amphotericin is seen as effective, it is deemed a second-line agent due to its adverse effect profile (Samaranayake et al., 2009; Fosses Vuong and Waymack, 2022).

Cryptococcosis

Cryptococcosis is a chronic fungal disease involving the lungs, the central nervous system, and occasionally the skin and the mouth. The causative agent is *Cryptococcus neoformans* (Swe Han et al., 2009). The disease is usually a pulmonary infection, but oral lesions occur in the disseminated form. Oral lesions range from violaceous nodules of granulation tissue or swellings to ulcers, and are usually seen in the gingiva, hard and soft palate, pharynx, oral mucosa, and tooth sockets after extraction (Iatta et al., 2009). Diagnosis is confirmed by microscopy, and nonimmunosuppressed patients suspected of having a pulmonary cryptococcal infection with mild to moderate symptoms can be treated with fluconazole at a dose of 400 mg daily for 6–12 months (Samaranayake et al., 2009).

Blastomycosis

Blastomycosis, caused by *Blastomycosis dermatitidis*, is a relatively uncommon male-predominant disease, presenting as pulmonary, disseminated, or localized cutaneous lesions. The disease is initiated on inhalation of the spores, and the clinical and histopathological findings are similar to those of squamous cell carcinoma. Oral blastomycosis is uncommon, but when present it is seen as single or multiple ulcerations, sessile projections, and granulomatous or verrucous lesions (Kruse et al., 2010). Diagnosis is based on biopsy, smear, and culture (Samaranayake et al., 2009).

Itraconazole is the treatment of choice for all forms of the disease, except in severe, life-threatening cases. It is recommended that 600 mg be given orally daily for three days, followed by 200–400 mg per day for 6–12 months. Other azoles, including ketoconazole and fluconazole, can be used, but are not preferred due to lower efficacy and, in the case of ketoconazole, a worse side effect profile. Voriconazole has good cerebrospinal fluid penetration and thus plays a role in central nervous system disease (Miceli and Krishnamurthy, 2022).

Mucormycosis

Mucormycosis, caused by the saprophytic fungus *Mucorales*, is often found in the nasal cavity of healthy individuals. Infection arises through inhalation of spores that are deposited in the pulmonary alveoli and spreads to different locations, such as the paranasal, rhino-orbital, rhino-cerebral, cerebral, pulmonary, and gastrointestinal areas. The fungi erode the arteries, resulting in thrombosis and subsequent necrosis of surrounding tissues. Auluck (2007) described maxillary erosion (which is rare due to high vascularity) by mucormycosis in a patient with uncontrolled diabetes, outlining its severity. Six cases with mucormycosis affecting the periodontal ligament have been described in the literature (McDermott et al., 2010). Oral ulcerations, sinusitis, and facial cellulitis are common with mucormycosis, along with blood-tinged nasal discharge and unilateral facial pain or numbness (Tabachnick and Levine, 1975). Radiological imaging studies are required to investigate areas with suspected mucormycosis, specifically in the brain, paranasal sinuses, lungs, and abdomen, always guided by the clinic. The first intervention in the suspicion of rhino-cerebral mucormycosis is with the endoscopic evaluation and biopsy of the sinuses to examine for tissue necrosis and to obtain examples of tissue; the presence of the characteristic hyphae provides a presumptive diagnosis. The area of highest yield, and greatest accuracy, is to biopsy the middle turbinate. A CT scan can help evaluate contiguous structures such as the eyes and brain; findings on CT scan include soft tissue edema of cavity mucosa, sinus mucoperiosteal thickening, bone erosions, and orbital invasions.

Amphotericin B is considered the first-line therapy for mucormycosis. The lipid formulation of amphotericin B is administered in high doses IV once a day as initial therapy. The initial starting dose is 5 mg/kg daily, with a maximum dose of 10 mg/kg. Treatment duration depends on the patient's clinical picture. Surgical debridement of infected tissue should be urgently performed to limit the further spread of infection. Aggressive surgical debridement of necrotic tissue should take place immediately. This may involve radical facial resections, partial pneumonectomy, colectomy, and so on, in accordance with the site of disease. Similar to necrotizing fasciitis, mucormycosis requires very aggressive surgical management and often carries dramatic morbidity (Samaranayake et al., 2009; Hernández and Buckley, 2022).

Histoplasmosis

Histoplasmosis, a localized or systemic fungal infection caused by *Histoplasma capsulatum*, appears when microconidiae or hyphae are inhaled into the lungs. Clinical presentation of this infection includes acute or chronic pulmonary cutaneous histoplasmosis, with or without disseminated disease. Oral lesions are mostly chronic, with nodular, indurated, or granular masses and ulceration affecting the oral mucosa, tongue, palate, gingiva, and periapical region of the teeth (Epifanio et al., 2007;

Narayana et al., 2009). Diagnosis is confirmed by microscopy, culture, and serological tests such as complement fixation, immunodiffusion, and enzyme immunoassays (Samaranayake et al., 2009). Acute pulmonary infections, with symptoms for less than four weeks, do not need treatment. If the symptoms persist beyond this period, a three-month course of itraconazole is recommended.

Paracoccidioidomycosis

Paracoccidioidomycosis is caused by *Paracoccidioides brasiliensis*, which produces a granulomatous disease, primarily affecting the lungs and then disseminating to the nasal mucosa and other organ systems. The disease is restricted to South and Central America, especially Brazil, hence the name South American blastomycosis. The source of the organism is the soil, and infection occurs through inhalation or by direct contact (Ramos-E-Silva and Saraiva, 2008). Oral manifestations are common, and the lesions usually appear as small papules and vesicles, which then ulcerate to form shallow ulcers with a rolled edge and a white exudative base studded with small hemorrhagic dots (Jham et al., 2008). In severe cases, infection may penetrate deep into the bone with perforation of the hard palate. Lesions can occur anywhere in the oral cavity, including the hard and soft palate, tongue, gingiva, and tonsils, and may lead to mobility of teeth due to periodontal infection. The face becomes readily swollen (Godoy and Reichart, 2003; Silva et al., 2007; Samaranayake et al., 2009). The diagnosis includes visualization of fungal elements suggestive of *Paracoccidioides* spp. by direct microscopy (with potassium hydroxide) and/or culture specimens, biopsy, and histopathology, as well as serological testing. Treatment is usually carried out using antifungal agents including ketoconazole, itraconazole, voriconazole, posaconazole, terbinafine, and amphotericin B. Fluconazole is not commonly used because of its lower response rate and more frequent relapses (Cordova and Torres, 2022).

Sporotrichosis

Sporotrichosis is a chronic nodular mycotic disease, the causative agent of which is *Sporotrichium schenckii*, a fungus found in soil and rotting wood. The fungi gain access through traumatic ulcerations, and usually affect the skin (Mahlberg et al., 2009). Proliferation of the organism leads to formation of a nodule or small ulcer. The nodules turn into “bumps” on the skin and after several weeks the initial lesions heal with scarring, as new nodules and new bumps develop in other areas. Oral lesions are initially erythematous, ulcerative, and suppurative, but eventually become granulomatous, vegetative, and papillomatous. These lesions are painful, with enlarged and hard regional lymph nodes, and may resemble aphthous ulcerations, lichen planus, or cutaneous leishmaniasis (Aarestrup et al., 2001). Definitive diagnosis is based on the culture, where one must demonstrate the dimorphism of the fungus. Diagnosis of cutaneous sporotrichosis can be made through direct examination of the specimen such as tissue biopsy or pus from lesions, while sputum culture aids in diagnosing pulmonary sporotrichosis.

Before the introduction of azole compounds in the 1990s, potassium iodide was the treatment of choice for sporotrichosis. Due to the adverse effects of this drug, itraconazole is now the treatment of choice. The dose varies from 100 to 200 mg/day PO for cutaneous forms, while a dose of 400 mg/day PO should be used for pulmonary

forms. For children weighing <20 kg, 5–10 mg/kg/day is recommended. Itraconazole cannot be used in patients who are pregnant; amphotericin B may be used after 12 weeks of pregnancy (Sizar and Talati, 2022).

Parasitic infections

The common parasitic infections of particular interest to dentists and orthodontists are listed in Table 10.4.

Trichomonas and *Entamoeba*

Local protozoan infections, caused by *Trichomonas tenax* and *Entamoeba gingivalis*, which may occur as harmless commensals of the oral cavity, are observed in conditions of poor oral hygiene and in people with a low standard of living. The etiological role of these organisms in oral infections is unclear, but they have been isolated from periodontal tissues of immunocompromised patients with necrotic gingivitis. This finding has led to an assumption that parasitic infections are uncommon in healthy individuals and are more frequently observed in immunocompromised individuals. Diagnosis is based on microscopic examination of tissue scrapings after Giemsa staining, or after preculture in specific media, such as Kupferberg Trichomonas broth. In addition, PCR amplification techniques can be employed. Metronidazole is the drug of choice in both *Trichomonas* and *Entamoeba* infections, with a dosage of 400 mg three times daily for 1 week. There are no vaccines for these diseases (Bergquist, 2009).

Table 10.4 Parasitic infections of interest to the dentist and orthodontist.

Adapted from Bergquist (2009).

Type of infection	Microorganisms involved	Clinical manifestation	Treatment	Comment
Local oral parasitic infection	*Entamoeba gingivalis*	Associated with aggressive periodontitis in immunocompromised patients	Metronidazole	
	Trichomonas tenax	Associated with aggressive periodontitis in immunocompromised patients	Metronidazole	
Systemic parasitic infections (leishmaniasis)	*Leishmania brasiliensis, L. mexicana* (in the mucocutaneous form)	Cutaneous, mucocutaneous, and visceral forms The mucocutaneous forms may have oral manifestations	No efficient drugs available Amphotericin B and antimonite have some effect	Transmitted by a vector (sand fly)

Leishmaniasis

Leishmaniasis, a systemic parasitic infection, is caused by *Leishmania*, a protozoan parasite that is found worldwide. Transmission relies on the sand fly, which constitutes a vector for the parasite and is part of the life cycle of *Leishmania*. Leishmaniasis has a spectrum of clinical symptoms ranging from superficial self-resolving skin patches to systemic mutilating forms resembling leprosy (Motta et al., 2007). The clinical spectrum also includes cutaneous, mucocutaneous, and visceral leishmaniasis. Cutaneous leishmaniasis, often referred to as oriental sore, is a localized skin lesion that does not spread beyond the area of inoculation. This is the least serious form of the disease (Reithinger et al., 2007). When the organism invades mucosal tissues, it is called mucocutaneous leishmaniasis, and has a predilection for oto-nasopharyngeal areas. The most common symptom is nasal irritation or stiffness due to infiltration of the parasite into the septum and inferior turbinates. Extension of this lesion can lead to granulomas in the oral, laryngeal, and pharyngeal areas, and as the disease progresses severe facial deformities develop, sometimes resulting in total loss of the nose and upper lip (Di Lella et al., 2006). The involvement of the palate, tongue, pharynx, and larynx can lead to dysphagia or dysphonia. Bacterial superinfections can occur over these areas, further complicating the problem (Bergquist, 2009). Visceral leishmaniasis is otherwise known as kala azar, in which there is hematogenous dissemination of *Leishmania* spp., which then infect macrophages in the liver, spleen, bone marrow, and lymph nodes. This condition usually develops gradually, and the patient becomes progressively weak with abdominal distension, nausea, and vomiting, followed by lymphadenopathy, petechiae, ecchymoses, and edema. The skin becomes dry and scaly, and can acquire a grayish tone, especially on the hands and face (Gupta et al., 2010).

Aspirates and biopsy specimens from the raised edges of skin lesions can be used to make a direct diagnosis. Giemsa staining will reveal amastigotes, which tend to be found in the periphery of infected host cells (Bergquist, 2009). Aspirates can be cultured in specialized media such as Novy-McNeal-Nicolle medium (Limoncu et al., 2004). Several rapid and reliable tests are available, such as the Montenegro skin test, immunochromatographic test, and molecular diagnostic tests using PCR (Bergquist, 2009).

Pentavalent antimonials, such as sodium stibogluconate (Pentostam®, GSK, Brentford, UK) and methylglucamine antimonite (Glucantime®, Sanofi, Gentilly, France), are the drugs used in treatment of leishmaniasis of all forms. A dose of 20 mg/kg/day is recommended and should be administered only under medical supervision. The second line of drugs such as pentamidine, amphotericin B, and macrolide polyenes can also be used, from which amphotericin B has the highest cure rate (Bergquist, 2009; van Griensven et al., 2010). There is no vaccine available for this disease and prevention is the only option. Use of insecticide-treated nets is a good method and is recommended as a preventive measure (Bergquist, 2009).

The oral cavity as a source for focal infections

Focal oral infections can be defined as infections occurring in different locations in the human body that are caused by microorganisms normally inhabiting the oral cavity or

their products. Dental procedures such as tooth extraction, endodontic treatment, periodontal surgery, orthodontic separator placement, or banding and debonding procedures can introduce oral microorganisms into the bloodstream and the lymphatic system. The number of bacteria in the bloodstream required to cause transient bacteremia is around 1–10 per ml of blood; this usually lasts for no more than 15–30 minutes. The bacterial spread is mainly by three routes (Gendron et al., 2000):

- Metastatic infection – caused by translocation of bacteria.
- Metastatic injury – through microbial toxins.
- Metastatic inflammation – due to immune injury.

Studies have confirmed the role of oral microorganisms in focal infections that can lead to coronary heart disease, preterm low-birthweight babies, and aspiration pneumonia (Destefano et al., 1993; Offenbacher et al., 1996; Scannapieco et al., 1998). The susceptibility of certain groups of individuals, such as older patients and the immunocompromised (HIV infected, organ transplanted), to this process is well established (Gendron et al., 2000).

Infective endocarditis

Infective endocarditis is the most common heart disease caused by oral bacterial metastasis. Congenital heart diseases, presence of valvular defects, and a previous history of congestive cardiac diseases all predispose patients to infective endocarditis when exposed to surgical dental procedures (Bascones-Martinez et al., 2009). The outcome of the disease varies from debilitation to death due to valvular malfunction, congestive cardiac failure, or renal complication. About 50% of cases are due to viridans streptococci (alpha streptococci), more particularly the polysaccharide-producing *Strep. sanguinis*, *Strep. mutans*, *Strep. oralis*, *Strep. mitis*, and *Strep. salivarius* (Douglas et al., 1993). Production of extracellular polysaccharide glucan by these bacteria favors their attachment to heart surfaces or fibrin-platelet clots. Fiehn et al. (1995) reported that bacteria colonizing in the oral cavity may invade through the bloodstream and cause infective endocarditis. It has been reported that cardiovascular complications are more frequent in patients with periodontitis, and studies have provided evidence of a close association between periodontitis and myocardial infarction, atherosclerosis or stroke, and fatal coronary artery diseases (Scannapieco et al., 2010). For a more detailed discussion of the subject and the management strategies, see Chapter 15.

Brain abscess

A focal suppurative process in the brain parenchyma can result from transient bacteremia from oral infections or dental treatment. Around 0.09–0.84 cases of brain abscess reported per million population per year can be attributed to oral infectious causes. In most cases of brain abscess from oral infections, the lesions are located in the frontal or temporal lobes, and reach the brain via direct extension or cavernous sinus thrombosis through the hematogenous or anatomical routes (Gendron et al., 2000). Syrjanen et al. (1989) found an increased prevalence of periodontitis, periapical abscess, poor oral hygiene, and carious lesions in patients with ischemic cerebral

infarction. All types of microorganisms, Gram-positive cocci, Gram-negative cocci and rods, and anaerobic bacteria have been isolated from brain abscess lesions (Schuman and Turner, 1994).

Chronic meningitis

Various oral infections, such as dental abscesses and dental caries, have been implicated in chronic meningitis. Bacteria found at these sites can contaminate the cerebrospinal fluid and reach the central nervous system. Moreover, the spread of oral infections into the tissues surrounding the oral cavity may give rise to chronic maxillary sinusitis and facial plane infections. The extreme form of infection in this regard is Ludwig angina, which involves life-threatening swelling of the posterior floor of the mouth as it can cause obstruction of the airway (Gilon et al., 2002; Jimenez et al., 2004). Oral infections have also been implicated in eye infections such as uveitis, endophthalmitis, and chronic conjunctivitis (Gendron et al., 2000).

Pneumonia

Pneumonia is infection of the pulmonary parenchyma caused by anaerobic bacteria and a dental source of the infection has been demonstrated in the form of dental plaque, associated with periodontitis (Sharma and Shamsuddin, 2011). Lung abscesses caused by *Streptococcus intermedius*, *Actinomyces* spp., and *Campylobacter rectus* have been reported to originate from oral infectious sources and dental treatment-induced bacteremia (Scannapieco and Mylotte, 1996). Dental plaque containing *Pseudomonas aeruginosa* has been implicated in the development of chronic infection of the respiratory tract in patients with cystic fibrosis. The mechanisms by which these bacteria produce respiratory infections have been described by Scannapieco (1999), who suggests that the host-derived enzymes in the saliva uncover receptors on the mucosal surface, allowing colonization by respiratory pathogens. From this site, periodontal pathogens such as *Porphyromonas gingivalis* and *A. actinomycetemcomitans* are aspirated into the lung where they initiate infections. At the same time, cytokines derived from periodontal tissues may alter the respiratory epithelium, promoting infection by respiratory pathogens.

Helicobacter pylori infection

H. pylori, which persists in dental plaque even after its eradication with triple drug therapy, may get reactivated in some instances to produce reinfection. Zaric et al. (2009) reported that 77.3% of their patients treated with combined periodontal therapy and triple therapy with antibiotics, antimicrobials, and proton pump inhibitors showed successful eradication of gastric *H. pylori* infection, in comparison with 47.6% who received only triple therapy. Oral microorganisms such as *A. actinomycetemcomitans*, *Fusobacterium nucleatum*, *Prevotella intermedia*, and *Peptostreptococcus micros* (now *Parvimonas micra*) can also cause skin infections following direct inoculation (Gendron et al., 2000). In the same way, chronic urticaria can be triggered by pathogenic oral microorganisms that favor release of histamine from mast cells, or formation of circulating immune complexes (Thyagarajan and Kamalam, 1982).

Osteomyelitis

Osteomyelitis has been reported in association with *A. actinomycetemcomitans*, *P. micros*, and *Eikenella corrdens*. In addition, fusobacteria and *C. albicans* have been implicated in some cases of osteomyelitis following dental treatment (Hudson, 1993; Navazesh and Mulligan, 1995; Gendron et al., 2000).

Preterm birth

Approximately 7% of all infants weigh less than 2500 g at birth, and these infants account for two-thirds of neonatal deaths. There are many risk factors involved in preterm birth, such as maternal smoking, alcohol abuse, drug use, and infection. Periodontal disease has also been implicated as a risk factor in this phenomenon. It had been suggested that periodontal disease provides a chronic systemic source of lipopolysaccharides, which stimulate the production of interleukin-1β and prostaglandin E2, which are closely associated with preterm delivery (Heimonen et al., 2009; Kumar and Samelson, 2009). Katz et al. (2009) isolated *P. gingivalis* colonies from the placental tissue of women delivering preterm babies. Han et al. (2004) proposed *F. nucleatum* as a cause of preterm delivery. However, further evidence is required to clarify the precise role of this microorganism.

Conclusions

Orthodontic care is available to people regardless of age, sex, and geographical location. Most orthodontic patients are healthy or have health problems that are of minor significance as far as mechanotherapeutics is concerned. However, some individuals have preexisting conditions that may endanger their well-being, and sometimes their life. Some of these diseases may be contagious and spread to other people who are otherwise healthy. The individuals at risk are the orthodontist, the orthodontic office staff, and all other patients who are being treated in the same clinic. Therefore, it is of prime importance for the orthodontist to identify patients who carry these diseases in the initial diagnosis. The most important duty of orthodontists is to protect themselves, their assistants, and all their patients from being infected by contagious diseases carried by persons who are receiving orthodontic care in the same office.

The orthodontist may be the first to diagnose a contagious disease in a patient before or during orthodontic treatment. In addition to looking for physical evidence of specific pathological conditions, many laboratory tests are available that can confirm or alter the initial diagnosis. Orthodontists may prescribe medications for the diagnosed diseases, based on their knowledge, but frequently they would benefit from seeking the advice of the patient's physician or a specialist in contagious diseases.

In addition to the external dangers associated with contagious diseases, these pathological conditions and the medications used to treat them may adversely affect the biological response to orthodontic forces. Tooth movement is facilitated by the remodeling of mineralized and nonmineralized tissues, under the control of the nervous, immune, and endocrine systems. Changes in any or all of these systems, caused by either the disease or its medications, may affect processes such as inflammation, which is a core part of the cellular and tissue response to

mechanotherapy. Little is known about these associations and their effects on the course and outcome of orthodontic treatment, but our knowledge about the nature of these diseases and the development of means to cure them effectively continues to grow, enabling the orthodontist to provide the best care, alongside protection from undesirable diseases.

References

Aarestrup, F.M., Guerra, R.O., Vieira, B.J. et al. (2001). Oral manifestation of sporotrichosis in AIDS patients. *Oral Diseases* 7: 134–136.

Aaron, S.L., and DeBlois, K.W. (2022). Acute necrotizing ulcerative gingivitis. In: *StatPearls*. Treasure Island, FL: StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK562243.

Aas, J.A., Paster, B.J., Strokes, L.N. et al. (2005). Defining the normal bacterial flora of the oral cavity. *Journal of Clinical Microbiology* 43: 5721–5732.

Adigun, R., and Singh, R. (2022). Tuberculosis. In: *StatPearls*. Treasure Island, FL: StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK441916.

AlDahash, F., AlShamali, D., AlBander, W. et al. (2020). Oral mucosal ulceration during orthodontic treatment: The perception of patients and knowledge and attitude of the orthodontic practitioners. *Journal of Family Medicine and Primary Care* 9(11): 5537.

Alvarenga-Brant, R., Costa, F.O., Mattos-Pereira, G. et al. (2023). Treatments for burning mouth syndrome: A network meta-analysis. *Journal of Dental Research* 102(2): 135–145.

Arduino, P.G., and Porter, S.R. (2008). Herpes simplex virus type 1 infection: Overview of relevant clinic-pathologic features. *Journal of Oral Pathology and Medicine* 37: 107–121.

Auluck, A. (2007). Maxillary necrosis by mucormycosis: A case report and literature review. *Medicina Oral Pathologia Oral y Cirugia Bucal* 12: E360–E364.

Axell, T., Samaranayake, L.P., Reichart, P.A. et al. (1997). A proposal for reclassification of oral candidosis. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics* 84: 111–112.

Ayoade, F., and Kumar, S. (2022). Varicella zoster. In: *StatPearls*. Treasure Island, FL: StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK448191.

Barzilai, O., Sherer, Y., Ram, M. et al. (2007). Epstein-Barr virus and cytomegalovirus in autoimmune diseases: Are they truly notorious? A preliminary report. *Annals of the New York Academy of Sciences* 1108: 567–577.

Bascones-Martinez, A., Munoz-Corcuera, M., and Meurman, J.H. (2009). Odontogenic infections in the etiology of infective endocarditis. *Cardiovascular and Hematologic Disorders Drug Targets* 9: 231–235.

Bennett, L.K., and Hinshaw, M. (2009). Heck's disease: Diagnosis and susceptibility. *Pediatric Dermatology* 26: 87–89.

Bergquist, R. (2009). Parasitic infections affecting the oral cavity. *Periodontology 2000* 49: 96–105.

Bhandari, J., Awais, M., Robbins, B.A. et al. (2021). Leprosy. In: *StatPearls*. Treasure Island, FL: StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK559307.

Birek, C. (2000). Herpes virus induced diseases: Oral manifestations and current treatment options. *Journal of California Dental Association* 28: 911–921.

Broderick, A.L., and Jonas, M.M. (2003). Hepatitis B in children. *Seminars in Liver Diseases* 23: 59–68.

Brook, I. (2008). Actinomycosis: diagnosis and management. *Southern Medical Journal* 101: 1019–1023.

Brook, I. (2009). Current management of upper respiratory tract and head and neck infections. *European Archives of Otorhinolaryngology* 266: 315–323.

Brook, I. (2010). Treatment modalities for bacterial rhinosinusitis. *Expert Opinion on Pharmacotherapy* 5: 755–769.

Brook, I., Frazier, E.H., and Thompson, D.H. (1991). Aerobic and anaerobic microbiology of acute suppurative parotitis. *Laryngoscope* 101: 170–172.

Bruce, A.J., and Rogers, R.S., 3rd (2004). Oral manifestations of sexually transmitted diseases. *Clinics in Dermatology* 22: 520–527.

Buensalido, J.A.L., and Nepomuceno, M.J. (2022). Bacterial pharyngitis. *Medscape*, November 11. https://emedicine.medscape.com/article/225243-overview.

Carneiro, T.E., Marinho, S.A., Verli, F.D. et al. (2009). Oral squamous papilloma: Clinical, histologic and immunohistochemical analysis. *Journal of Oral Science* 51: 367–372.

Cascella, M., Rajnik, M., Aleem, A. et al. (2022). Features, evaluation, and treatment of coronavirus (COVID-19). In: *StatPearls*. Treasure Island, FL: StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK554776.

Chaudhary, A.K., Singh, M., Sundaram, S. et al. (2009). Role of human papilloma virus and its detection in potentially malignant and malignant head and neck lesions: An updated review. *Head and Neck Oncology* 1: 22.

Chen, C., Zhang, Q., Yu, W. et al. (2020). Oral mucositis: An update on innate immunity and new interventional targets. *Journal of Dental Research* 99(10): 1122–1130.

Childs, W.B. (1933). The value of orthodontia as a health service. *International Journal of Orthodontia and Dentistry for Children* 19: 184–190.

Chue, P.W. (1975). Gonorrhea – its natural history, oral manifestations, diagnosis, treatment and prevention. *Journal of American Dental Association* 90: 1297–1301.

Civen, R., Chaves, S.S., Jumaan, A. et al. (2009). The incidence and clinical characteristics of herpes zoster among children and adolescents after implementation of varicella vaccination. *Pediatric Infectious Disease Journal* 28: 954–959.

Coelho, C.M., Sousa, Y.T., and Dare, A.M. (2004). Denture-related oral mucosal lesions in a Brazilian school of dentistry. *Journal of Oral Rehabilitation* 31: 135–139.

Cordova, L.A., and Torres, J. (2022). Paracoccidioidomycosis. In: *StatPearls*. Treasure Island, FL: StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK563188.

D'Agostino, J. (2010). Pediatric airway nightmares. *Emergency Medicine Clinics of North America* 28: 119–126.

Dahlén, G. (2009). Bacterial infections of the oral mucosa. *Periodontology 2000* 49: 13–38.

Dahlén, G., Blomquist, S., and Carlen, A. (2009). A retrospective study on the microbiology in patients with oral complaints and oral mucosal lesions. *Oral Diseases* 15: 265–272.

Destefano, F., Anda, R.F., Kahn, S. et al. (1993). Dental disease and risk of coronary heart disease and mortality. *British Medical Journal* 306: 688–691.

Dhariwal, S.K., Cubie, H.A., and Southam, J.C. (1995). Detection of human papilloma virus in oral lesions using commercially developed typing kits. *Oral Microbiology and Immunology* 10: 60–63.

Di Lella, F., Vincenti, V., Zennaro, D. et al. (2006). Mucocutaneous leishmaniasis: Report of a case with massive involvement of nasal, pharyngeal and laryngeal mucosa. *International Journal of Oral and Maxillofacial Surgery* 35: 870–872.

Douglas, C.W.I., Hearth, J., Hampton, K.K. et al. (1993). Identity of viridians streptococci isolated from cases of infective endocarditis. *Journal of Medical Microbiology* 39: 179–182.

Dufty, J., Gkranias, N., and Donos, N. (2017). Necrotising ulcerative gingivitis: A literature review. *Oral Health & Preventive Dentistry* 15(4): 321–327.

Dykewicz, M.S., and Hamilos, D.L. (2010). Rhinitis and sinusitis. *Journal of Allergy and Clinical Immunology* 125: S103–S115.

Ellner, P.D., Kiehn, T.E., Cammarata, R. et al. (1988). Rapid detection and identification of pathogenic mycobacteria by combining radiometric and nucleic acid probe methods. *Journal of Clinical Microbiology* 26: 1349–1352.

Epifanio, R.N., Brannon, R.B., and Muzyka, B.C. (2007). Disseminated histoplasmosis with oral manifestation. *Special Care in Dentistry* 27: 236–239.

Evans, M., Davies, J.K., Sundqvist, G. et al. (2002). Mechanisms involved in the resistance of *Enterococcus faecalis* to calcium hydroxide. *International Endodontic Journal* 35(3): 221–228.

Faergemann, I., and Dahlèn, G. (2009). Facial skin infections. *Periodontology 2000* 49: 194–209.

Feder, H.M. (1990). Actinomycosis manifesting as an acute painless lump of the jaw. *Paediatrics* 85: 858–863.

Fiehn, N.E., Gutschik, E., Larsen, T. et al. (1995). Identity of streptococcal blood isolates and oral isolates from two patients with infective endocarditis. *Journal of Clinical Microbiology* 33: 1399–1401.

Fischler, B. (2007). Hepatitis C virus infection. *Seminars in Fetal Neonatology and Medicine* 12: 168–173.

Flores, J., Tan, A.J., and Mehta, N. (2022). Peritonsillar abscess in emergency medicine. *Medscape*, October 13. https://emedicine.medscape.com/article/764188-overview.

Fosses Vuong, M., and Waymack, J.R. (2022). Aspergillosis. In: *StatPearls*. Treasure Island, FL: StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK482241.

Gendron, R., Grenier, D., and Maheu-Robert, L.F. (2000). The oral cavity as a reservoir of bacterial pathogens for focal infections. *Microbes and Infection* 2: 897–906.

Ghosh, S., Gadda, R.B., Vengal, M. et al. (2009). Orofacial aspects of leprosy: Report of two cases with literature review. *Medicina Oral Patologia Oral y Cirugia Bucal* 15: e459–e462.

Gilden, D., Cohrs, R.J., Mahalingam, R. et al. (2010). Neurological disease produced by varicella zoster virus reactivation without rash. *Current Topics in Microbiology and Immunology* 342: 243–253.

Gilon, Y., Brandt, L., Lahaye, T. et al. (2002). Systemic infections of dental origin. *Reveue de Stomatologie et de Chirurgie Maxilla-Faciale* 103: 26–29.

Godoy, H., and Reichart, P.A. (2003). Oral manifestations of paracoccidiodomycosis: Report of 21 cases from Argentina. *Mycoses* 46: 412–417.

Gohean, R.J., Pantera, E.A., and Schuster, S.G. (1990). Indirect immunofluorescence microscopy for the identification of Actinomyces sp. in endodontic disease. *Journal of Endodontics* 16: 318–322.

Gonzalez, X., Correnti, M., Rivera, H. et al. (2010). Epstein Barr virus detection and latent membrane protein 1 in oral hairy leukoplakia in HIV+ Venezuelan patients. *Medicina Oral Pathologia Oral y Virugia Bucal* 15: e297–e302.

Greenberg, M.S. (1996). Herpesvirus infections. *Dental Clinics of North America* 40: 359–368.

Guerra, A.M., Orille, E., and Waseem, M. (2022). Hand foot and mouth disease. In: *StatPearls*. Treasure Island, FL: StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK431082.

Guerra, A.M., and Waseem, M. (2021). Epiglottitis. In: *StatPearls*. Treasure Island, FL: StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK430960.

Guinta, J.L., and Fiumara, N.J. (1986). Facts about gonorrhoea and dentistry. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics* 62: 529–531.

Gupta, G., and McDowell, R.H. (2022). Peritonsillar abscess. In: *StatPearls*. Treasure Island, FL: StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK519520.

Gupta, M., and Shorman, M. (2022). Cytomegalovirus. In: *StatPearls*. Treasure Island, FL: StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK459185.

Gupta, S., Pal, A., and Vyas, S.P. (2010). Drug delivery strategies for therapy of visceral leishmaniasis. *Expert Opinion on Drug Delivery* 7: 371–402.

Hale, R.G., and Tucker, D.I. (2008). Head and neck manifestations of tuberculosis. *Oral and Maxillofacial Surgery Clinics of North America* 20: 635–642.

Halkai, R., Hegde, M.N., and Halkai, K. (2014). Evaluation of the presence of Enterococcus faecalis in root cementum: A confocal laser scanning microscope analysis. *Journal of Conservative Dentistry*, 17(2): 119.

Han, Y.W., Redline, R.W., Li, M. et al. (2004). Fusobacterium nucleatum induces premature and term stillbirths in pregnant mice: Implication of oral bacteria in preterm birth. *Infection and Immunity* 72: 2272–2279.

Heimonen, A., Janket, S.J., Kaaja, R. et al. (2009). Oral inflammatory burden and preterm birth. *Journal of Periodontology* 80: 884–891.

Helovuo, H., Hakkarainen, K., and Paunio, K. (1993). Changes in the prevalence of subgingival enteric rods, staphylococci and yeasts after treatment with penicillin and erythromycin. *Oral Microbiology and Immunology* 8: 75–79.

Hernández, J.L., and Buckley, C.J. (2022). Mucormycosis. In: *StatPearls*. Treasure Island, FL: StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK544364.

Hoelzer, D. (2009). Update on Burkitt lymphoma and leukemia. *Clinical Advances in Hematology and Neurology* 7: 728–729.

Hoover, K., and Higginbotham, K. (2022). Epstein Barr virus. In: *StatPearls*. Treasure Island, FL: StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK559285.

Horning, G.M., and Cohen, M.E. (1995). Necrotizing ulcerative gingivitis, periodontitis and stomatitis: Clinical staging and predisposing factors. *Journal of Periodontology* 66: 990–998.

Hudson, J.W. (1993). Osteomyelitis of jaws: A 50 year perspective. *Journal of Oral and Maxillofacial Surgery* 51: 1294–1301.

Hviid, A., Rubin, S., and Muhlemann, K. (2008). *Mumps. Lancet* 371: 932–944.

Iatta, R., Napoli, C., Borghi, E. et al. (2009). Rare mycoses of the oral cavity: A literature epidemiologic review. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics* 108: 647–655.

Jenkins, I.A., and Saunders, M. (2009). *Infections of the airway. Paediatric Anesthesia* 19: 118–130.

Jham, B.C., Fernandes, A.M., Duraes, G.V. et al. (2008). The importance of intraoral examination in the differential diagnosis of paracoccidioidomycosis. *Brazilian Journal of Otorhinolaryngology* 74: 946.

Jimenez, Y., Bagan, J.V., Murillo, J. et al. (2004). Odontogenic infections, complications, systemic manifestations. *Medicina Oral Patologia Oral y Cirugia Bucal* 9: 139–147.

Kakisi, O.K., Kechagia, A.S., Kakisis, I.K. et al. (2010). Tuberculosis of the oral cavity: A systematic review. *European Journal of Oral Sciences* 118: 103–109.

Karkos, P.D., Asrani, S., Karkos, C.D. et al. (2009). Lemierre's syndrome. A systematic review. *Laryngoscope* 119: 1552–1559.

Katz, J., Chengini, N., Shiverick, K.T. et al. (2009). Localization of P. gingivalis in preterm delivery placenta. *Journal of Dental Research* 88: 575–578.

Klug, T.E., Rusan, M., Fuursted, K. et al. (2009). Fusobacterium necrophorum: Most prevalent pathogen in peritonsillar abscess in Denmark. *Clinical Infectious Diseases* 49: 1467–1472.

Kononen, E. (2000). Development of oral bacterial flora in young children. *Annals of Medicine* 32: 107–112.

Krawiec, C., and Hinson, J.W. (2022). Rubeola (measles). In: *StatPearls*. Treasure Island, FL: StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK557716.

Kruse, A.L., Zwahlen, R.A., Bredell, M.G. et al. (2010). Primary blastomycosis of oral cavity. *Journal of Craniofacial Surgery* 21: 121–123.

Kui, L.L., Xiu, H.Z., and Ning, L.Y. (2003). Condyloma acuminatum and human papilloma virus infection in the oral mucosa of children. *Pediatric Dentistry* 25: 149–153.

Kumar, J., and Samelson, R. (2009). Oral health care during pregnancy – recommendations for oral health professionals. *New York State Dental Journal* 75: 29–33.

Kushner, D., and Caldwell, B.D. (1996). Hand-foot and mouth disease. *Journal of American Pediatric Medical Association* 86: 257–259.

Laskaris, G. (1996). Oral manifestations of infectious diseases. *Dental Clinics of North America* 40: 395–423.

Lauritano, D., Moreo, G., Oberti, L. et al. (2020). Oral manifestations in HIV-positive children: A systematic review. *Pathogens* 9(2): 88.

Leao, J.C., Ribeiro, C.M., Carvalho, A.A. et al. (2009). Oral complications of HIV disease. *Clinics* 64: 459–470.

Limoncu, M.E., Ozbilgin, A., Balcioglu, I.C. et al. (2004). Evaluation of three new culture media for cultivation and isolation of Leishmania parasites. *Journal of Basic Microbiology* 44: 197–202.

Little, J.W. (2005). Syphilis: An update. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics* 100: 3–9.

Lopez-Jornet, P., Camacho-Alonso, F., Andujar-Mateos, P. et al. (2010) Burning mouth syndrome: An update. *Medicina Oral Patologia Oral y Cirugia Bucal* 15: e562–e568.

Lucchese, A., and Bondemark, L. (2021). The influence of orthodontic treatment on oral microbiology. In: V. Krishnan, A.M. Kuijpers-Jagtman, and Z. Davidovitch (eds.), *Biological Mechanisms of Tooth Movement*, 2nd ed. Chichester: Wiley, pp. 139–158.

Mahlberg, M.J., Patel, R., Rosenman, K. et al. (2009). Fixed cutaneous sporotrichosis. *Dermatology Online Journal* 15: 8.

McCullough, M.J., Abdel-Hafeth, S., and Scully, C. (2007). Recurrent aphthous stomatitis revisited: Clinical features, associations and new association with infant feeding practices? *Journal of Oral Pathology and Medicine* 36: 615–620.

McCullough, M.J., and Savage, N.W. (2005a). Oral candidosis and therapeutic use of antifungal agents in dentistry. *Australian Dental Journal* 50: S36–S39.

McCullough, M.J., and Savage, N.W. (2005b). Oral viral infections and the therapeutic use of antiviral agents in dentistry. *Australian Dental Journal* 50: s31–s35.

McDermott, N.E., Barrett, J., Hipp, J. et al. (2010). Successful treatment of periodontal mucormycosis: Report of a case and literature review. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics* 109: e64–e69.

Meltzer, E.O., Hamilos, D.L., Hadley, J.A. et al. (2004). Rhinosinusitis: Establishing definitions for clinical research and patient care. *Journal of Allergy and Clinical Immunology* 114: 155–212.

Mendoza, N., Diamantis, M., Arora, A. et al. (2008). Mucocutaneous manifestations of Epstein-barr virus infection. *American Journal of Clinical Dermatology* 9: 295–305.

Miceli, A., and Krishnamurthy, K. (2022). Blastomycosis. In: *StatPearls*. Treasure Island, FL: StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK441987.

Miller, C.S. (1996). Viral infections in the immunocompromised patient. *Dermatologic Clinics* 14: 225–241.

Moore, H.N. (1939). Changing concepts in diagnosis. *American Journal of Orthodontics and Oral Surgery* 25: 875–882.

Motta, A.C.F., Lopes, M.A., Ito, F.A. et al. (2007). Oral leishmaniasis: A clinicopathological study of 11 diseases. *Oral Diseases* 13: 335–340.

Motta-Silva, A.C., Aleva, N.A., Chavasco, J.K. et al. (2010). Erythematous oral candidiasis in patients with controlled type II diabetes mellitus and complete dentures. *Mycopathologia* 169: 215–223.

Murayama, Y., Kurihara, H., Nagai, A. et al. (1994). Acute necrotizing ulcerative gingivitis: Risk factors involving host defence mechanisms. *Periodontology 2000* 6: 116–124.

Narayana, N., Gifford, R., Giannini, P. et al. (2009). Oral histoplasmosis: An unusual presentation. *Head and Neck* 31: 274–277.

Navazesh, M., and Mulligan, R. (1995). Systemic dissemination as a result of oral infection in individuals 50 years of age and older. *Special Care Dentist* 15: 11–19.

NIH Office of AIDS Research (2021). Guidelines for the use of antiretroviral agents in adults and adolescents with HIV. https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/whats-new-guidelines.

Noorizan, Y., Chew, Y.K., Khir, A. et al. (2009). Parotid abscess: An unusual case of facial nerve palsy. *Medical Journal of Malaysia* 64: 172–173.

Offenbacher, S., Katz, V., Fertik, G. et al. (1996). Periodontal disease as a possible risk factor for preterm low birth weight. *Journal of Periodontology* 67: 1103–1113.

Ørstavik, D., and Haapasalo, M. (1990). Disinfection by endodontic irrigants and dressings of experimentally infected dentinal tubules. *Dental Traumatology* 6(4): 142–149.

Ortega, K.L., Ceballos-Salobrena, A., Gaitan-Cepeda, L.A. et al. (2008). Oral manifestations after immune reconstitution in HIV patients on HAART. *International Journal of STD and AIDS* 19: 305–308.

Pajukoski, M., Meurman, J.H., Halonen, P. et al. (2001). Prevalence of subjective dry mouth and burning mouth in hospitalized elderly patients and outpatients in relation to saliva, medication and systemic diseases. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics* 92: 641–649.

Persson, A., Bergstrom, T., Lindh, M. et al. (2009). Varicella zoster virus CNS disease – viral load, clinical manifestations and sequels. *Journal of Clinical Virology* 46: 249–253.

Peterson, L.R., and Thomson, R.B. (1999). Use of clinical microbiology laboratory for the diagnosis of infectious diseases related to the oral cavity. *Infectious Disease Clinics of North America* 13: 775–795.

Phalen, J.A., Jimenez, V., and Tompkins, D.C. (1996). Tuberculosis. *Dental Clinics of North America* 40: 327–341.

Pleming, W., Barco, S., Voci, D. et al. (2022). Cardiac and cerebral arterial complications of Lemierre syndrome: Results from a systematic review and individual patient data meta-analysis. *Hamostaseologie* 42(4): 261–267.

Raad, I.L., Sabbagh, M.F., and Caranasos, G.J. (1990). Acute bacterial sialadenitis: A study of 29 cases and review. *Reviews of Infectious Diseases* 12: 591–602.

Ramos-E-Silva, M., and Saraiva, L. do E.S. (2008). Paracoccidioidomycosis. *Dermatologic Clinics* 26: 257–269.

Reichart, P.A. (2003). Oral manifestation in HIV infection: Fungal and bacterial infections, Kaposi's sarcoma. *Medical Microbiology and Immunology* 192: 165–169.

Reithinger, R., Dujardin, J.C., Louzir, H. et al. (2007). Cutaneous leishmaniasis. *Lancet Infectious Diseases* 7: 581–596.

Ridgeway, J.M., Parikh, D.A., Wright, R. et al. (2010). Lemierre syndrome: A pediatric case series and review of literature. *American Journal of Otolaryngology* 31: 38–45.

Ristevska, I., Armata, R.S., D'Ambrosio, C. et al. (2015). Xerostomia: Understanding the diagnosis and the treatment of dry mouth. *Journal of Family Medicine and Disease Prevention* 1(8): 1–5.

Rivera-Hidalgo, F., and Stanford, T.W. (1999). Oral mucosal lesions caused by infective microorganisms I. *Viruses and bacteria*. *Periodontology 2000* 21: 106–124.

Rosenwasser, L. (2007). New insights into the pathophysiology of allergic rhinitis. *Allergy and Asthma Proceedings* 28: 10–15.

Sahin, S., Saygun, I., Kubar, A. et al. (2009). Periodontitis lesions are the main source of salivary cytomegalovirus. *Oral Microbiology and Immunology* 24: 340–342.

Saleh, D., Yarrarapu, S.N.S., and Sharma, S. (2022). Herpes simplex type 1. In: *StatPearls*. Treasure Island, FL: StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK482197.

Sales, M. da P.U. (2009). Chapter 5—Aspergillosis: From diagnosis to treatment. *Journal Brasiliero de Pnemologia* 35: 1238–1244.

Sällberg, M. (2009). Oral viral infections of children. *Periodontology 2000* 49: 87–95.

Samaranayake, L.P., Keung Leung, W., and Jin, L. (2009). Oral mucosal fungal infections. *Periodontology 2000* 49: 39–49.

Scala, A., Checchi, L., Montevecchi, M. et al. (2003). Update on burning mouth syndrome: Overview and patient management. *Critical Reviews in Oral Biology and Medicine* 14: 275–291.

Scannapieco, F.A. (1999). Role of oral bacteria in respiratory infection. *Journal of Periodontology* 70: 793–802.

Scannapieco, F.A., Dasanayake, A.P., and Chhun, N. (2010). Does periodontal therapy reduce the risk of systemic diseases? *Dental Clinics of North America* 54: 163–181.

Scannapieco, F.A., and Mylotte, J.M. (1996). Relationships between periodontal disease and bacterial pneumonia. *Journal of Periodontology* 67: 1114–1122.

Scannapieco, F.A., Papandonatos, G.D., and Dunford, R.G. (1998). Associations between oral conditions and respiratory disease in a national sample survey population. *Annals of Periodontology* 3: 251–256.

Schuman, N.J., and Turner, J.E. (1994). Brain abscess and dentistry: A review of literature. *Quintessence International* 25: 411–413.

Scott, D.A., Coulter, W.A., Biagioni, P.A. et al. (1997). Detection of herpes simplex virus type I shedding in the oral cavity by polymerase chain reaction and enzyme linked immunosorbant assay at the prodromal stage of recrudescent herpes labialis. *Journal of Oral Pathology and Medicine* 26: 305–309.

Scully, C., Epstein, J., and Sonis, S. (2003). Oral mucositis: A challenging complication of radiotherapy, chemotherapy and radiochemotherapy: Part I: Pathogenesis and prophylaxis of mucositis. *Head and Neck* 25: 1057–1070.

Seigel, M.A. (1996). Syphilis and gonorrhoea. *Dental Clinics of North America* 40: 369–383.

Sharma, N., and Shamsuddin, H. (2011). Association between respiratory disease in hospitalized patients and periodontal disease: A cross-sectional study. *Journal of Periodontology* 82(8): 1155–1160.

Sharma, S., Hashmi, M.F., and Valentino, D.J., III (2022). Actinomycosis. In: *StatPearls*. Treasure Island, FL: StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK482151.

Ship, J.A., Chavez, E.M., Doerr, P.A. et al. (2000). Recurrent aphthous stomatitis. *Quintessence International* 31: 95–112.

Silva, C.O., Almeida, A.S., Pereira, A.A. et al. (2007). Gingival involvement in oral paracoccidiodomycosis. *Journal of Periodontology* 78: 1229–1234.

Sitheeque, M.A., and Samaranayake, L.P. (2003). Chronic hyperplastic candidosis/candidiasis (candidal leukoplakia). *Critical Reviews in Oral Biology and Medicine* 14: 253–267.

Sizar, O., and Talati, R. (2022). Sporotrichosis. In: *StatPearls*. Treasure Island, FL: StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK532255.

Slots, J. (2009). Oral viral infections of adults. *Periodontology 2000* 49: 60–86.

Sonis, S.T. (2007). Pathobiology of oral mucositis: Novel insights and opportunities. *Journal of Supportive Oncology* 5: 3–11.

Steichen, O., and Dautheville, S. (2009). Koplik spots in early measles. *Canadian Medical Association Journal* 180: 583.

Swe Han, K.S., Bekker, A., Greeff, S. et al. (2009). Cryptococcus meningitis and skin lesions in an HIV negative child. *Journal of Clinical Pathology* 61: 1138–1139.

Sweeney, M.P., Bagg, J., Fell, G.S. et al. (1994). The relationship between micronutrient depletion and oral health in geriatrics. *Journal of Oral Pathology and Medicine* 23: 168–171.

Syrjanen, J., Peltola, J., Vatonen, V. et al. (1989). Dental infections in association with cerebral infection in young and middle aged men. *Journal of Internal Medicine* 225: 179–184.

Tabachnick, T.T., and Levine, B. (1975). Mucormycosis of the craniofacial structures. *Journal of Oral Surgery* 33: 464–469.

Taylor, M., Brizuela, M., and Raja, A. (2022). Oral candidiasis. In: *StatPearls*. Treasure Island, FL: StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK545282.

Templer, S.P., Rohner, P., and Baumgartner, A. (2008). Relation of *Enterococcus faecalis* and *Enterococcus faecium* isolates from foods and clinical specimens. *Journal of Food Protection* 71: 2100–2104.

Thyagarajan, K., and Kamalam, A. (1982). Chronic urticaria due to abscessed teeth roots. *International Journal of Dermatology* 21: 606.

Tovaru, S., Parlatescu, I., Tovaru, M. et al. (2009). Primary herpetic gingivostomatitis in children and adults. *Quintessence International* 40: 119–124.

Treister, N.S., and Woo, S.B. (2010). Topical n-docosanol for management of recurrent herpes labialis. *Expert Opinion on Pharmacotherapy* 11: 853–860.

Tudor, M.E., Al Aboud, A.M., Leslie, S.W. et al. (2022). Syphilis. In: *StatPearls*. Treasure Island, FL: StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK534780.

van Griensven, J., Balasegaram, M., Meheus, F. et al. (2010). Combination therapy for visceral leishmaniasis. *Lancet Infectious Diseases* 10: 184–194.

Van Heerden, W.F.P. (2006). Oral manifestations of viral infections. *SA Family Practice* 48: 20–24.

Wallace, D.V., Dykewicz, M.S., Bernstein, D.I. et al. (2008). Joint task force on practice: American Academy of Allergy, Asthma and Immunology. The diagnosis and management of rhinitis: An updated practice parameter. *Journal of Allergy and Clinical Immunology* 122: S1–S84.

Wang, Y.P., Chen, H.M., Kuo, R.C. et al. (2009). Oral verrucous hyperplasia: Histologic classification, prognosis and clinical implications. *Journal of Oral Pathology and Medicine* 38: 651–656.

Weg, J.G. (1976). Diagnostic standards of tuberculosis – revised. *Journal of the American Medical Association* 235: 1329–1330.

Weinberger, B.W. (1938). Medical problems relating to orthodontia. *American Journal of Orthodontics and Oral Surgery* 24: 213–234.

Wilson, S.S., Fakioglu, E., and Herold, B.C. (2009). Novel approaches in fighting herpes simplex virus infections. *Expert Review of Anti-Infective Therapy* 7: 559–568.

Woo, S.B., and Sonis, S.T. (1996)., Recurrent aphthous ulcers; a review of diagnosis and treatment. *Journal of American Dental Association* 127: 1202–1213.

Wu, I.B., and Schwartz, R.A. (2007). Herpetic whitlow. *Cutis* 79: 193–196.

Zaric, S., Bojic, B., Jankovic, L.J. et al. (2009). Periodontal therapy improves gastric helicobacter pylori eradication. *Journal of Dental Research* 88: 946–950.

Zhang, X., Reichart, P.A., and Song, Y. (2009). Oral manifestations of HIV/AIDS in China: A review. *Oral and Maxillofacial Surgery* 13: 63–68.

11
Unveiling and Managing Upper Airway Problems in the Orthodontic Patient

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Summary

Snoring and obstructive sleep apnea (OSA) are the most common types of sleep-disordered breathing (SDB). The patient with SDB presents clinical heterogeneity with complex multifactorial etiologies that demand different solutions at different ages. A synergistic blend of dentistry, medicine, and surgery in managing the compromised and collapsible upper airway has evolved over the past century, initiated by a French dentist, Pierre Robin. The ongoing challenge is collaborative interdisciplinary diagnostics to identify the sleep phenotype for the right treatment at the right time. Understanding the different sleep phenotypes paves the way for precision health strategies in optimizing and improving treatment modalities. The current gold standard in treatment is continuous positive airway pressure (CPAP) therapy, with good outcomes in both young and old patients with OSA. However, compliance with long-term CPAP therapy to manage upper airway issues can be challenging. Dentofacial orthopedic treatment options for maxillary expansion and/or protraction and mandibular growth in growing children are upstream treatment for prevention, and can be considered as adjunctive therapy in the management of blocked noses and hyperplastic adenotonsillar lymphoid tissues. Alternative therapies for adults include mandibular advancement devices, tongue stabilizing devices, upper airway soft tissue surgery, hypoglossal nerve stimulation, and maxillomandibular advancement surgery. The orthodontist should always identify preexisting SDB in patients with narrow upper airway space before embarking on orthodontic or orthognathic treatment. Interdisciplinary collaborative treatment planning and management are necessary to ensure upper airway patency.

Obstructive sleep apnea (OSA) occurs when there is limitation of upper respiratory airflow due to partial or complete upper airway obstructions despite persistent respiratory effort. With reduced airflow, gaseous exchange is impaired and sleep is fragmented from recurrent arousals (Carberry et al., 2016). The afflicted individual is

usually unaware of the problem. Snoring and sleep apnea are often reported by bed partners who witness the patient's sleep-breathing problems, or there may be suspicion of OSA from associated medical comorbidities of long-term OSA; that is, metabolic, cardiovascular, neurological, ophthalmological, and urological disorders (Javaheri et al., 2017; Marrone and Bonsignore, 2020).

The spectrum of sleep-disordered breathing

The signs and symptoms of what we now know as the sleep-disordered breathing (SDB) spectrum were recognized centuries ago. They were described in literary works by William Shakespeare and Charles Dickens in the seventeenth and nineteenth centuries, respectively. In Shakespeare's last play, *The Tempest*, Sebastian says to Antonio as they circle the sleeping bodies, "Thou dost snore distinctly; there is meaning in thy snores" (Shakespeare, 1987: Act II Scene 1). In his first novel, the *Posthumous Papers of the Pickwick Club*, Dickens (1837) described one of his characters, Joe, as "a wonderfully fat boy – habited as a serving lad, standing upright on a mat, with his eyes closed as if in sleep." Obesity-hypoventilation or Pickwickian syndrome was named with reference to Joe in the Pickwick Papers. Patients with this syndrome present with morbid obesity, hypersomnolence, periodic respiration, intermittent cyanosis, polycythemia, and heart failure (Burwell et al., 1956).

Snoring and OSA are events in a wide-ranging SDB spectrum with variable severity and overlapping signs and symptoms that can occur in both adults and children (Schwab, 2003). There are different forms of SDB: primary or simple snoring without arousals or other symptoms is at the mildest end of the spectrum, while upper airway resistance syndrome (UARS) is more severe and associated with multiple respiratory effort-related arousals (RERAs). Sleep hypopnea syndrome is characterized by snoring with symptoms increasing in severity, but with the absence of apnea, and this is followed by mild, moderate, and severe OSA, which progressively increases in severity along the continuum (Figure 11.1).

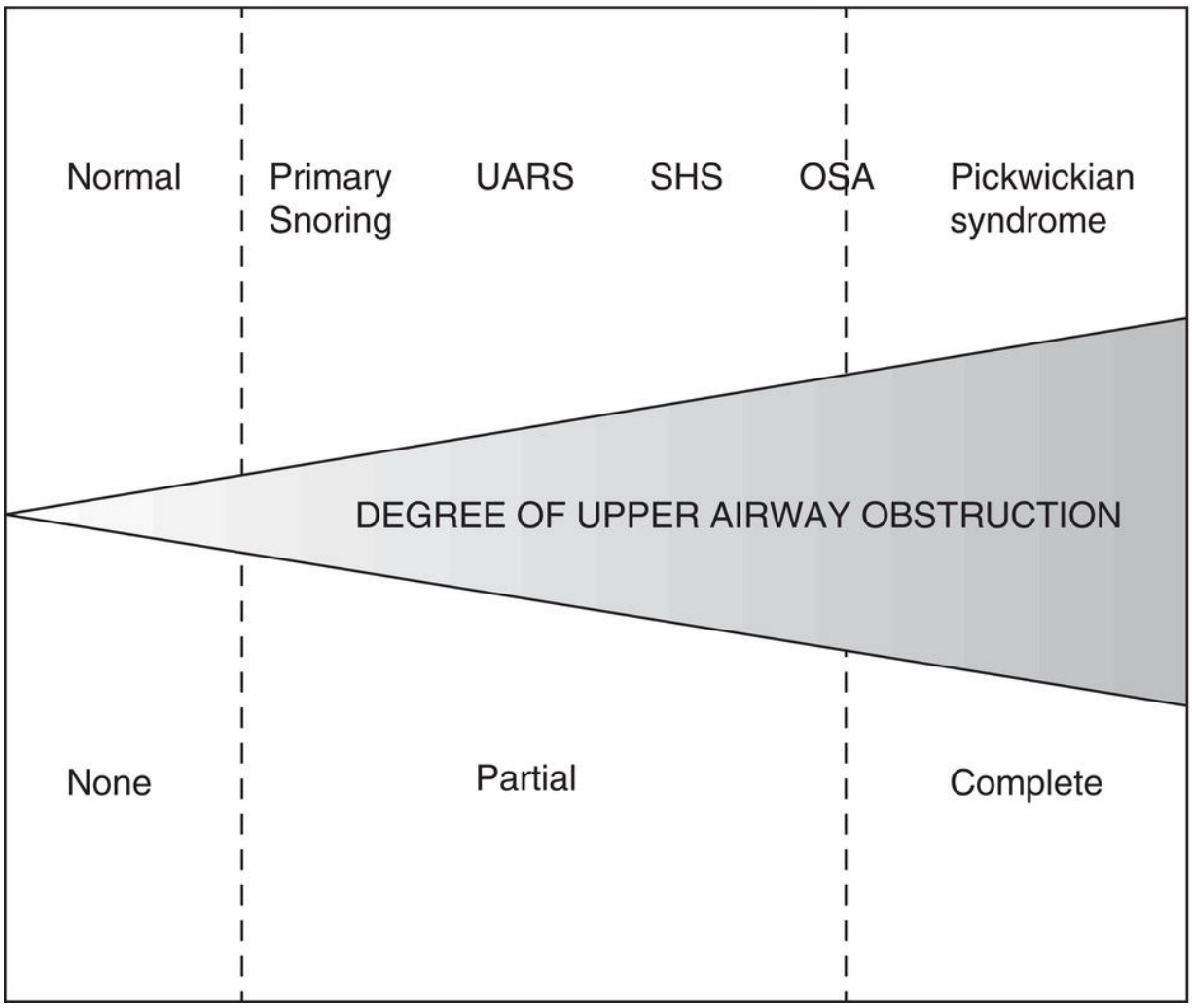


Figure 11.1 The spectrum of sleep-disordered breathing: snoring; upper airway resistance syndrome (UARS); sleep hypopnea syndrome (SHS); obstructive sleep apnea (OSA); obesity hypoventilation syndrome (Pickwickian syndrome).

Decoding obstructive sleep apnea

A thorough examination of the patient with snoring and OSA is necessary in diagnosis. Coexistence of a wide range of other medical conditions such as cranio-dentofacial anomalies, obesity, hypertension, cardiac dysfunction, chronic obstructive pulmonary disease, restrictive lung diseases, metabolic disease, muscular dystrophy, kyphoscoliosis, hypothyroidism, and pituitary tumors highlights the importance of interactive collaboration in overall management (Davila, 1995; Mathur and Douglas, 1995).

The gold standard test to confirm SDB is an attended overnight polysomnography (PSG). This is a hospital-based test that records specific physiological parameters during sleep, which enables the diagnosis of OSA and other types of sleep disorders. The total number of respiratory events in an hour is expressed as the apnea–hypopnea index (AHI). AHI is derived from the sum of apneas and hypopneas in an hour of sleep.

Adult

An adult apneic event is defined as complete cessation of airflow, for 10 seconds or more, despite persistent respiratory effort. Hypopnea occurs when airflow reduces, by 30% or more, in a partially obstructed airway. Each episode of reduced airflow is significant if it lasts for at least 10 seconds with an arterial oxygen desaturation of 4% or more; or if there is a 50% or greater reduction in airflow for at least 10 seconds associated with an arousal due to hypercapnia. The criteria of apneas and hypopneas of 10 seconds' duration are based on two lost breaths of adult normal respiration rate. Classification of mild OSA is 5–15 apnea and/or hypopnea events per hour; more than 15 and up to 30 events per hour is moderately severe OSA; and more than 30 events per hour is classified as severe OSA (Guilleminault et al., 1978; Berry et al., 2020).

Child

The polysomnographic criteria for defining pediatric OSA differ from those of adult OSA (Table 11.1). In children, the International Classification of Sleep Disorders, third edition (ICSD-3) polysomnographic criteria for diagnosis of OSA are either (i) one or more obstructive events (obstructive or mixed apnea or obstructive hypopnea) per hour of sleep; or (ii) obstructive hypoventilation, as manifest by $PaCO_2$ >50 mmHg for >25% of sleep time, together with snoring, paradoxical thoracoabdominal movement, or flattening of the nasal airway pressure waveform implying flow limitation. OSA consists of shorter apnea and hypopnea duration associated with pediatric respiration rates. An apneic event lasts for the duration of two lost breaths in children, about 6 seconds. Hypopnea in children refers to a drop in airflow by at least 30% for the duration of two

breaths and associated with an arousal or 3% desaturation of arterial oxygen. An AHI of 1–4 events per hour indicates mild OSA, 5–9 events per hour is moderately severe OSA, and 10 or more events per hour is severe OSA in children (Iber et al., 2007).

Polysomnographic values of note are the AHI and the apnea index (AI) in grading the severity of OSA. Based on positive clinical findings, even if the AHI value is low, a diagnosis of OSA with an AHI of 1 is significant in children. Clinical information is as important as AHI and AI values in determining the clinical severity and morbidity of pediatric sleep-disordered breathing (Marcus et al., 1992; Chan et al., 2004). Affected children demonstrate behavioral problems and learning difficulties, hyperactivity, inattention, aggression, and neurocognitive deficits with impact on memory, learning, and executive functions. A child who snores at least two nights per week or more is significantly at risk of negative behavioral outcomes and decline in cognitive functions. The frequency of snoring regardless of AHI scores was predictive of adverse outcomes and cognitive functions (Smith et al., 2017).

Table 11.1 Characteristics of children and adults with obstructive sleep apnea.

Parameters	Child	Adult
Peak age	2–6 years	30–60 years
Sex ratio (female: male)	1 : 1	1 : 2
Apnea–hypopnea index	≥1	≥5
Estimated prevalence		
–General population	1–3%	2–4%
–Habitual snorers	9%	10–40%
–Morbidly obese	37–55%	>50%
Body mass index (BMI)	Low: failure to thrive <3rd percentile High: >95th percentile	≥28 Asian; ≥30 Caucasian
Common causes	Adenotonsillar hypertrophy Craniofacial anomalies	Obesity Dentofacial anomalies

Research findings suggest that neurocognitive deficits are partially reversible, but there may be a residual learning deficit representing a "learning debt" (Gozal and Pope, 2001; Larkin et al., 2005). Children with AHI ≥5 have raised levels of C-reactive protein (CRP), which is known to increase the risk of cardiovascular disease. Children with OSA may also have autonomic dysfunction with increased sympathetic activity (Gozal and O'Brien, 2004). In addition, there is evidence of systemic inflammation in OSA patients (Li et al., 2008). The inflammatory mediator cysteinyl leukotriene (cys-LT) has been found in exhaled breath condensates of children and is related to the severity of SDB (Goldhart et al., 2006).

In children, OSA is complex and cannot be excluded on the basis of history and physical examination (Gottlieb and Young, 2009). A diagnosis of OSA based on history and physical examination is

inadequate (sensitivity 63% and specificity 60%). Home-based three-night pulse oximetry is a better screening tool. Test results with an oxygen desaturation index (ODI) >10 demonstrated a sensitivity of 93% and specificity of 75% for moderately severe to severe OSA (Chung et al., 2016; Galway et al., 2021). If there is high clinical suspicion, the patient should be referred to a sleep-trained pediatrician or a multidisciplinary sleep team for possible causes and confirmation of the diagnosis. Studies conducted on the predictive value of screening tools using history, clinical signs and symptoms, and overnight pulse oximetry indicated there was no foolproof method for confirming OSA (Hoffstein and Szalai, 1993). Full-night (type 1) polysomnography is still the gold standard test and is recommended for the diagnosis of OSA in both adults and children (Kushida et al., 2005).

Epidemiology

Prevalence

Snoring and OSA are common. Reported prevalence of snoring in adults ranges from 32% to 52.8%, and 16.7% to 30.6% in children from different countries (Ferreira et al., 2000; Teculescu et al., 2001). In another study, the global prevalence for adults with OSA based on data from 16 countries exceeded 50%, affecting 936 million people aged between 30 and 69 years of age. Global prevalence for those with moderate to severe OSA was 45% (Benjafield et al., 2019). In most children, primary snoring does not progress to OSA and resolves spontaneously except in about 11%. In a Caucasian group of 3–6-year-olds who were habitual snorers, 13% had OSA, whereas in an Asian population of 7-year-olds who were habitual snorers, 9% developed OSA after three years (Castronovo et al., 2003; Anuntaseree et al., 2005). Among morbidly obese children between the ages of 6 and 19 years, OSA prevalence increases to 55% (Chay et al., 2000). There is evidence linking OSA with cardiovascular and metabolic diseases, affecting not only children with OSA, but also children with primary or habitual snoring (Ali et al., 1993; Brunetti et al., 2001; Ferreira et al., 2000; Gozal and Pope, 2001; Chervin et al., 2002; Chng et al., 2004; Gottlieb et al., 2004).

Risk factors

Body mass index (BMI) is an independent factor that correlates with severe OSA. In the morbidly obese, the incidence of OSA increases by at least 12–30 times (Young et al., 1993; Kyzer and Charuzi, 1998; Resta et al., 2001). Weight gain and obesity are important factors in the development and progression of OSA in middle-aged patients. The World Health Organization (WHO) recommends cutoff points to indicate obesity at BMI ≥30 kg/m^2 for Caucasian adults and ≥28 kg/m^2 for Asian adults; Asians have a higher body fat percentage at a lower BMI (WHO Expert Consultation, 2004). Other than age, sex, and obesity, general characteristics of OSA patients are low waist–hip ratio and high serum cholesterol concentration (Tishler et al., 2003). Different physical features characterize patients with OSA (Table 11.1).

Respiration: Effect of anatomy and sleep

Effect of anatomy on respiration

The upper airway tract comprises three components: the nose, the pharynx, and the larynx. The nose, portal to the upper airway, is divided into two openings by the nasal septum; there is an alternative route should one nostril be blocked. The nasal airway is the preferred route for resting ventilation and infants are obligatory nasal breathers (Hall et al., 2000). The structures maintaining the patency of the anterior nares are the alar, procerus, compressor, and dilator naris muscles. The anterior nasal valves are responsible for much of the nasal resistance in patients with normal nasal apertures. The nose contributes up to half of the total airway resistance in the normal awake patient (Ferris et al., 1964). The lateral nasal walls contain several protuberances, the nasal turbinates, which serve two functions: creation of air turbulence to slow down airflow to prolong air contact with the highly vascularized nasal mucosa for temperature and humidity control; and production of nasal secretions with antimicrobial actions on inhaled air before it is channeled into the lungs. With increased ventilatory drives to meet physiological demands, the nasal apertures widen, and nasal mucosa

constricts to reduce airflow resistance. At an individual physiological threshold of ventilatory demand, a secondary route of oral breathing is established to bypass nasal resistance, thereby increasing the volume per breath.

Inspired air passes through the nasal airway to the pharynx via the bilateral choanae. The pharynx traverses three regions: the nasopharynx, which extends from the posterior nasal choanae to the hard palate; the oropharynx, which comprises the retropalatal and retroglossal segments – the former extends from the level of the hard palate to the caudal margin of the soft palate and tip of the uvula, and the latter from the soft palate margins to the base of the epiglottis; and the laryngopharynx, which is the segment from the base of the tongue to the larynx. Narrowing of the posterior nasal choanae occurs in patients with craniofacial abnormalities. Pharyngeal airway narrowing or collapse is common in the retropalatal and retroglossal aspects of the pharynx, with a majority of patients having more than one site of obstruction (Hudgel, 1988; Horner et al., 1989; Launois et al., 1993; Morrison et al., 1993; Suto et al., 1993; Trudo et al., 1998; Ciscar et al., 2001). Nasendoscopic studies describe the mechanics of pharyngeal airway narrowing as a function of sphincteric movement of the lateral pharyngeal walls together with backward movement of the anterior structures. Posterior pharyngeal wall movement is not implicated in airway narrowing (Weitzman et al., 1978) and the narrow parts of the pharyngeal lumen are potential choke points (Wellman et al., 2014).

The larynx connects the pharynx with the lower airway, the trachea. It is responsible for phonation as well as protection of the trachea. It is bounded superiorly by the epiglottis, inferiorly by the vocal cords, and laterally by the aryepiglottic folds. These structures work in synchrony to channel air into the anterior tract, the trachea, whereas food and liquids are directed into the posterior tract, the esophagus. The epiglottis acts as a valve to separate the trachea from the esophagus during deglutition and to maintain a patent airway during respiration. The posterior cricoarytenoid is the only abductor muscle that widens the glottic aperture during inspiration and expiration. The tongue and lingual tonsils, which stud the dorsum of the posterior third of the tongue, may hinder the function of the

epiglottis if the lingual tissues are enlarged and encroach into the posterior airway space (Suzuki and Kirchner, 1969; Wyke, 1974).

Redundant mucosa in the arytenoid–aryepiglottic region has been associated with OSA. Vocal cord abnormalities are rarely implicated in symptomatic OSA; however, bilateral vocal cord paralysis has been reported to be associated with snoring. Rarely, congenital vallecula cysts occur between the base of the tongue and the epiglottis. When cysts are present in this region or in the larynx, they are sometimes associated with airway obstruction, stridor, pyoceles, or vocal cord paralysis (Griffith et al., 1993).

Many cephalometric studies show an association between craniofacial characteristics and OSA. These include hard and soft tissue features such as reduced mandibular body length (Miles et al., 1996), posteriorly positioned maxilla, and inferiorly positioned hyoid bone (deBerry-Borowiecki et al., 1988; Bacon et al., 1990; Pracharktam et al., 1994; Lowe et al., 1995). Other distinguishing craniofacial features of OSA patients are reduced cranial base length, mandibular or maxillomandibular retrusion, increased lower face height, an elongated soft palate, a large tongue, and a smaller upper airway compared with normal individuals (Horner et al., 1989; Ciscar et al., 2001).

The oropharyngeal airway is usually narrow in individuals with OSA (Shepard and Thawley, 1989; Schwab et al., 1993, 2003). Reduced size of the posterior airway space and increased distance of the hyoid bone to the mandible are also associated with those with OSA. The two cephalometric parameters that are used as indicators of OSA are posterior airway space of <11 mm and a hyoid to mandible distance of >15.4 mm (Riley et al., 1983). Severe respiratory disturbance indices are associated with a posterior airway space of <5 mm at the base of the tongue and a distance of the hyoid bone to the lower border of the mandible of ≥24 mm (Partinen et al., 1988). There is a low probability of OSA if the airway cross-sectional area is >110 mm^2, but a high probability of severe OSA if the area measures <52 mm^2. Most constrictions are located in the oropharynx (Lowe et al., 1986; Avrahami and Englender, 1995; Ogawa et al., 2007).

There are also differences in the soft tissue characteristics of OSA patients compared with those without OSA; besides a larger tongue, OSA patients have thicker and longer soft palates and parapharyngeal fat pads in the lateral pharyngeal walls (Schwab, 2003; Schwab et al., 2003).

Effects of sleep on respiration

The diaphragm is the main driver of ventilation during sleep. Pharyngeal airway patency is well maintained during wakefulness, but during sleep pharyngeal and genioglossal muscle activity is reduced, which predisposes to sleep-dependent pharyngeal airway collapse (McNicholas, 2002; Jordan and White, 2008). Sleep adversely affects tonic and phasic skeletal muscle functions. There is evidence suggesting that in OSA, the intrinsic upper airway muscle function and central neural regulation of the upper airway dilator muscles and genioglossus may be impaired. Recurrent apnea during sleep induces intermittent hypoxia that alters respiratory muscle contraction, reducing muscle endurance with diminished pharyngeal electromyographic (EMG) responses to physiological changes (Bradford et al., 2005).

Sleep reduces the strength of muscular tone and, consequent to that, the negative pressures of inspiration may suck the tongue into the pharyngeal airway (Remmers et al., 1978). The mechanical properties of the upper airway that maintain tissue tone and stiffness to preserve airway patency are reliant on intrinsic physiological properties. In patients with OSA, there is reduced effectiveness of upper airway dilator muscle contractions and genioglossal reflex. The genioglossal negative pressure reflex declines with age, which may explain age-related onset of OSA. Current evidence suggests a biomechanical basis for OSA in patient with anatomical and sleep-positional predisposition to pharyngeal collapse (White et al., 1985; Sériès, 2002; Malhotra et al., 2004; Dempsey et al., 2010).

Mechanical influences on respiration

There are several mechanical influences on the airway diameter, causing it to be open, narrowed, or closed. These factors can be

either static or dynamic. Static factors are surface adhesive forces, neck and jaw posture, tracheal tug, gravity, and sleep position. Dynamic factors comprise upstream resistance within the nasal airway and pharynx: the Bernoulli effect and dynamic compliance (Schwab et al., 2005).

Several studies have demonstrated a smaller upper airway width in patients with OSA compared with patients without OSA. The reduction in size of the upper airway has been attributed to the enlargement of the surrounding soft tissues: fat, muscles, and lymphoid tissues in the tongue, soft palate, and lateral and parapharyngeal walls. Reduced airway diameter affects airway resistance the most, as described by Poiseuille's law: $R = 8nl/pr^4$; the resistance (R) and the length of the tube (l) are inversely related to its radius (r) and pressure (p). By halving the size of the tube, intraluminal resistance increases by 16 times (Shepard and Thawley, 1989; Schwab et al., 1993, 2003; Schwab, 2003).

Nasal obstruction has been implicated as a cause of OSA due to nasal resistance and mouth breathing. Nasal resistance, measured by posterior rhinomanometry, is reported to be higher in individuals with OSA. Nasal resistance during inspiration places the upper airway at a greater risk of collapse (Isono et al., 2004). During sleep, the genioglossal activity increases when an infant switches from oral to nasal breathing. There is evidence correlating increased genioglossal EMG activity with changes in airway resistance and carbon dioxide levels (Roberts et al., 1986).

Mouth breathing plays a role in pharyngeal airway obstruction by changed dynamics of the airway that reduces airway caliber and patency. With mouth opening, the mandible and its soft tissue attachments rotate down and back, restricting the retroglossal and hypopharyngeal airway. When the tongue is lowered, it detaches from the soft palate and becomes free moving. With gravity and poor tongue muscle tone, it falls downward and backward into the pharyngeal airway, causing partial or complete obstruction. Reduced surface adhesion forces of mucosal surfaces are also contributory to airway obstruction (Issa and Sullivan, 1984; Roberts et al., 1985).

The child with sleep-disordered breathing

The clinical morbidities associated with obstructed upper airways were first reported in medical publications more than a century ago. In 1889, Ambroise Guye described "the impairment of cerebral functions by disorders of the nose." The obstructive effect of enlarged adenoid masses, particularly during sleep, was observed to produce "aprosexia" – the inability to fix the attention on any abstract subject. With removal of the adenoid mass from the nasopharynx, headaches ceased and learning difficulties were prevented (Guye, 1889).

This observation was confirmed soon after by William Hill (1889), who was "much struck by the fact that operations on children, undertaken for the relief of deafness associated with adenoid growths, enlarged tonsils, and hypertrophic catarrhal conditions of the nose, have frequently resulted in such an immediate improvement in the mental acuteness of the patients as was altogether incommensurate with the often, immediate improvement in the sense of hearing." He advised that the "stupid looking lazy child who frequently suffers from headache at school, breathes through his mouth instead of his nose, snores and is restless at night, and wakes up with a dry mouth in the morning, is well worthy of the solicitous attention of the medical officer."

Similar to Hill's and Guye's observations and advice, the current evidence-based management calls for screening of children for snoring and recommendation of adenotonsillectomy in children diagnosed with OSA (Marcus et al., 2012; Venekamp et al., 2015).

History, physical examination, and diagnosis

All children should be screened for snoring as part of well-child visits to identify at-risk children who will benefit from a thorough evaluation and confirmation of OSA by sleep-trained physicians (Marcus et al, 2012). A child with a mild form of SDB without diagnosis and treatment could progress to a more severe condition in over two years (Li et al., 2010). Habitual snoring of more than two nights per week warrants evaluation (Marcus et al., 2012; Smith et al., 2017). Early detection leads to prevention-driven management of

chronic comorbidities and poor quality of life associated with established SDB (Guilleminault et al., 2019; Tan et al., 2020).

Habitual snoring, if present, should prompt for a more detailed history of other signs and symptoms. Symptoms are commonly classified into night symptoms and daytime symptoms. Night symptoms include unusual sleeping postures, restless sleep, labored sleep breathing, and observed apneas. Daytime symptoms include unrefreshed sleep, morning headaches, hyperactivity, attention deficit, learning difficulties, and behavioral problems. Hyperactivity is more likely to be present in the child with OSA than is excessive daytime sleepiness; the latter occurs more often in adults with OSA (Leach et al., 1992; Carroll, 1996). Selective screening of high-risk children with craniofacial syndromes and craniofacial synostosis is effective in picking up children with OSA, particularly in those with complex craniosynostosis and fusion of at least two cranial sutures. Snoring is common in 77% of children with craniofacial syndromes and there is a 40% chance of developing OSA (Bannink et al., 2010). In a study of children with Apert, Crouzon, Muenke, Pfeiffer, and Saethre–Chotzen craniosynostotic syndromes, the critical clinical question that identified children with OSA was “Has the child difficulty with breathing during sleep?” A negative response excluded clinically significant OSA (high negative predictive value of 91% and sensitivity of 64%). Many pediatric sleep questionnaires have been developed to screen children for the presence of SDB, though none of them is widely accepted. An approach to screening children for SDB is the use of a simple instrument, a five-item BEARS questionnaire (Tan et al., 2020). The questionnaire increases the likelihood of identifying sleep problems among preschoolers, school-aged children, and adolescents in a primary care setting.

A good physical examination and identifying sites of airway obstruction form the basis for diagnosis and effective treatment of pediatric SDB. It is important to start with a general examination of the child presenting with SDB symptoms. The risks of OSA are higher in children with a family history of SDB, cranio/dentofacial structural anomalies, prematurity, neuromuscular disorders, Down syndrome, cleft lip and palate after pharyngoplasty, morbid obesity, asthma, and atopic disease (Brouillette et al., 1982; Mallory et al., 1989; Marcus et al., 1991; Silvestri et al., 1993; Guilleminault et al.,

1995; Chng et al., 2004; Savini et al., 2019). There is a positive correlation between OSA and children with obesity and without adenotonsillar hypertrophy (Verhulst et al., 2008). Obesity in a child is defined as having a BMI that is above the 95th percentile in their age and sex cohort. It is a primary independent factor in increased respiratory disturbance index (RDI) in children. Children with BMI ≥180% of ideal body weight are deemed to be morbidly obese, and between 37% and 55% of such children have OSA (Brooks et al., 1998; Chay et al., 2000; Mei et al., 2002). Besides the body habitus of the child, a note should be made about the presence of retrognathia or micrognathia and craniofacial abnormalities like midface hypoplasia, narrow nasal aperture, and open mouth posture.

Adenotonsillar hypertrophy reduces pharyngeal airway caliber and it is the most common finding in otherwise well children with SDB. The adenoid size may be examined via the use of flexible nasendoscopy or lateral cephalometry. The region of greatest pharyngeal airway narrowing is the area where the adenoid and tonsil masses overlap (Arens et al., 2003). The Brodsky grading of enlarged adenoids and tonsils (Brodsky, 1989) is reliable and easy, with good interrater agreement (ICC 0.721 and Cronbach alpha 0.911; Kumar et al., 2014). The Scammon growth curves demonstrate accelerated growth of the lymphoid tissue from birth, reaching its maximum at 11–13 years. Total body lymphoid tissue of a 13-year-old may attain a mass of almost 200% greater than that of an adult. Craniofacial skeletal growth follows a different timing and growth trajectory from lymphoid tissue growth; the latter tails off between 14 and 20 years of age, while the cranial vault and upper face follow the neural pattern of growth, which peaks between 8 and 12 years of age, with growth ceasing between 12 and 16 years of age. Growth of the lower face and mandible follows the general adolescent growth spurt that peak between 14 and 18 years and slows down or stops after 20 years of age (Scammon, 1930). As a result, the skeletal "container" may be too small to accommodate enlarged lymphoid tissues due to mismatched timing of skeletal and soft tissue growth.

Another common area of airway obstruction is the nose. Examination of the nose is important to identify structural abnormalities such as the presence of a deviated nasal septum and inferior turbinate hypertrophy, often resulting from a history of

allergic rhinitis. When the nose is obstructed, the secondary respiratory route or mouth breathing takes over, with postural and functional changes of the lip, tongue, and bucco-facial musculature. Some children with mouth breathing from an obstructed nasal and/or nasopharyngeal airway develop specific dentofacial characteristics: long narrow face or “adenoid facies,” increased anterior lower face height, downward and backward rotation of the mandible, high-vaulted narrow palate, lowered tongue posture, incompetent lips, excessive upper gingival show, anterior open bite with retrognathic mandible and/or retrognathic maxilla, and forward head posture (Guilleminault et al., 2016; Brożek-Mądry et al., 2021). Research findings attribute the bidirectional ramifications of dentofacial and oral features to altered breathing and its effects on craniofacial growth and development (Vargervik et al., 1984; Huang and Guilleminault, 2013; Grippaudo et al., 2016).

Using history taking, questionnaires to elicit sleep-related symptoms, and clinical assessment will fail to detect OSA for one in five children (Chay et al., 2000). The American Academy of Pediatrics recommends an overnight polysomnogram (PSG) to confirm the diagnosis of SDB or OSA. However, a study showed that only 10% of pediatric otolaryngologists would obtain a diagnostic PSG prior to surgical treatment (Mitchell et al., 2006). Reasons cited for not obtaining PSG include concerns about a child’s emotional distress over the testing, high cost, and lack of access to a sleep laboratory. The American Academy of Otolaryngology published a guideline advocating preoperative PSG in the subgroup of high-risk children who are syndromic, have craniofacial abnormalities, obesity, neuromuscular disorders, sickle cell disease, and mucopolysaccharidoses. The role of PSG in this high-risk group is to identify nonobstructive (central) apneas that will not benefit from surgery, provide diagnostic certainty in patients who have increased risk of surgery, ascertain the need for preoperative anesthetic assessment and postoperative monitoring, and document the baseline severity of SDB for comparison after surgery if persistent SDB is anticipated (Marcus et al., 2012).

Cephalometrics

In children with adenotonsillar hypertrophy, narrowing of the airway is usually at the retropalatal region where the soft palate, adenoid, and tonsils overlap (Isono et al., 1998; Fregosi et al., 2003; Figure 11.2). There is high sensitivity in identifying adenoid hypertrophy by using lateral cephalograms (Duan et al., 2019). Orthodontic two- or three-dimensional (3D) diagnostic imaging by lateral cephalometry or ultra low dose-low dose cone beam computed tomography (van Bunningen et al., 2022) are precise and able to show potential obstructions in the upper airway space that require further investigations:

- Percentage of nasopharynx occupied by the adenoid mass compared to percentage airway norm for a 6-year-old is more than 51% (Handelman and Osborne, 1976; Schulof, 1978).
- Reduced distance from the posterior nasal spine (PNS) to the nearest adenoid mass measured along the PNS-basion; normal distance in a 6-year-old is approximately 15–21 mm (Linder-Aronson, 1970; Schulof, 1978).

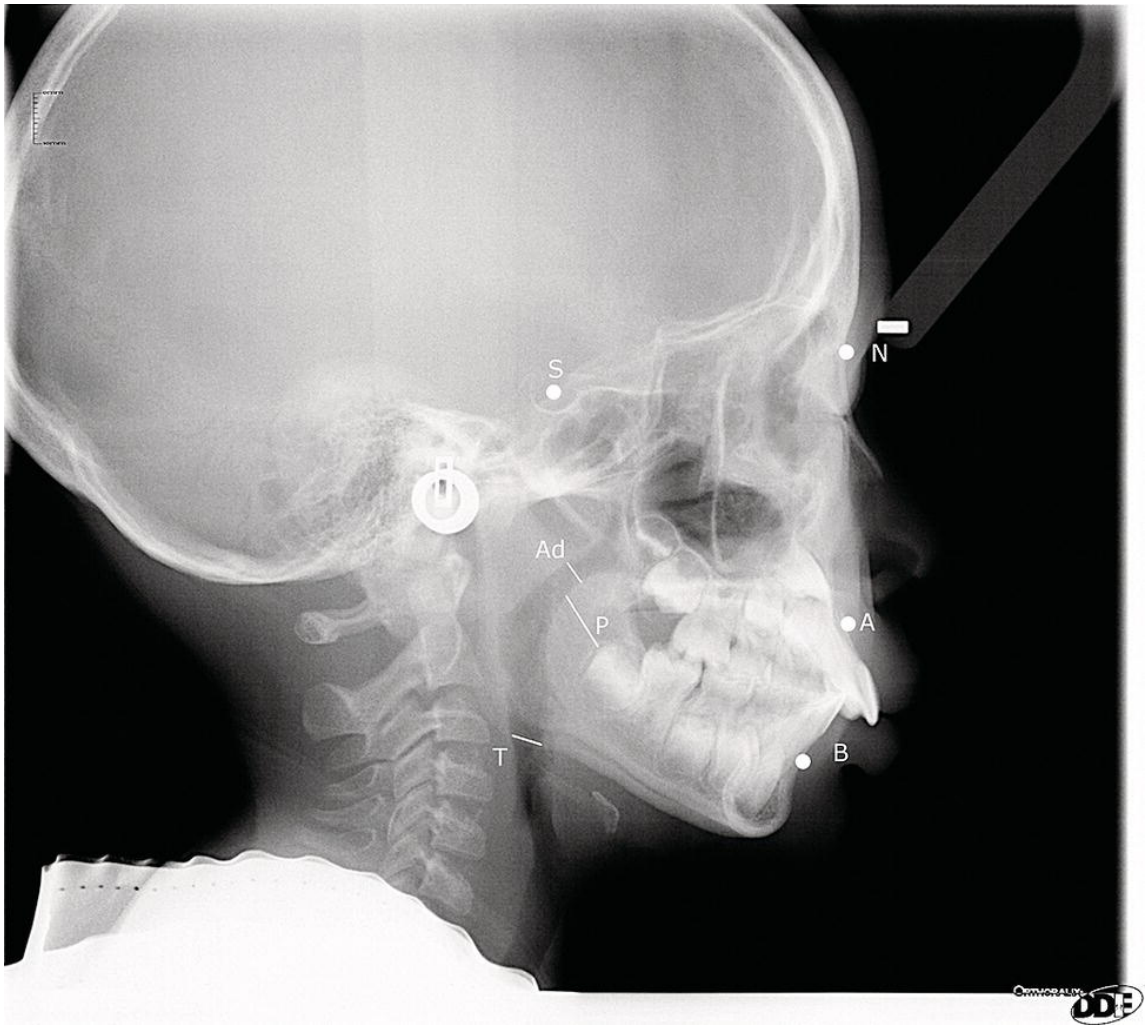


Figure 11.2 Significant parameters in a lateral cephalogram of a child with obstructive sleep apnea: Large adenoids and tonsils causing narrowing of the nasopharyngeal and oropharyngeal airway.

- Reduced distance from the PNS to the nearest adenoid mass measured along a line through the PNS perpendicular to the sella-basion; normal measurement in a 6-year-old is approximately 15–16 mm (Schulof, 1978; Linder-Aronson and Leighton, 1983).
- Reduced distance to the nearest adenoid mass from a point on the pterygoid vertical 5 mm above the PNS; the normal value is approximately 7 mm (Ricketts, 1954; Schulof, 1978).

Assessment of the upper airway by drug-induced sleep endoscopy (DISE) or cine-magnetic resonance imaging is used for dynamic characterization of structures at the obstructed site(s) for surgical treatment planning in children with persistent OSA (Li et al., 2023).

Orthodontic management

Growth modification of the maxilla and mandible

Rapid maxillary expansion (RME) with maxillary protraction increases the transverse width of the maxilla and enlarges the palatal and retropalatal areas. This improves the ratio of airway space relative to adenotonsillar size. Enlargement of the dental arches, transversely and antero-posteriorly, increases the intraoral space for accommodating lingual and sublingual tissues by removing the constraints of narrow maxillary and mandibular arches (Viva et al., 1992; Defabjanis, 2003). Systematic review of prepubertal RME treatment showed increased widths of the nasal and maxilla lateral walls by 3.3 mm and 3.4 mm, respectively (Seif-Eldin et al., 2019). Villa et al. (2007) reported that the majority of children (78.5%) treated with RME had significantly reduced AHI and 85.7% of the children switched from oral to nasal breathing. A Cochrane systematic review showed that treatment with orthodontic appliances in children with mild OSA could reduce AHI, nasal congestion, and habitual snoring. Although the evidence is equivocal, dentofacial growth modification can be considered as adjunctive therapy for OSA management in children with dentofacial anomalies (Carvalho et al., 2016; Figure 11.3).

Correction of antero-posterior or maxillo-mandibular deficiencies in children have been shown to improve SDB. Forward repositioning of the mandible with functional appliances enlarges the upper airway and improves respiratory function after six months. The AHI improved in more than 60% of patients (Villa et al., 2002). Results of studies on the effects of maxillary protraction on airway dimensions in children with Class III malocclusion are nonconclusive. In one study, significant favorable skeletal changes of the maxilla and mandible did not result in short-term or long-term changes in sagittal airway dimensions of the nasopharynx and oropharynx

(Baccetti et al., 2010). Another study reported a favorable increase in airway dimensions with maxillary protraction. Maxillary protraction increased the antero-posterior width of the upper airway and nasopharyngeal airway area (Oktay and Ulukaya, 2008). The increased airway size remained significant after four years. The oropharyngeal airway area, however, did not increase immediately after active treatment, although it increased significantly during a four-year follow-up period (Kaygisiz et al., 2009). The study suggested that increasing oropharyngeal airway caliber post active treatment may be an effect of accelerated growth.

A randomized control study of nonobese 4–10-year-old children with OSA (AHI ≥1) reported normalization of AHI in 50% of patients who used customized oral appliances to advance the mandible for six months. The use of oral appliances was associated with reduced tonsillar hypertrophy in about 67% of patients compared with 14% of children in the control group. About 74% of the patients tolerated the appliance treatment well (Villa et al., 2002).

A review of dentofacial orthopedic appliances showed them to be effective as nonsurgical alternatives in the management of childhood OSA in the short term. Longitudinal data are needed to confirm if orthodontic and dentofacial orthopedic treatment for children with OSA can be curative (Carvalho et al., 2007).

Treatment of children with sleep-disordered breathing and the role of surgery

Sleep-disordered breathing in children is a heterogeneous condition with overlapping phenotypes. As such, polysomnographic diagnosis and clinical findings are equally important in determining the treatment plan. Phenotypic features can be divided into anatomical and nonanatomical factors. Anatomical hard and soft tissues comprise craniofacial anomalies, nasal anatomy, adenotonsillar enlargements, and body habitus. The nonanatomical factors are arousal threshold, loop gain, and muscle reactivity (Carberry et al., 2018).

Practice guidelines from the American Academy of Pediatrics and American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS; Trosman, 2013) both recommend adenotonsillectomy as

primary therapy for OSA in healthy children older than 2 years. These healthy children have the commonest anatomical phenotype in pediatric SDB: adenotonsillar hypertrophy, possibly associated with a long face, narrow palate, and minor malocclusions. Enlarged tonsils, of Brodsky grade 2+ or larger associated with oxygen desaturation, are good predictors for the success of adenotonsillectomy (Heath et al., 2021). Removal of the tonsils in the group has a cure rate of up to 72%, as defined by AHI <1 (Lee et al., 2016). For children with mild OSA and parents who decline surgical treatment, conservative treatment of allergic rhinitis may be effective in some patients. Meta-analysis of treatment with intranasal steroids showed a reduction of AHI by 1.1 events per hour (Liu et al., 2015), while there was a reduction of AHI by 4.2 events per hour when intranasal steroids were used in combination with oral montelukast medication (Liming et al., 2018).

(a) (b)

Figure 11.3 Dentofacial orthopedic appliances to increase maxillary/nasal width and protract the mandible. (a) Hyrax rapid maxillary expander (RME) with upper twin block appliance (TBA). (b) Lower TBA with upper RME and upper TBA.

Another anatomical phenotype comprises children with congenital anatomical features that predispose them to SDB, such as micrognathia and the Pierre Robin sequence, maxillary hypoplasia, mid-nasal stenosis, and craniofacial synostosis. The cornerstone in planning optimal treatment for this group is the ability to determine the specific causes and locations of upper airway narrowing and collapse. Without precision profiling of the phenotypes, the gold standard treatment is continuous positive airway pressure (CPAP)

therapy to pneumatically splint the airway open. It is 90% effective, but limited by low compliance of 50% or more in nonadherence to treatment (Sawunyavisuth et al., 2021). A detrimental side effect from long-term CPAP therapy is midface hypoplasia from the CPAP mask that retards maxillary growth (Ghadiri and Grunstein, 2020).

Surgical procedures of the hard and soft tissues are alternative options to establish patency of the upper airway when conservative management with positive airway pressure therapy fails. Adenotonsillectomy is considered to be the first-line approach in managing OSA of otherwise well children who are 2 years and older with significant adenotonsillar hypertrophy and OSA. RME in growing children improved much more in the short term (under three years) for those with previous adenotonsillectomy or who have small tonsils. The cure rate was 25.6% in AHI reduction to below 1 event per hour and ODI increased to above 90% (Camacho et al., 2017). Mandibular distraction osteogenesis and maxillary protraction are other options to relieve upper airway constriction from disproportion in craniofacial growth (Garg et al., 2017). Early tracheostomy may also be considered for syndromic infants with an obstructed or unstable upper airway (Katz et al., 2012).

A third separate phenotype of children with SDB is best described as an “adult” phenotype, where the child is older with obesity in addition to the facial features of chronic nasal obstruction such as midface hypoplasia and open mouth posture. These children may have adenotonsillar hypertrophy, or the lymphoid tissues may have started regressing in size. Treatment of such children will have a large emphasis on weight management. Adenotonsillectomy success rates as defined by AHI <1 have been reported to be much lower, at 12–34% (Lee et al., 2016). Patients who have “failure” of adenotonsillectomy to cure OSA may be offered positive airway pressure therapy or site-specific airway procedures, which target the nose, oropharynx, and/or hypopharynx.

The adult with sleep-disordered breathing

History

Clinical assessment with a thorough history and examination is an important tool for evaluating adults with suspected SDB to identify those who need further evaluation and polysomnography. Symptoms associated with SDB can be classified into nocturnal and daytime symptoms.

Common nocturnal symptoms include persistent snoring, witnessed apneas, choking, nocturia, frequent awakenings, and restless sleep. The most commonly reported nocturnal symptom is snoring. Loud heavy snoring interspersed with periods of silence, which are apneic episodes, is associated with OSA. The history of snoring is best obtained from the bed partner, as most patients are unaware of their own snoring. Apart from snoring, it is important to ask about witnessed apneas or choking episodes. Patients who wake up two or more times per night to pass urine may have nocturia, a common symptom in OSA, reported to occur in up to 84% of OSA patients (Miyauchi et al., 2015). The occurrence of nocturia associated with OSA is postulated to be due to increased secretion of atrial natriuretic peptide, which increases urine production, coupled with increased abdominal pressure transmitted to the bladder due to ongoing inspiratory effort against an obstructed upper airway. Patients and/or bed partners sometimes report loud snorts, vocalization, or body movements associated with brief awakenings, which usually occur during the termination of apneic episodes.

Common daytime symptoms include excessive daytime sleepiness (EDS), dry mouth in the morning, morning headaches, impaired neurocognitive function, and mood disorders. EDS in individuals with OSA results from respiratory arousal-related sleep fragmentation and poor-quality sleep. The perception of EDS is subjective and can be hard to quantify. Screening for EDS in adults is easily accomplished with the Epworth Sleepiness Scale (ESS), an eight-item questionnaire where patients score their likelihood of falling asleep in various scenarios, such as monotonous soporific situations or during driving. A summative ESS score of >10 predicts a possibility of hypersomnolence (Johns, 1991, 1992). However, EDS can also be a result of insufficient sleep and it is therefore important to enquire about the patient's sleep and wake times.

Approximately 12–18% of patients complain of morning headaches that are usually described as dull and generalized (Russell et al., 2014). The exact mechanism is unclear, but is thought to be due to nocturnal oxygen desaturation and hypercapnia that results in cerebral vessel dilation and increased intracranial pressure. Neurocognitive impairments such as reduced vigilance, impairment in short- and long-term memory, as well as reduced executive functioning are commonly associated with OSA. EDS and its consequent impact on quality of life and daytime functioning result in mood disturbances in some patients. Depression is the most common mood symptom among other mood disorders like anxiety, irritability, and emotional lability. Individuals with OSA have a constellation of medical comorbidities (Bonsignore et al., 2019) and the comorbidity burden increases with OSA severity (Tveit et al., 2018).

Physical examination

A comprehensive physical examination of the OSA patient includes body habitus, craniofacial and dental characteristics, as well as upper airway soft tissue factors that influence the size and collapsibility of the upper airway

Measurement of height and weight and calculation of the BMI is an important part of examination, as obesity is frequently associated as an independent risk factor for OSA (Jehan et al., 2017). Increased circumference and the degree of fat deposition around the neck have been shown to be a reliable indicator for OSA. Prior studies have shown that neck circumference measurements of ≥43 cm for men and ≥37 cm for women are associated with increased risk of OSA, and further investigation of these patients should be performed (Katz et al., 1990; Kushida et al., 1997).

Mandibular deficiency is the most common craniofacial deformity associated with OSA. Retroposition of the mandible results in posterior displacement of the tongue base and a narrow retroglossal airway. These patients with mandibular deficiency generally fall into several growth patterns: primary mandibular deficiency, long face growth pattern, or maxillomandibular deficiency. Craniofacial assessment should be done with the patient's head positioned in the

natural head posture to determine the skeletal class. Examination of the mandible should encompass assessment of both antero-posterior and transverse dimensions considering the transverse width, chin–throat length, and chin-to-neck angle. A small or sunken midface and narrow high-arched palate are suggestive of maxillary deficiency in different planes of space, which has an impact on the size of the piriform aperture that forms the bony boundaries of the nasal passage. There can be linea alba or white lines in the buccal mucosa, torus mandibularis, buccal dentoalveolar exostosis, attrition, structural damage to teeth and dental restorations, hypersensitive teeth, masticatory muscle pain, temporomandibular disorders, and headaches stemming from sleep bruxism (SB; Palm et al., 2014; Lee et al., 2021). Co-occurrence of SB and OSA is common and the former occurs during arousals from apneic episodes. There is an increased risk of OSA (odds ratio 1.8) in patients with SB (Balasubramaniam et al., 2014) and screening for OSA is recommended (Puvanendran et al., 2020; Kuang et al., 2022).

Oropharyngeal findings typically seen in OSA include macroglossia, erythema and/or telangiectasia of the uvula, long and redundant soft palate, and tonsillar hypertrophy. Macroglossia is often associated with the presence of scalloping along the lateral border of the tongue due to pressure against adjacent teeth. Erythema and telangiectasia of the uvula result from vibratory trauma associated with chronic snoring. Snoring-associated intermittent hypoxia and vibratory trauma are potentially damaging, with progressive neuropathy and myopathy of the soft palate and pharyngeal dilators (Saboisky et al., 2012; Patel et al., 2018; Shah and Stål, 2022). The forces that result from repeated airway obstruction can cause stretching of the soft palate, creating redundancy and webbing of the soft palate and tonsillar pillars. Tonsillar hypertrophy is graded on a scale from 0 to 4, depending on the relation of tonsil size to the posterior tonsillar pillars: Grade 0: absence of tonsils; Grade 1: tonsils within pillars; Grade 2: tonsils extending to the posterior pillars; Grade 3: tonsils extending past the posterior pillars; Grade 4: tonsils meeting in midline. The Friedman tongue position (FTP) is a simple means to approximate obstruction at the hypopharyngeal level. FTP is the evaluation of the tongue's position relative to the tonsils, uvula, soft palate, and hard palate and is done with the tongue in the neutral,

unprotruded position. Depending on the soft palate structures visualized, patients are scored as FTP I–IV, whereby patients with a high FTP score have a higher likelihood of hypopharyngeal obstruction (Friedman et al., 2017).

Awake nasendoscopic examination of the upper airway underpins evaluation of any patient with OSA (Figures 11.4–11.9). Nasal findings that are common in patients with OSA can be structural or mucosal causes that contribute to nasal obstruction. Structural causes include nasal septal deviation, inferior turbinate hypertrophy, middle turbinate concha bullosa, and collapse of the internal or external nasal valves.

Common causes of nasal mucosa inflammation include allergic rhinitis and sinusitis. Chronic mucosal inflammation leads to the formation of nasal polyps in some patients, contributing to nasal obstruction. Adenoid hypertrophy, particularly in the pediatric population, also contributes to nasal obstruction in the nasopharynx. Nasendoscopy allows direct visualization of retropalatal (velum) and retroglossal cross-sectional dimensions, lingual tonsils, epiglottis, and the vocal cords. Lingual tonsil hypertrophy is a common cause of retroglossal obstruction. The degree of lingual tonsil hypertrophy is graded on a scale of 0 to 4 depending on the estimated vertical thickness of the lingual tonsil visualized during nasendoscopy (Friedman et al., 2017). The shape and position of the epiglottis are also important factors in airway evaluation, whereby a tubular, redundant, or retropositioned epiglottis can predispose to obstruction.

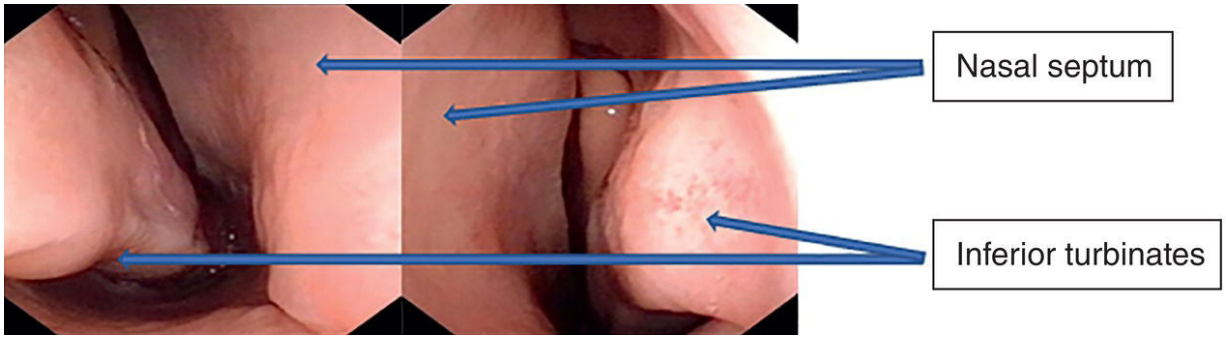


Figure 11.4 Nasoendoscopic view of normal patent nasal airway.

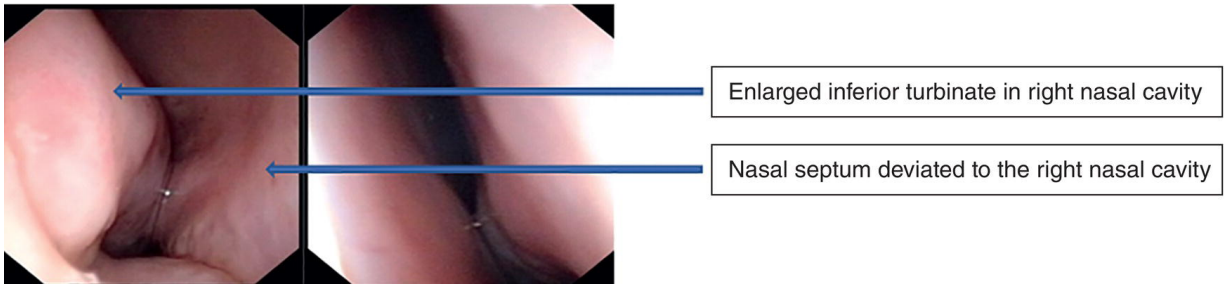


Figure 11.5 Nasoendoscopic view of patient with nasal septal deviation to the right with blocked right nasal cavity and patent left nasal cavity.

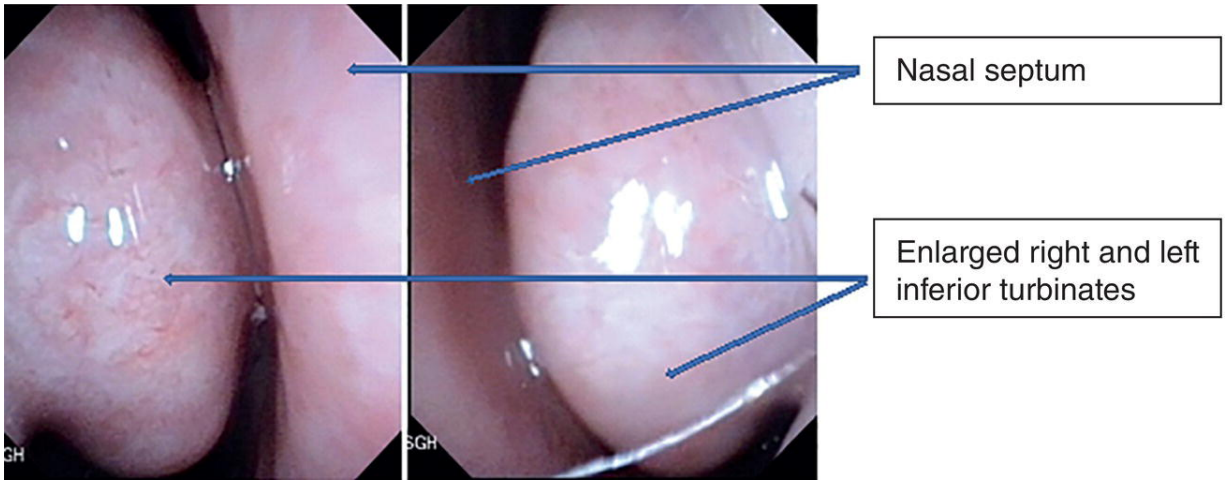


Figure 11.6 Nasoendoscopic view of patient with allergic rhinitis.

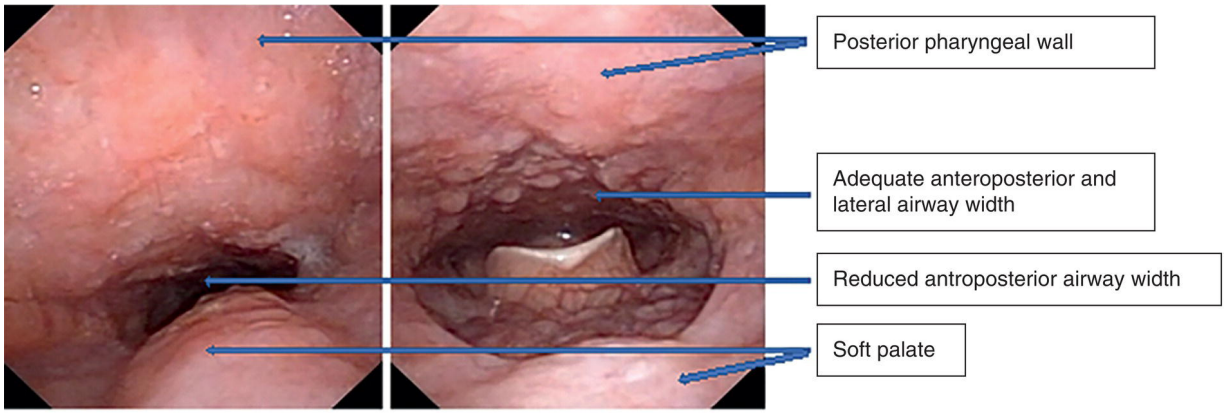


Figure 11.7 Nasoendoscopic views of the retropalatal airway.

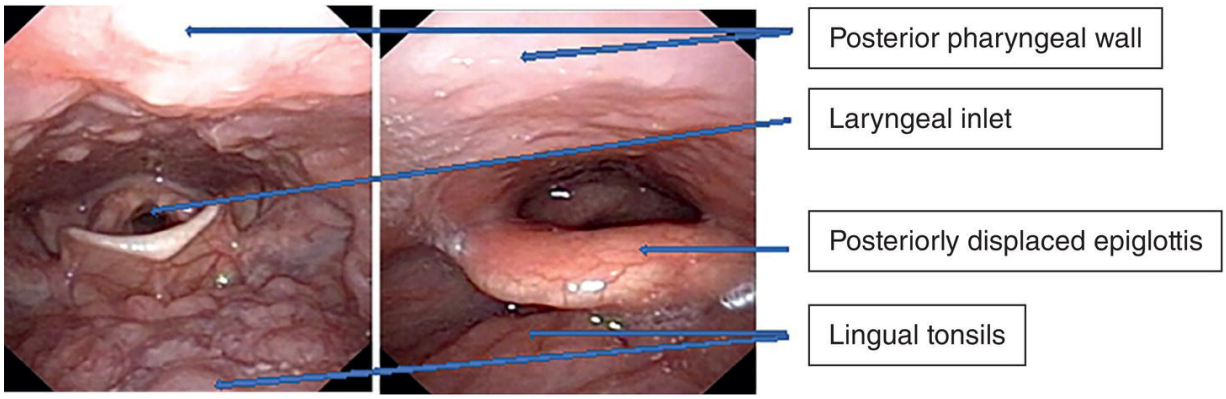


Figure 11.8 Nasoendoscopic view of the retroglossal airway. (a) No lingual tonsil hypertrophy. Laryngeal inlet visualized. (b) Lingual tonsil hypertrophy causing posterior displacement of the epiglottis. The laryngeal inlet cannot be visualized.

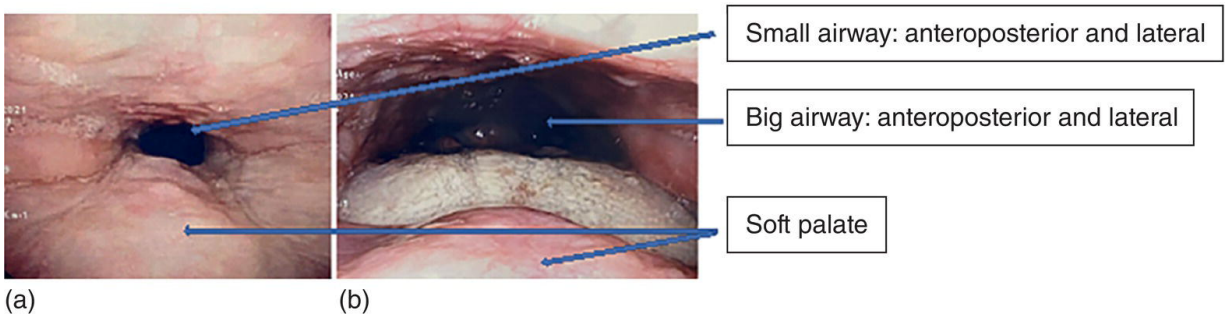


Figure 11.9 Nasoendoscopic view of the retropalatal airway (a) before and (b) after uvulopalatopharyngoplasty. Note the lateral and antero-posterior widening as the palate is suspended forward.

Cephalometrics and imaging

Lateral cephalometry is routinely used in treatment planning of orthodontic patients presenting for treatment of malocclusions. Cephalometric studies of upright as well as supine patients reveal structural differences between apneic and nonapneic subjects. Cephalometric features associated with OSA are brachycephalic craniofacial configuration, short antero-posterior cranial base length, reduced nasion-sella-basion angle, inferiorly positioned hyoid, retrognathic maxilla, retrognathic and micrognathic mandible, smaller than normal values for SNA and/or SNB, increased Frankfort mandibular plane angle or maxillary-mandibular plane angle (anterior divergent face), and increased anterior lower face height.

Soft tissue features associated with OSA are narrow retropalatal and retroglossal airway spaces, thicker and longer soft palate, reduced angle between the uvula tip and posterior nasal spine, and a greater tongue mass (Miles et al., 1996; Ingman et al., 2004; Hsu et al., 2005). Snoring children and children with OSA demonstrated mildly increased ANB angle due to reduced SNB angle that were statistically significant compared to controls, but they were not clinically significant; however, airway width reduction due to adenoid enlargement was significant (Katyal et al., 2013).

Airway imaging using CBCT and magnetic resonance imaging improved diagnostic capabilities by providing accurate visualization of the airway and enabling volumetric airway measurements. The mean total airway volume, from the anterior nasal cavity to the epiglottic level, is found to be significantly smaller in patients with retrognathic mandibles and significantly correlated with antero-posterior and vertical cephalometric variables, notably the ANB angle and anterior face height (Kim et al., 2010). The availability of CBCT acquisition of accurate 3D information provided the key to understanding the biomechanical role of the craniofacial structures in the etiology of OSA (Strauss and Burgoyne, 2008; White and Pharoah, 2008), although it is not needed for clinical decision making.

Orthodontic management

Given the complexity of multiple and overlapping etiologies, interdisciplinary team diagnosis and management of the patient with OSA involving different specialists and coordination of treatment are essential. The sleep team comprising some or all of the following members depends on the needs of the patient: endocrinologist, general dentist, neurologist, nutritionist, oral and maxillofacial surgeon, orthodontist, otolaryngologist, prosthodontist, psychiatrist, psychologist, and respiratory physician.

Treatment entails both general and specific measures to manage the varied causes and sequelae of OSA. Treatment is important in managing the patient's general health indicators: weight, cardiovascular health, and respiratory and metabolic functions. Specific treatment decisions are based on the appropriate treatment modality for the probable cause or causes of airway obstruction during sleep. Orthodontic treatment planning takes into consideration breathing, tongue and soft palate, tonsils, and locations of potential choke points in the pharyngeal airway. Where appropriate, the orthodontic treatment plan should enlarge narrow dental arches to acceptable limits rather than extract teeth to manage crowding. Retraction of the upper and lower incisors in managing bimaxillary proclination of incisors or compensation for a Class II malocclusion with a retrusive mandible may reposition the tongue postero-inferiorly, thereby posing a risk of compromising an existing narrow oropharyngeal airway.

A combination of clinical, craniofacial, and polysomnographic variables is used to design effective prescriptions for oral appliance treatment. Positive predictors of successful outcomes with the use of oral appliances in OSA in patients with mild to moderate OSA are AHI ≥5 to ≤30 events per hour (Schmidt-Nowara et al., 1995; Yow, 2009; Ng and Yow, 2020), posture-dependent or supine-related OSA (Marklund et al., 1998), retrognathic mandible, single-site obstruction at the retroglossal region, and an oropharyngeal lumen that is narrowed antero-posteriorly but not laterally. Negative predictors are severe OSA with AHI >30 events per hour; BMI >30 kg/m^2; multiple-level obstructions; nonpositional-dependent OSA;

inability to protrude the mandible >5 mm; and Class III malocclusion with a large mandible (Johnston et al., 2002).

In adult patients with mild to moderate OSA, AHI ≥5 to ≤30, intraoral appliances for mandibular advancement, similar in design to functional appliances for dentofacial growth in children, have been shown to be effective in managing OSA. However, mandibular advancement splints are not recommended as first-line treatment as they are not as efficacious as CPAP, the latter being the gold standard in treating OSA (Barnes et al., 2004; Hoekema et al., 2004; Lim et al., 2006).

Oral appliance treatment in adult OSA increases the posterior airway space by enlarging the lumen of the pharyngeal airway with increased muscular activity of the pharynx and tongue. Studies of users of mandibular advancement splints using 3D imaging and endoscopy have shown increased cross-sectional dimensions at the multiple levels of the pharynx (Liu et al., 2000). Anterior re-positioning of the mandible displaces the soft tissues, most importantly, the genioglossus, away from the oropharynx. The upper airway muscle activity is increased through stretching the palatoglossus and palatopharyngeus (Lowe et al., 1990).

Different studies use different indicators to denote success in OSA management. Some use AHI reduction by 50% as a success criterion, while others maintain the polysomnographic yardstick of the norm as AHI ≤5 events per hour as the criterion of cure. Even though there is computerized tomographic evidence of enlarged airway measurements due to mandibular advancement appliances (Gale et al., 2000), follow-up polysomnography studies of the patient sleeping with the mandibular advancement splint are necessary to confirm the effectiveness in managing SDB (Kushida et al., 2005).

There are many types and designs of appliances used in SDB. The two main ones are the mandibular advancement and tongue-retainer devices. The mandibular advancement device is the OSA appliance that is most widely used. Efficacy and outcomes of treatment with oral appliances with an anterior tongue-retention bulb, with or without mandibular advancement, are not well reported in the literature. The magnitude of mandibular advancement is an important factor in the reduction of AHI. A monobloc or a one-piece

intraoral appliance works well in patients who can manage good mandible protrusion of at least 5 mm. For the purposes of comfort and titratability, the initial mandibular advancement can be 75% of the maximum protrusion. The desired mandibular position is achieved by using two-piece mandibular advancement splints with telescoping connectors, similar to the Herbst appliance or the twin-block appliance with anteroposterior screws for gradual titration of mandibular advancement. Oligodontia, with fewer than 10 teeth per jaw, is usually a contraindication to prescribing an oral appliance. There are exceptions, however, and mandibular advancement appliances can sometimes be successfully retained in edentulous patients with good dentoalveolar ridges.

Tongue-stabilizing devices are monobloc appliances, with or without built-in mandibular advancement. The splint incorporates an anterior bulb, in front of the upper and lower incisors, for accommodating the tongue in a forward position. The tongue-stabilizing bulb is made from a soft polyvinyl material, which when squeezed produces negative pressure that draws the tongue forward into the retaining bulb. The best predictor of success of the tongue-stabilizing appliance is the presence of a single-site airway obstruction in supine-dependent OSA (Cartwright, 1985). Studies have shown no greater efficacy of the tongue-stabilizing device in reduction of the AHI compared to the mandibular advancement splint. In a randomized control trial, more than 90% of patients preferred to use the mandibular advancement appliance without the tongue bulb (Deane et al., 2009). Patients also preferred mandibular advancement splints to CPAP machines, even though the oral appliance is less efficacious than the CPAP device. The reasons include the effectiveness of the mandibular advancement appliance in managing mild to moderate OSA with fewer side effects and greater patient comfort (Ferguson et al., 1996). Furthermore, the oral appliance is small, which makes it easy to carry on journeys, and it does not need to be powered by electricity. The added incentive with an intraoral device is the lack of external visibility and the fact that it does not generate noise. There are none of the claustrophobic and cumbersome straps and tubes of the CPAP machine to deal with.

Oral appliance treatment does have its drawbacks. Soreness of the teeth, occlusion changes, and facial muscle and temporomandibular joint pain are commonly reported in the first few hours of waking. Long-term side effects occur after two or more years of oral appliance wear, and these include dental and skeletal changes. They present as reduction of overbite and overjet, proclination and retroclination of the lower incisors and upper incisors, respectively, and about 26% of patients experience irreversible changes in their occlusion. Oral appliances with greater advancements of the mandible have a greater impact on the skeletal system; there is downward and forward positioning of the mandible with increased anterior lower face height (Clark et al., 2000). In a report on the practice parameters of snoring and OSA, the American Academy of Sleep Medicine recommends fitting and follow-up of oral appliances by trained dental practitioners in dental sleep medicine. Follow-up overnight polysomnography is necessary to establish efficacy of the oral appliance with long-term monitoring of OSA signs and symptoms, dental and periodontal health, as well as the occlusion (Kushida et al., 2006).

Surgical management

Even though CPAP therapy remains the gold standard for management of OSA, adherence to treatment remains a challenge. Up to 83% of patients are unable to use the CPAP device for more than four hours per night (Weaver et al., 2008). As discussed in the previous section, not all patients are suitable for nor respond fully to oral devices. In these cases, surgery is an option.

Surgical procedures for OSA can be broadly divided into site-specific airway procedures that target the nose, oropharynx, and/or hypopharynx versus global airway procedures that seek to address the entire length of the upper airway, such as maxillo-mandibular advancement (MMA) or bariatric surgery. The surgical management strategy of OSA can be device based, whereby surgery is performed to complement and facilitate device use (CPAP or oral appliance), or for surgical cure. The decision on which surgical management strategy to adopt is dependent on the following factors: the patient's willingness to continue using CPAP/oral appliance; identification of

factors that contribute to poor device comfort and compliance; and the physician's overall assessment of the key contributing factors to the patient's OSA.

A device-based strategy can be adopted in patients who have poor compliance with CPAP or an oral device due to nasal obstruction. In a study that evaluated various physical, psychological, device-related, and socioeconomic factors that influenced CPAP adherence, nasal obstruction and CPAP pressure levels were found to be key contributing factors to poor adherence (Archbold and Parthasarathy, 2009). Nasal surgeries like septoplasty, inferior turbinoplasty, concha bullosa excision, nasal valve suspension, endoscopic sinus surgery, and polypectomy can improve nasal airway patency. A meta-analysis evaluating the effect of nasal surgery on CPAP device use and therapeutic treatment pressures reported reduction of CPAP pressures from 11.6 ± 2.2 to 9.5 ± 2.0 cmH_2O after nasal surgery. In addition, 89.1% of patients who were not using CPAP prior to nasal surgery accepted, adhered to, or tolerated CPAP after surgery and device usage increased from a mean of 3.0 ± 3.1 to 5.5 ± 2.0 hours (Camacho et al., 2015). Tonsillectomy and/or adenoidectomy are performed in patients with severe adenotonsillar hypertrophy, with the same overall aim of improving upper airway patency and reducing CPAP pressure requirements. Partial epiglottidectomy is performed in patients with a floppy closing door epiglottis who experience difficulty with CPAP due to displacement of the epiglottis against the laryngeal inlet by airway pressure.

Multilevel soft tissue surgery to address all obstructions in the upper airway is required when the aim is device-free surgical cure. The overall success rate of multilevel soft tissue surgery has been reported to be between 61.6% and 66.4% (Lin et al., 2017). DISE allows examination of the dynamic status of the upper airway during sleep to determine the sites and pattern of airway obstruction. With precise identification of the sites and types of obstruction, surgery can be tailored to address them such that surgical success rates are maximized (Lee et al., 2012; De Vito et al., 2018).

In adult patients with mid-palatal suture maturation, surgically assisted palatal expansion (SARPE) and miniscrew-assisted rapid palatal expansion (MARPE) are recently introduced options in

improving nasal function by widening the maxilla. Increased upper airway volume by palatal expansion is well established (Calvo-Henriquez et al., 2021). The change in anatomy reduces airflow speed and negative pressure effects on the pharyngeal airway. This correlates with reductions in AHI and ODI (Iwasaki et al., 2020). The evidence for long-term efficacy is yet to be established.

MMA surgery is a strategy to establish multilevel upper airway patency (Yu et al., 2020; Figure 11.10). A meta-analysis of 518 patients from 45 studies showed MMA surgery to be effective in treating OSA. Surgical success criteria were reductions in AHI ≥50% with fewer than 10 events per hour. Post-MMA AHI ≤5 indicated cure of OSA for the patient. Surgical success in managing the severity and the cure rate were 85.5% and 38.5%, respectively. The strongest predictive factor for a surgical cure was AHI ≤60 (Zaghi et al., 2016). Using dynamic assessment with DISE, the anatomical structures of the upper airway that stabilized after successful MMA interventions were the lateral pharyngeal wall, soft palate, and tongue base. Individuals with the largest improvements in respiratory parameters of AHI and ODI had the greatest reduction in lateral pharyngeal collapsibility (Liu et al., 2015).

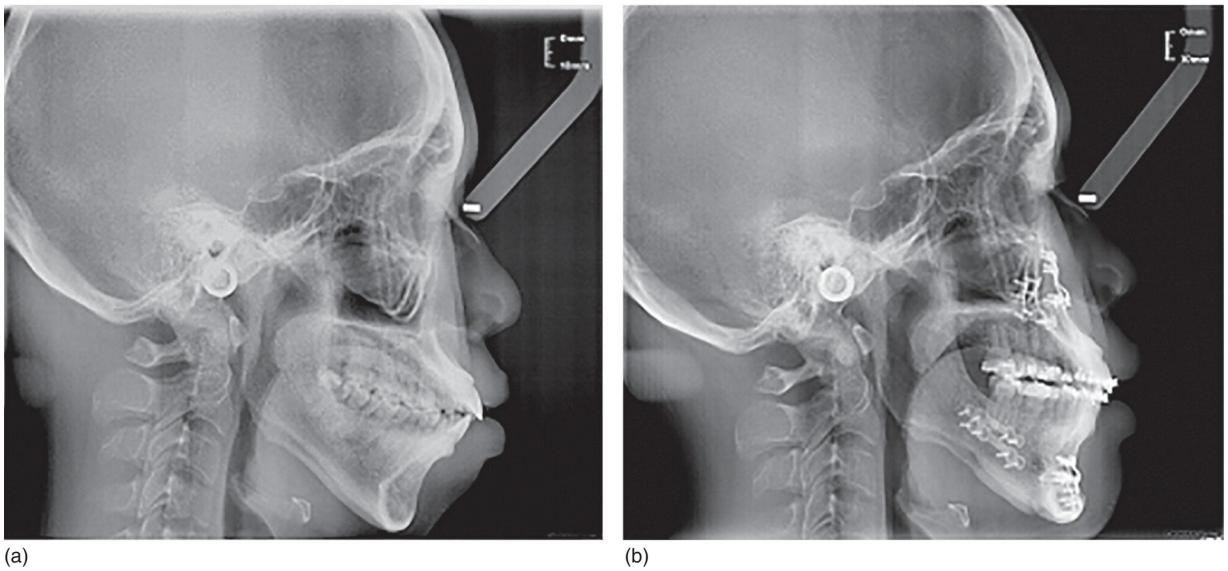

(a) (b)

Figure 11.10 (a) Lateral cephalogram before maxillo-mandibular advancement (MMA) surgery. (b) Lateral cephalogram after MMA with counter-clockwise rotation of the maxillo-mandibular complex and multilevel enlargement of the upper airway

Conclusion

The causes of SDB are multifactorial. The etiologies and pathogenesis are neither well defined nor completely understood. Although the likely anatomical areas and obstructing structures in the nose and choke points at different levels of the pharynx are clinically identifiable, their roles in SDB may not always be one of direct cause and effect. There are nonanatomical contributors to the heterogeneous disorder to consider; that is, muscle reactivity, loop gain, and arousal threshold. Identification of the sleep phenotypic traits is necessary for a precise treatment approach.

In children, the important consideration in management is to rule out the common causes of nasal and/or nasopharyngeal obstructions. Although surgical management by tonsillectomy and adenoidectomy is the mainstay in treatment of childhood OSA, treatment with dentofacial orthopedic appliances can alleviate compromised upper airways in growing patients where the adenotonsillar size is incompatible with dentofacial structure for upper airway function. Without proper diagnosis and treatment, approximately one-third of children with mild SDB will progress in two years or more to a more severe form of the condition. The rationale behind the approach to treatment is either to increase the volume of the hard tissue “container” to accommodate the enlarged soft tissue contents, or to remove the contents that have become too large for the container.

Orthodontic treatment protocols include management of dentofacial morphometric risk factors to alleviate OSA in the short term by widening the maxilla and protraction of retruded maxilla and mandible. Long-term studies are needed to provide an evidence-based cure for OSA. For some patients OSA is not curable, but treatment is possible to manage the severity and attendant medical comorbidities. Comprehensive interdisciplinary management is necessary to address all possible causes, structural as well as nonstructural.

Caution should be exercised in certain surgical procedures that are known to cause OSA, such as pharyngoplasty to improve speech in cleft lip and palate patients, and orthognathic setback procedures of

the maxilla or mandible to manage dentofacial esthetics. There is evidence to substantiate that these surgeries can permanently reduce the caliber of the upper airway. It is recommended to screen all patients for SDB before subjecting them to procedures that can reduce airway patency.

In adults, the first-line management strategy is to rule out nasal obstructions and the use of the gold standard therapy with CPAP to pneumatically splint the airway open. Unfortunately, the lack of adherence to CPAP therapy is high. Consequent to that, there is a plethora of other airway-opening strategies with positional sleep devices, mandibular advancement appliances, tongue stabilizers, and surgical procedures. In severe cases when all types of treatment to establish a functionally patent upper airway are exhausted, the obstructed upper airway is bypassed with tracheostomy.

Patients with SDB may have associated excessive daytime sleepiness and associated medical comorbidities that adversely affect the cardiovascular and cerebrovascular systems as well as metabolic and neurocognitive functions. Evaluation by an interdisciplinary team trained in sleep medicine is vital for orthodontic or orthognathic patients presenting with SDB for treatment. Identification of patients at risk of SDB before orthodontic and orthognathic treatment prevents compromising of a narrow upper airway that worsens a collapsible upper airway. Multidisciplinary collaboration adds to the decision-making process in treatment planning. The treatment plan to manage dentofacial esthetics and occlusion should include the maintenance of or improvement to the patency of the upper airway. The patient with SDB and medical comorbidities requires multiple treatment considerations from the cardiologist, endocrinologist, neurologist, orthodontist, oral and maxillofacial surgeon, otorhinolaryngologist, pediatrician (for a child), psychiatrist, psychologist, and respiratory medicine physician. Orthodontic treatment in patients with SDB, dentofacial deformities, and malocclusion should be done in close collaboration with a sleep medicine team.

A collaborative interdisciplinary approach is essential to optimize the care of patients with SDB. The challenge for the orthodontist or dentist is in recognizing patients who are at risk of a collapsible

upper airway to initiate early investigations and interventions. Orthodontic patients can be easily screened using a combination of family history, sleep history, clinical assessment, and imaging (Boxes 11.1 and 11.2; Figures 11.11 and 11.12).

Box 11.1 Practice points in screening and management of children.

Screen with the BEARS questionnaire. Signs and symptoms for the at-risk child:

- Snoring and frequency ≥3 nights per week
- Mouth breathing, laborious breathing, restless sleep, enuresis
- Daytime drowsiness, attention deficit/hyperactivity, poor academic performance

Nonstructural signs and symptoms:

- Obesity: body mass index (BMI) ≥95th percentile in age and sex cohorts
- Allergies and nasal congestion
- Hyotonia, muscular dystrophy, or neurological disorders

Structural signs and symptoms from clinical assessment and orthodontic x-rays or cone beam computed tomography:

- Complex syndromes, craniofacial abnormalities, macroglossia
- Micrognathia or retrognathia of the maxilla and/or mandible
- Nasal septum deviation, enlarged inferior turbinates, enlarged adenoids and tonsils obstructions in the posterior airway space, narrowing of the nasopharynx, oropharynx, and hypopharynx, hyoid distance from the lower border of the mandible

Collaborate with pediatric specialists/sleep team to confirm the diagnosis and comorbidities:

- Comprehensive assessment of the upper airway including oral and nasal cavities
- Nasendoscopic examination for nasal abnormalities, locations of upper airway narrowing, adenotonsillar size relative to upper airway size
- Establish orthodontic diagnosis and sites of dentofacial deformity (DFD)

Concomitant orthodontic and medical treatment for the following groups of children: with mild to moderate obstructive sleep apnea (OSA); residual OSA after adenotonsillectomy; findings of sleep-disordered breathing inconsistent with adenoid and/or tonsil hypertrophy:

- Prepubertal treatment
- Maxillary expansion, maxillary advancement and/or mandibular advancement according to the type of jaw discrepancy, malocclusion, and site of airway obstruction
- Collaborate with the pediatric specialists/sleep team to manage allergic rhinitis, nasal congestion, adenotonsillar hypertrophy, obesity, and other medical comorbidities
- Collaborate with the craniomaxillofacial/sleep team for children with syndromes, severe DFD, neuromuscular disease, chronic lung disease, sickle cell disease, metabolic disease, laryngomalacia, severe OSA, and obesity

Source: SingHealth Duke-NUS Sleep Centre.

Box 11.2 Practice points in screening and management of adults.

Screen with STOP-BANG questionnaire for at-risk patients:

- Low risk of moderately severe to severe obstructive sleep apnea: 0–2 yes responses
- Intermediate risk: 3–4 yes responses
- High risk: 5–8 yes responses

Screen for nonstructural signs and symptoms:

- Obesity: body mass index (BMI) ≥28 for Asians; ≥30 for Caucasians
- Allergies and nasal congestion
- Hyotonia, muscular dystrophy, or neurological disorders

Screen for structural signs and symptoms:

- Craniofacial abnormalities, syndromes or conditions with macroglossia
- Micrognathia or retrusion of the maxilla and/or mandible
- Oropharyngeal congestion – enlarged palatine and/or lingual tonsils, large crenated tongue, long droopy soft palate, narrow high-vaulted hard palate, linea alba in the buccal mucosa, tori and tooth wear from bruxism

Structural signs and symptoms from clinical assessment and orthodontic x-rays or cone beam computed tomography:

- Nasal septum deviation, enlarged inferior turbinates, narrow upper airway width, increased distance of greater horn tip of the hyoid to mandibular plane
- Nasendoscopic examination for nasal abnormalities, locations of upper airway narrowing, airway collapsibility with Müller maneuver, airway caliber changes with simulated mandibular advancement

Collaborate with sleep specialists/sleep team to confirm the diagnosis and comorbidities:

- Comprehensive assessment of the upper airway including oral and nasal cavities
- Nasendoscopic examination for nasal abnormalities, locations of upper airway narrowing, upper airway narrowing in the oropharynx and hypopharynx
- Establish orthodontic diagnosis and sites of dentofacial deformity (DFD)

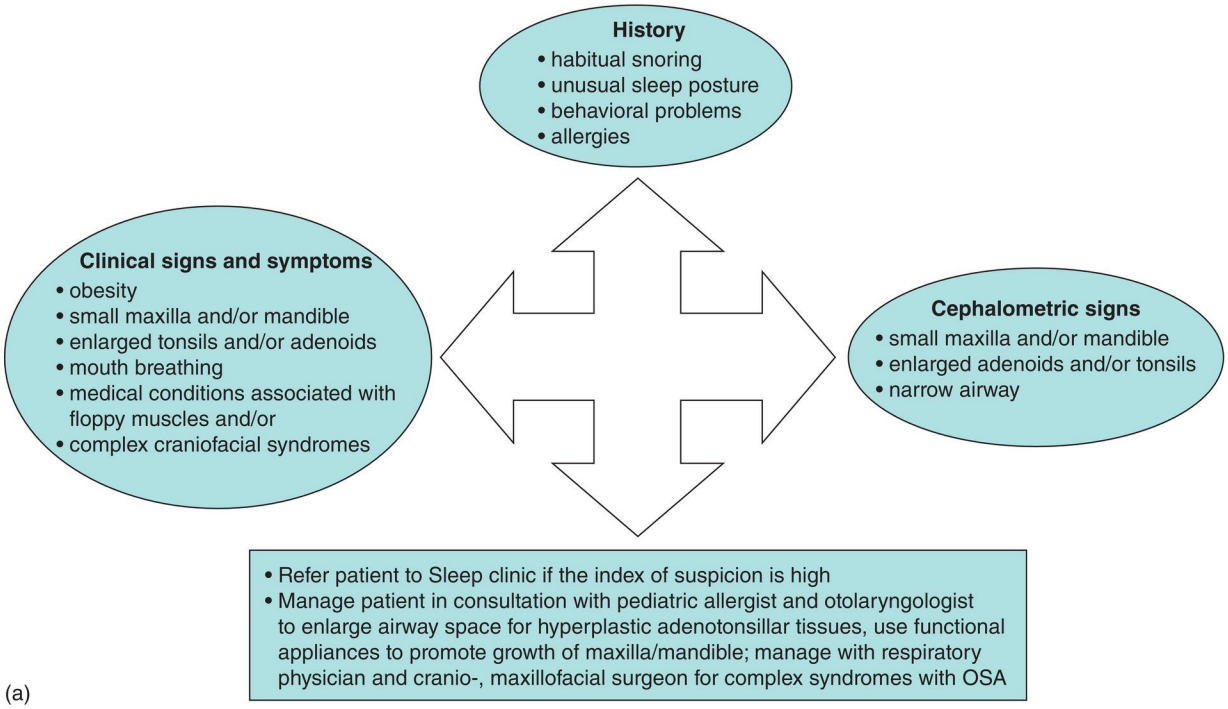
Orthodontic and presurgical orthodontic treatment recommendations:

- Establish orthodontic diagnosis
- Define sites of DFDs
- Expand transversely and antero-posteriorly rather than constrict maxillary and mandibular arches with extractions; treat to orthodontically acceptable limits of occlusion and psychosocial function
- If appropriate, plan orthognathic surgery to advance the maxilla and mandible. In correction of mandibular prognathism, reduce the magnitude of mandibular setback with bimaxillary orthognathic surgery
- Presurgical screen for sleep-disordered breathing (SDB) in all patients planned for setback osteotomies

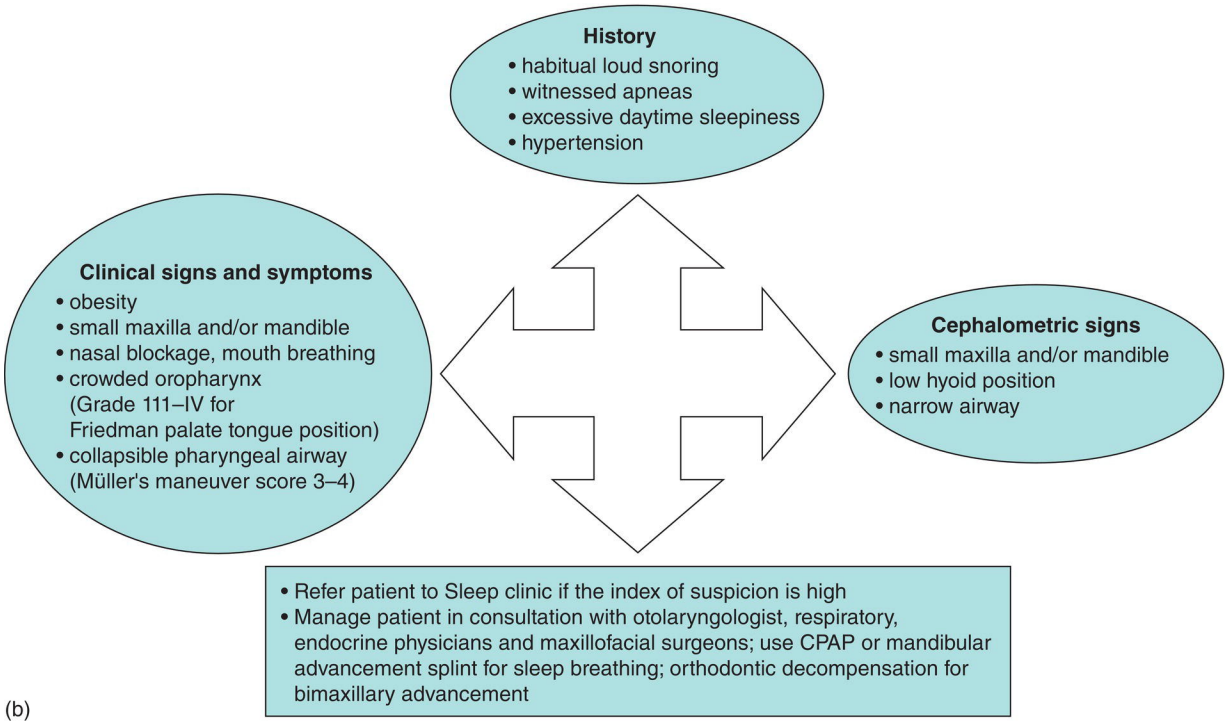
Concomitant treatment recommendations:

- Collaborate with the sleep specialist/team for joint medical and/or surgical management of orthodontic patients with confirmed SDB

Source: SingHealth Duke-NUS Sleep Centre.


History
• habitual snoring
• unusual sleep posture
• behavioral problems
• allergies
Clinical signs and symptoms
• obesity
• small maxilla and/or mandible
• enlarged tonsils and/or adenoids
• mouth breathing
• medical conditions associated with floppy muscles and/or
• complex craniofacial syndromes
Cephalometric signs
• small maxilla and/or mandible
• enlarged adenoids and/or tonsils
• narrow airway
• Refer patient to Sleep clinic if the index of suspicion is high
• Manage patient in consultation with pediatric allergist and otolaryngologist to enlarge airway space for hyperplastic adenotonsillar tissues, use functional appliances to promote growth of maxilla/mandible; manage with respiratory physician and cranio-, maxillofacial surgeon for complex syndromes with OSA

(a)


History
• habitual loud snoring
• witnessed apneas
• excessive daytime sleepiness
• hypertension
Clinical signs and symptoms
• obesity
• small maxilla and/or mandible
• nasal blockage, mouth breathing
• crowded oropharynx (Grade 111–IV for Friedman palate tongue position)
• collapsible pharyngeal airway (Müller's maneuver score 3–4)
Cephalometric signs
• small maxilla and/or mandible
• low hyoid position
• narrow airway
• Refer patient to Sleep clinic if the index of suspicion is high
• Manage patient in consultation with otolaryngologist, respiratory, endocrine physicians and maxillofacial surgeons; use CPAP or mandibular advancement splint for sleep breathing; orthodontic decompensation for bimaxillary advancement

(b)

Figure 11.11 (a) Management pathway for a child with dentofacial deformity and malocclusion suspected of having sleep-disordered breathing. OSA, obstructive sleep apnea. (b) Management pathway for an adult with dentofacial deformity and malocclusion suspected of having sleep-disordered breathing. CPAP, continuous positive airway pressure.

Source: National Dental Centre Singapore.

OSA EXAMINATION CHART PAGE 1

National Dental Centre Singapore
SingHealth

Patient's Particulars

Weight: _____ kg

Height: _____kg

BMI: _____ (At risk Asian ≥ 28 Caucasian ≥30)

Neck circumference: ____cm (At risk ♀≥37 ♂ ≥43)

BP: Systolic/Diastolic_____ (At risk >120/80)

ESS: ____ (Excessive daytime sleepiness ≥ 9)

Referred by: _____

Complaint: _____

Previous OSA Treatment, Dr and date: _____

Sleep history: _____

Child: Difficulty breathing during sleep: □Yes □No Unusual sleep posture: □Yes □No

Adult: Habitual snorer: □Yes □No Witnessed apnea: □Yes □No

Medical History: _____

Medication: _____

Relevant dental history: _____

CPAP usage: □Yes □No From:_____ (year) Current CPAP pressure: _____cmH_20

Polysomnograph (PSG) Results/Date: _____

AHI: _____ AI: _____ Lowest $Sa0_2$: _____%

Facial Examination:

Deviation of nose	□ Straight	□ Right	□ Left
Facial form	□ Square	□ Ovoid	□ Tapering
Facial profile	□ Convex	□ Straight	□ Concave
Maxilla	□ Protrusive	□ Normal	□ Retrusive
Mandible	□ Protrusive	□ Normal	□ Retrusive

Oropharyngeal examination:

Respiration	□ Nasal	□ Mouth	□ Mixed
Nasal obstruction	□ Right	□ Left	
Swallowing	□ Normal	□ Abnormal	
Palatal Vault	□ Low	□ Normal	□ High

Tonsil Size (Please circle the appropriate number) Grade 0, 1, 2, 3, 4 (Refer to Fig 18-4)
0: Tonsils fit within tonsillar fossa
1: Tonsils < 25% of space between pillars
2: Tonsils < 50% of space between pillars
3: Tonsils < 75% of space between pillars
4: Tonsils > 75% of space between pillars

Friedman Palate/Tongue Position (Please circle the appropriate number)

Grade I, II, III, IV (Refer to Fig 18-5)

OSA EXAMINATION CHART PAGE 2

National Dental Centre Singapore
SingHealth

TMJ Function:

_____

(Deviation, joint sounds, joint or muscle pain)

Range of motion:

Maximum mouth opening: _____mm

Lateral excursion: (Right) _____mm (Left) _____mm

Protrusion (max): _____mm Deviation in protrusion: □ R □ L

Intraoral Exam:

Hygiene: □ Good □ Adequate □ Poor

Periodontal Status: _____

Dentition:

8	7	6	5	4	3	2	1	1	2	3	4	5	6	7	8

Occlusion:

Class I II/1 II/2 III Overjet: ____ mm Overbite: ____ mm

Nasopharyngoscopic Examination:

External nasal valve	□ Normal	□ Collapsed	
Deviated septum	□ None	□ Present	□ R / □ L
Turbinate hypertrophy	□ None	□ Present	□ R / □ L
Nasal Polyps	□ None	□ Present	□ R / □ L
Sinusitis	□ None	□ Present	□ R / □ L
Adenoid hypertrophy	□ None	□ Present	
Retropalatal narrowing	□ None	□ Present	□ AP □ Lateral
Müller's Maneuvre	0 1	2 3	4

(0= no collapse, 1= 25% collapse, 2 = 50% collapse, 3= 75% collapse and 4=100% collapse)

Retrolingual narrowing	□ None	□ Present	□ AP □ Lateral
Lingual Tonsils	□ Normal	□ Hypertrophy	
Hypopharynx	□ Normal	□ Anomaly:_____	

Radiographic examination:

OPG: _____

Lat Ceph: Retropalatal airway space ____ mm Retrolingual airway space ____ mm (At risk <10mm)

Maxilla	□ Normal	□ Hypoplastic	□ Hyperplastic
Soft Palate	□ Normal	□ Long	□ Thick
Mandible	□ Normal	□ Hypoplastic	□ Hyperplastic
Chin	□ Normal	□ Retrogenia	□ Progenia
Hyoid	□ Normal	□ Low _____	mm (At risk ≥ 24mm)

Examiner's name & signature: _____ Date: _____

Figure 11.12 Sample clinical examination chart for obstructive sleep apnea.

Source: National Dental Centre Singapore.

Acknowledgments

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References

Ali, N.J., Pitson, D.J., and Stradling, J.R. (1993). Snoring, sleep disturbance and behaviour in 4–5 year olds. *Archives of Disease in Childhood* 68: 360–366.

Anuntaseree, W., Kuasirikul, S., and Suntornlohanakul, S. (2005). Natural history of snoring and obstructive sleep apnea in Thai school-age children. *Pediatric Pulmonology* 39(5): 415–420.

Archbold, K.H., and Parthasarathy, S. (2009). Adherence to positive airway pressure therapy in adults and children. *Current Opinion in Pulmonary Medicine* 15(6): 585–590.

Arens, R., McDonough, J.M., Corbin, A.M. et al. (2003). Upper airway size analysis by magnetic resonance imaging of children with obstructive sleep apnea syndrome. *American Journal of Respiratory and Critical Care Medicine* 167: 65–70.

Avrahami, E., and Englender, M. (1995). Relation between CT axial cross-sectional area of the oropharynx and obstructive sleep apnea syndrome in adults. *American Journal of Neuroradiology* 16(1): 135–140.

Baccetti, T., Franchi, L., Mucedero, M. et al. (2010). Treatment and post-treatment effects of facemask therapy on the sagittal pharyngeal dimensions in Class III subjects. *European Journal of Orthodontics* 32: 346–350.

Bacon, W.H., Turlot, J.C., Kriegor, J. et al. (1990). Cephalometric evaluation of pharyngeal obstructive factors in patients with sleep apnea syndrome. *Angle Orthodontist* 60: 115–122.

Balasubramaniam, R., Klasser, G.D., Cistulli, P.A. et al. (2014) The link between sleep bruxism, sleep disordered breathing and temporomandibular disorders: an evidence-based review. *Journal of Dental Sleep Medicine* 1(1): 27–37.

Bannink, N., Mathijssen, I.M.J., and Joosten, K.F.M. (2010). Can parents predict obstructive sleep apnea in children with syndromic or complex cranio-synostosis? *International Journal of Oral & Maxillofacial Surgery* 39: 421–423.

Barnes, M., McEvoy, R.D., Banks, S. et al. (2004). Efficacy of positive airway pressure and oral appliance in mild to moderate obstructive sleep apnea. *American Journal of Respiratory and Critical Care Medicine* 170(6): 656–664.

Benjafield, A.V., Ayas, N.T., Eastwood, P.R. et al. (2019). Estimation of the global prevalence and burden of obstructive sleep apnoea: A literature-based analysis. *Lancet Respiratory Medicine* 7(8): 687–698.

Berry, R.B., Quan, S.F., Abreu, A.R. et al. (2020). *The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications, Version 2.6*. Darien, IL: American Academy of Sleep Medicine.

Bonsignore, M.R., Baiamonte, P., Mazzuca, E. et al. (2019). Obstructive sleep apnea and comorbidities: A dangerous liaison. *Multidisciplinary Respiratory Medicine* 14(14): 8.

Bradford, A., McGuire, M., and O'Halloran, K.D. (2005). Does episodic hypoxia affect upper airway dilator muscle function?

Implications for the pathophysiology of obstructive sleep apnoea. *Respiratory Physiology & Neurobiology* 147(2–3): 223–234.

Brodsky, L. (1989). Modern assessment of tonsils and adenoids. *Pediatric Clinics of North America* 36(6): 1551–1569.

Brooks, L.J., Stephens, M.B., and Bacevice, A.M. (1998). Adenoid size is related to severity but not the number of episodes of obstructive sleep apnea in children. *Journal of Pediatrics* 132: 682–686.

Brouillette, R.C., Fernbach, S.K., and Hunt, C.E. (1982). Obstructive sleep apnea in infants and children. *Journal of Pediatrics* 100: 31–40.

Brożek-Mądry, E., Burska, Z., Steć, Z. et al. (2021). Short lingual frenulum and head-forward posture in children with the risk of obstructive sleep apnea. *International Journal of Pediatric Otorhinolaryngology* 144: 110699.

Brunetti, L., Rana, S., Lospalluti, M.L. et al. (2001). Prevalence of obstructive sleep apnea syndrome in a cohort of 1,207 children of southern Italy. *Chest* 120: 1930–1935.

Burwell, C.S., Robin, E.D., Whaley, R.D. et al. (1956). Extreme obesity associated with alveolar hypoventilation – a Pickwickian syndrome. *American Journal of Medicine* 21: 811–818.

Calvo-Henriquez, C., Megias-Barrera, J., Chiesa-Estomba, C. et al. (2021). The Impact of maxillary expansion on adults' nasal breathing: A systematic review and meta-analysis. *American Journal of Rhinology & Allergy* 35(6): 923–934.

Camacho, M., Chang, E.T., Song, S.A. et al. (2017). Rapid maxillary expansion for pediatric obstructive sleep apnea: A systematic review and meta-analysis. *Laryngoscope* 127(7): 1712–1719.

Camacho, M., Riaz, M., Capasso, R. et al. (2015). The effect of nasal surgery on continuous positive airway pressure device use and therapeutic treatment pressures: A systematic review and meta-analysis. *Sleep* 38(2): 279–286.

Carberry, J.C., Amatoury, J., and Eckert, D.J. (2018). Personalized management approach for OSA. *Chest* 153(3): 744–755.

Carberry, J.C., Jordan, A.S., White, D.P. et al. (2016). Upper airway collapsibility (Pcrit) and pharyngeal dilator muscle activity are sleep stage dependent. *Sleep* 39(3): 511–521.

Carroll, J.L. (1996). Sleep-related upper airway obstruction in children and adolescents. *Child and Adolescent Psychiatry Clinics of North America* 5: 617–647.

Cartwright, R.D. (1985). Predicting response to the tongue retaining device for sleep apnea syndrome. *Archives of Otolaryngology* 111(6): 385–388.

Carvalho, F.R., Lentini-Oliveira, D., Machado, M.A. et al. (2007). Oral appliances and functional orthopaedic appliances for obstructive sleep apnoea in children. *Cochrane Database of Systematic Reviews* 18(2): CD005520. doi: 10.1002/14651858.CD005520.pub2.

Carvalho, F.R., Lentini-Oliveira, D.A., Prado, L.B. et al. (2016). Oral appliances and functional orthopaedic appliances for obstructive sleep apnoea in children. *Cochrane Database of Systematic Reviews* 10(10): CD005520. doi: 10.1002/14651858.CD005520.pub3.

Castronovo, V., Zucconi, M., Nosetti, L. et al. (2003). Prevalence of habitual snoring and sleep-disordered breathing in pre-school-aged children in an Italian community. *Journal of Pediatrics* 142(4): 377–382.

Chan, J., Edman, J.C., and Koltai, P.J. (2004). Obstructive sleep apnea in children. *American Family Physician* 69: 1147–1154.

Chay, O.M., Goh, A., Abisheganaden, J. et al. (2000). Obstructive sleep apnea syndrome in obese Singapore children. *Pediatric Pulmonology* 29: 284–290.

Chervin, R.D., Archbold, K.H., Dillon, J.E. et al. (2002). Inattention, hyperactivity and symptoms of sleep-disordered breathing.

Pediatrics 109: 449–456.

Chng, S.Y., Goh, D.Y., Wang, X.S. et al. (2004). Snoring and atopic disease: A strong association. *Pediatric Pulmonology* 38: 210–216.

Chung, F., Abdullah, H.R., and Liao, P. (2016). STOP-Bang questionnaire: A practical approach to screen for obstructive sleep apnea. *Chest* 149(3): 631–638.

Ciscar, M.A., Jaun, G., Martinez, V. et al. (2001). Magnetic resonance imaging of the pharynx in OSA patients and healthy subjects. *European Respiratory Journal* 17: 79–86.

Clark, G.T., Sohn, J.W., and Hong, C.N. (2000). Treating obstructive sleep apnea and snoring: Assessment of an anterior mandibular positioning device. *Journal of the American Dental Association* 131: 765–771.

Davila, D.G. (1995). Medical considerations in surgery for sleep apnea. *Oral and Maxillofacial Surgery Clinics of North America* 7: 205–219.

Deane, S.A., Cistulli, P.A., and Ng, A.T. (2009). Comparison of mandibular advancement splint and tongue stabilizing device in obstructive sleep apnea: A randomized controlled trial. *Sleep* 32(5): 648–653.

deBerry-Borowiecki, B., Kukwa, A., and Blanks, R.H. (1988). Cephalometric analysis for diagnosis and treatment of obstructive sleep apnea. *Laryngoscope* 98: 226–234.

Defabjanis, P. (2003) Impact of nasal airway obstruction on dentofacial development and sleep disturbances in children: Preliminary notes. *Journal of Clinical Pediatric Dentistry* 27(2): 95–100.

Dempsey, J.A., Veasey, S.C., Morgan, B.J. et al. (2010). Pathophysiology of sleep. *Physiology Review* 90: 47–112.

De Vito, A., Carrasco Llatas, M., Ravesloot, M.J. et al. (2018). European position paper on drug-induced sleep endoscopy: 2017

update. *Clinical Otolaryngology* 43(6): 1541–1552.

Dickens, C. (1837) *The Posthumous Papers of the Pickwick Club*. London: Chapman and Hall.

Duan, H., Xia, L., He, W. et al. (2019). Accuracy of lateral cephalogram for diagnosis of adenoid hypertrophy and posterior upper airway obstruction: A meta-analysis. *International Journal of Pediatric Otorhinolaryngology* 119: 1–9.

Ferguson, K.A., Ono, T., Lowe, A.A. et al. (1996). A randomized crossover study of an oral appliance vs nasal-continuous positive airway pressure in the treatment of mild-moderate obstructive sleep apnea. *Chest* 109(5): 1269–1275.

Ferreira, A.M., Clemente, V., Gozal, D. et al. (2000). Snoring in Portuguese primary school children. *Pediatrics* 106(5): e64.

Ferris, B., Mead, J., and Opie, L. (1964). Partitioning of respiratory flow resistance in man. *Journal of Applied Physiology* 19: 653–658.

Fregosi, R.F., Quan, S.F., Kaemingk, K.L. et al. (2003). Sleep disordered breathing, pharyngeal size and soft tissue anatomy in children. *Journal of Applied Physiology* 95: 2030–2038.

Friedman, M., Salapatas, A.M., and Bonzelaar, L.B. (2017). Future perspectives in sleep surgery. *Advances in Otorhinolaryngology* 80: 148–154.

Gale, D.J., Sawyer, R.H., Woodcock, A. et al. (2000). Do oral appliances enlarge the airway in patients with obstructive sleep apnoea? A prospective computerized tomographic study. *European Journal of Orthodontics* 22: 159–168.

Galway, N.C., Maxwell, B., Shields, M. et al. (2021). Use of oximetry to screen for paediatric obstructive sleep apnoea: Is one night enough and is 6 hours too much? *Archives of Disease in Childhood* 106(1): 58–61.

Garg, R.K., Afifi, A.M., Garland, C.B. et al. (2017). Pediatric obstructive sleep apnea: Consensus, controversy, and craniofacial

considerations. *Plastic and Reconstructive Surgery* 140(5): 987–997.

Ghadiri, M., and Grunstein, R.R. (2020). Clinical side effects of continuous positive airway pressure in patients with obstructive sleep apnoea. *Respirology* 25(6): 593–602.

Goldhart, A.D., Krishna, J., Li, R.C. et al. (2006). Inflammatory mediators in exhaled breath condensate of children with obstructive sleep apnea syndrome. *Chest* 130(1): 143–148.

Gottlieb, D.J., Chase, C., Vezina, R.M. et al. (2004). Sleep-disordered breathing symptoms are associated with poorer cognitive function in 5-year-old children. *Journal of Pediatrics* 145: 458–464.

Gottlieb, D.J., and Young, T.B. (2009). Natural history of sleep-disordered breathing: Shedding light on the early years. *Sleep* 32(6): 715–716.

Gozal, D., and O'Brien, L.M. (2004). Snoring and obstructive sleep apnoea in children: Why should we treat? *Paediatric Respiratory Review* 5(Suppl A): S371–S376.

Gozal, D., and Pope, D.W. (2001). Snoring during early childhood and academic performance at ages thirteen to fourteen. *Pediatrics* 107: 1394–1399.

Griffith, J.L., Ramadan, H.H., and Wetmore, S.J. (1993). Laryngocele: A cause of stridor and airway obstruction. *Otolaryngology—Head and Neck Surgery* 108: 760–762.

Grippaudo, C., Paolantonio, E.G., Antonini, G. et al. (2016). Association between oral habits, mouth breathing and malocclusion. *Acta Otorhinolaryngologica Italica* 36(5): 386–394.

Guilleminault, C., Huseni, S., and Lo, L. (2016). A frequent phenotype for paediatric sleep apnoea: Short lingual frenulum. *ERJ Open Research* 2(3): 00043–2016.

Guilleminault, C., Parinen, M., Lollman, K. et al. (1995). Familial aggregates in obstructive sleep apnea syndrome. *Chest* 107: 1545–

1551.

Guilleminault, C., Sullivan, S.S., and Huang, Y.S. (2019). Sleep-disordered breathing, orofacial growth, and prevention of obstructive sleep apnea. *Sleep Medicine Clinics* 14(1): 13–20.

Guilleminault, C., van den Hoed, J., and Mitler, M. (1978). Clinical overview of the sleep apnea syndrome. In: C. Guilleminault and W.C. Dement (eds.), *Sleep Apnea Syndromes*. New York: Alan R. Liss, pp. 1–12.

Guye, A.A. (1889). On aprosexia, being the inability to fix attention and other allied troubles in the cerebral functions caused by nasal disorders. *British Medical Journal* 2(1500): 709–711.

Hall, G.L., Hantos, Z., Petak, F. et al. (2000). Airway and respiratory tissue mechanics in normal infants. *American Journal of Respiratory and Critical Care Medicine* 162: 1397–1402.

Handelman, C.S., and Osborne, G. (1976). Growth of the nasopharynx and adenoid development from one to eighteen years. *Angle Orthodontist* 46(3): 243–259.

Heath, D.S., El-Hakim, H., Al-Rahji, Y. et al. (2021). Development of a pediatric obstructive sleep apnea triage algorithm. *Journal of Otolaryngology & Head and Neck Surgery* 50(1): 48.

Hill, W. (1889). On some causes of backwardness and stupidity in children: And the relief of these symptoms in some instances by naso-pharyngeal scarifications. *British Medical Journal* 2(1500): 711–712.

Hoekema, A., Stegenga, B., and de Bont, L.G. (2004). Efficacy and co-morbidity of oral appliances in the treatment of obstructive sleep apnoea-hypopnoea: A systematic review. *Critical Reviews in Oral Biology & Medicine* 15(3): 137–155.

Hoffstein, V., and Szalai, J.P. (1993). Predictive value of clinical features in diagnosing obstructive sleep apnea. *Sleep* 16(2): 118–122.

Horner, R.L., Shea, S.A., McIvor, J. et al. (1989). Pharyngeal size and shape during wakefulness and sleep in patients with obstructive sleep apnoea. *QJM* 72: 719–735.

Hsu, P.P., Tan, A.K.L., Chan, Y.H. et al. (2005). Clinical predictors in obstructive sleep apnoea patients with calibrated cephalometric analysis—a new approach 1. *Clinical Otolaryngology* 30(3): 234–241.

Huang, Y.S., and Guilleminault, C. (2013). Pediatric obstructive sleep apnea and the critical role of oral-facial growth: Evidences. *Frontiers in Neurology* 3:184.

Hudgel, D.W. (1988). Palate and hypopharyx – sites of inspiratory narrowing of the upper airway during sleep. *American Review of Respiratory Diseases* 138: 1542–1547.

Iber, C., Ancoli-Israel, S., Chesson, A.L. et al. (2007). *The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications*. Westchester, IL: American Academy of Sleep Medicine.

Ingman, T., Nieminen, T., and Hurmerinta, K. (2004). Cephalometric comparison of pharyngeal changes in subjects with upper airway resistance syndrome or obstructive sleep apnoea in upright and supine positions. *European Journal of Orthodontics* 26: 321–326.

Isono, S., Shimada, A., Utsugi, M. et al. (1998). Comparison of static mechanical properties of the passive pharynx between normal children and children with sleep-disordered breathing. *American Journal of Respiratory and Critical Care Medicine* 157(4): 1204–1212.

Isono, S., Tanaka, A., Tagaito, Y. et al. (2004). Influences of head positions and bite opening on collapsibility of the passive pharynx. *Journal of Applied Physiology* 97: 339–346.

Issa, F.G., and Sullivan, C.E. (1984). Upper airway closing pressures in snorers. *Journal of Applied Physiology* 57: 528–535.

Iwasaki, T., Yoon, A., Guilleminault, C. et al. (2020). How does distraction osteogenesis maxillary expansion (DOME) reduce severity of obstructive sleep apnea? *Sleep and Breathing* 24(1):287–296.

Javaheri, S., Barbe, F., Campos-Rodriguez, F. et al. (2017). Sleep apnea: Types, mechanisms, and clinical cardiovascular consequences. *Journal of the American College of Cardiology* 69(7): 841–858.

Jehan, S., Zizi, F., Pandi-Perumal, S.R. et al. (2017). Obstructive sleep apnea and obesity: Implications for public health. *Sleep Medicine and Disorders* 1(4): 00019.

Johns, M.W. (1991). A new method for measuring daytime sleepiness: The Epworth Sleepiness Scale. *Sleep* 14(6): 540–545.

Johns, M.W. (1992). Reliability and factor analysis of the Epworth Sleepiness Scale. *Sleep* 15(4): 376–381.

Johnston, C.D., Gleadhill, I.C., Cinnamond, M.J. et al. (2002). Mandibular advancement appliances and obstructive sleep apnea: A randomized clinical trial. *European Journal of Orthodontics* 24(3): 251–262.

Jordan, A.S., and White, D.P. (2008). Pharyngeal motor control and the pathogenesis of obstructive sleep apnea. *Respiratory Physiology and Neurobiology* 160(1): 1–7.

Katyal, V., Pamula, Y., Martin, A.J. et al. (2013). Craniofacial and upper airway morphology in pediatric sleep-disordered breathing: Systematic review and meta-analysis. *American Journal of Orthodontics and Dentofacial Orthopedics* 143(1): 20–30.e3.

Katz, E.S., Mitchell, R.B., and D'Ambrosio, C.M. (2012). Obstructive sleep apnea in infants. *American Journal of Respiratory and Critical Care Medicine* 185(8): 805–816.

Katz, I., Stradling, J., Slutsky, A.S. et al. (1990). Do patients with obstructive sleep apnea have thick necks? *American Review of Respiratory Diseases* 141: 1228–1231.

Kaygisiz, E., Tuncer, B.B., Yüksel, S. et al. (2009). Effects of maxillary protraction and fixed appliance therapy on the pharyngeal airway. *Angle Orthodontist* 79(4): 660–667.

Kim, Y.J., Hong, J.S., Hwang, Y.I. et al. (2010). Three-dimensional analysis of pharyngeal airway in preadolescent children with different anteroposterior skeletal patterns. *American Journal of Orthodontics and Dentofacial Orthopedics* 137(3): 306.e1–11.

Kuang, B., Li, D., Lobbezoo, F. et al. (2022). Associations between sleep bruxism and other sleep-related disorders in adults: A systematic review. *Sleep Medicine* 89: 31–47.

Kumar, D.S., Valenzuela, D., Kozak, F.K. et al. (2014). The reliability of clinical tonsil size grading in children. *JAMA Otolaryngology & Head and Neck Surgery* 140(11): 1034–1037.

Kushida, C.A., Efron, B., and Guilleminault, C. (1997). A predictive morphometric model for the obstructive sleep apnea syndrome. *Annals of Internal Medicine* 127: 581–587.

Kushida, C.A., Littner, M.R., Morgenthaler, T. et al. (2005). Practice parameters for the indications for polysomnography and related procedures: An update for 2005. *Sleep* 28(4): 499–521.

Kushida, C.A., Morgenthaler, T.I., Littner, M. et al. (2006). Practice parameters for the treatment of snoring and obstructive sleep apnea with oral appliances: An update for 2005. *Sleep* 29(2): 240–243.

Kyzer, S., and Charuzi, I. (1998). Obstructive sleep apnea in the obese. *World Journal of Surgery* 22(9): 998–1001.

Larkin, E.K., Rosen, C.L., Kirchner, H.L. et al. (2005). Variation of C-reactive protein levels in adolescents: Association with sleep-disordered breathing and sleep duration. *Circulation* 111: 1978–1984.

Launois, S.H., Feroah, T.R., Campbell, W.N. et al. (1993). Site of pharyngeal narrowing predicts outcome of surgery for obstructive

sleep apnea. *American Review of Respiratory Disease* 147: 182–189.

Leach, J., Olson, J., Hermann, J. et al. (1992). Polysomnographic and clinical findings in children with obstructive sleep apnea. *Archives of Otolaryngology & Head and Neck Surgery* 118: 741–744.

Lee, C.H., Hong, S.L., Rhee, C.S. et al. (2012). Analysis of upper airway obstruction by sleep videofluoroscopy in obstructive sleep apnea: A large population-based study. *Laryngoscope* 122(1): 237–241.

Lee, C.H., Hsu, W.C., Chang, W.H. et al. (2016). Polysomnographic findings after adenotonsillectomy for obstructive sleep apnoea in obese and non-obese children: A systematic review and meta-analysis. *Clinical Otolaryngology* 41(5): 498–510.

Lee, H.M., Kang, D.W., Yun, P.Y. et al. (2021). Associations between mandibular torus and types of temporomandibular disorders, and the clinical usefulness of temporary splint for checking bruxism. *BMC Oral Health* 21(1): 182.

Li, A.M., Au, C.T., Ng, S.K. et al. (2010). Natural history and predictors for progression of mild childhood obstructive sleep apnoea. *Thorax* 65(1): 27–31.

Li, A.M., Chan, M.H., Yin, J. et al. (2008). C-reactive protein in children with obstructive sleep apnea and the effects of treatment. *Pediatric Pulmonology* 43(1): 34–40.

Li, C., Kou, Y.F., DeMarcantonio, M.A. et al. (2023). Sleep endoscopy and cine-magnetic resonance imaging evaluation of children with persistent obstructive sleep apnea. *Otolaryngology & Head and Neck Surgery* 168(4): 848–855.

Lim, J., Lasserson, T., Fleetham, J. et al. (2006). Oral appliances for obstructive sleep apnoea. *Cochrane Database of Systematic Reviews* 1: CD004435. doi: 10.1002/14651858.CD004435.pub3.

Liming, B.J., Ryan, M., Mack, D. et al. (2018). Montelukast and nasal corticosteroids to treat pediatric obstructive sleep apnea: A systematic review and meta-analysis. *Otolaryngology & Head and Neck Surgery* 160(4): 594–602.

Lin, H.C., Weaver, E.M., Lin, H.S. et al. (2017). Multilevel obstructive sleep apnea surgery. *Advances in Otorhinolaryngology* 80: 109–115.

Linder-Aronson, S. (1970). Adenoids: Their effect on mode of breathing and nasal airflow and their relationship to characteristics of the facial skeleton and the dentition. A biometric, rhinomanometric and cephalometro-radiographic study on children with and without adenoids. *Acta Otolaryngologica Supplement* 265: 1–132.

Linder-Aronson, S., and Leighton, B.C. (1983). A longitudinal study of the development of the posterior nasopharyngeal wall between 3 and 16 years of age. *European Journal of Orthodontics* 5(1): 47–58.

Liu, S.Y., Huon, L.K., Powell, N.B. et al. (2015). Lateral pharyngeal wall tension after maxillomandibular advancement for obstructive sleep apnea is a marker for surgical success: Observations from drug-induced sleep endoscopy. *Journal of Oral & Maxillofacial Surgery* 73(8): 1575–1582.

Liu, Y., Zeng, X., Fu, M. et al. (2000). Effects of a mandibular repositioner on obstructive sleep apnea. *American Journal of Orthodontics and Dentofacial Orthopedics* 118(3): 248–256.

Lowe, A.A., Fleetham, J.A., Adachi, S. et al. (1995). Cephalometric and computed tomographic predictors of obstructive sleep apnea severity. *American Journal of Orthodontics & Dentofacial Orthopedics* 107: 589–595.

Lowe, A.A., Fleetham, J.A., Ryan, F. et al. (1990). Effects of a mandibular repositioning appliance used in the treatment of obstructive sleep apnea on tongue muscle activity. *Progress in Clinical and Biological Research* 345: 395–405.

Lowe, A.A., Gionhaku, N., Takeuchi, K. et al. (1986). Three-dimensional CT reconstructions of tongue and airway in adult subjects with obstructive sleep apnea. *American Journal of Orthodontics & Dentofacial Orthopedics* 90(5): 364–374.

Malhotra, A., Trinder, J., Fogel, R. et al. (2004). Postural effects on pharyngeal protective reflex mechanisms. *Sleep* 27(6): 1105–1112.

Mallory, G.B., Fiser, D.H., and Jackson, R. (1989). Sleep associated breathing disorders in morbidly obese children and adolescents. *Journal of Pediatrics* 115: 892–897.

Marcus, C.L., Brooks, L.J., Draper, K.A. et al. (2012). Diagnosis and management of childhood obstructive sleep apnea syndrome. *Pediatrics* 130(3): 576–584.

Marcus, C.L., Keens, T.G., Baustista, D.B. et al. (1991). Obstructive sleep apnea in children with Down syndrome. *Pediatrics* 88: 132–139.

Marcus, C.L., Omlin, K.J., Basinski, D.J. et al. (1992). Normal polysomnographic values for children and adolescents. *American Review of Respiratory Disease* 146: 1235–1239.

Marklund, M., Persson, M., and Franklin, K.A. (1998). Treatment success with mandibular advancement device is related to supine-dependent sleep apnea. *Chest* 114(6): 1630–1635.

Marrone, O., and Bonsignore, M.R. (2020). Obstructive sleep apnea and cancer: A complex relationship. *Current Opinion in Pulmonary Medicine* 26(6): 657–667.

Mathur, R., and Douglas, N.J. (1995). Family studies in patients with the sleep apnea-hypopnea syndrome. *Annals of Internal Medicine* 122(3): 174–178.

McNicholas, W.T. (2002). Impact of sleep on respiratory muscle function. *Monaldi Archives for Chest Disease* 57(5–6): 277–280.

Mei, Z., Grummer-Strawn, L.M., Pietrobelli, A. et al. (2002). Validity of body mass index compared with other body-composition screening indexes for the assessment of body fatness in children

and adolescents. *American Journal of Clinical Nutrition* 75: 978–985.

Miles, P.G., Vig, P.S., Weyant, R.J. et al. (1996). Craniofacial structure and obstructive sleep apnea syndrome – a qualitative analysis and meta-analysis of the literature. *American Journal of Orthodontics & Dentofacial Orthopedics* 109: 163–172.

Mitchell, R.B., Pereira, K.D., and Friedman, N.R. (2006). Sleep-disordered breathing in children: Survey of current practice. *Laryngoscope* 116(6): 956–958.

Miyauchi, Y., Okazoe, H., Okujyo, M. et al. (2015). Effect of the continuous positive airway pressure on the nocturnal urine volume or night-time frequency in patients with obstructive sleep apnea syndrome. *Urology* 85(2): 333–336.

Morrison, D.L., Launois, S.H., Isono, S. et al. (1993). Pharyngeal narrowing and closing pressures in patients with obstructive sleep apnea. *American Review of Respiratory Disease* 148: 606–611.

Ng, J.H., and Yow, M. (2020). Oral appliances in the management of obstructive sleep apnea. *Sleep Medicine Clinics* 15(2): 241–250.

Ogawa, T., Enciso, R., Shintaku, W.H. et al. (2007). Evaluation of cross-section airway configuration of obstructive sleep apnea. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics* 103(1): 102–108.

Oktay, H., and Ulukaya, E. (2008). Maxillary protraction appliance effect on the size of the upper airway passage. *Angle Orthodontist* 78(2): 209–214.

Palm, E., Franklin, K.A., and Marklund, M. (2014). Mandibular tori size is related to obstructive sleep apnea and treatment success with an oral appliance. *Sleep and Breathing* 18(2): 431–438.

Partinen, M., Guilleminault, C., Quera-Salva, M.A. et al. (1988). Obstructive sleep apnea and cephalometric roentgenograms. The role of anatomic upper airway abnormalities in the definition of abnormal breathing during sleep. *Chest* 93: 1199–1205.

Patel, J.A., Ray, B.J., Fernandez-Salvador, C. et al. (2018). Neuromuscular function of the soft palate and uvula in snoring and obstructive sleep apnea: A systematic review. *American Journal of Otolaryngology* 39(3): 327–337.

Pracharktam, N., Hans, M.G., Strohl, K.P. et al. (1994). Upright and supine cephalometric evaluation of obstructive sleep apnea syndrome and snoring subjects. *Angle Orthodontist* 64: 63–73.

Puvanendran, K., Thomas, M.N., and Chien, H.H. (2020). Sleep bruxism can be a harbinger of sleep disordered breathing. *Neurology Asia* 25(2): 183–187.

Remmers, J.E., DeGrott, W.T., Sauerland, E.K. et al. (1978). Pathogenesis of upper airway occlusion during sleep. *Journal of Applied Physiology* 44(6): 931–938.

Resta, O., Foschino-Barbaro, M.P., Legari, G. et al. (2001). Sleep-related breathing disorders, loud snoring and excessive daytime sleepiness in obese subjects. *International Journal of Obesity and Related Metabolic Disorders* 25(5): 669–675.

Ricketts, R.M. (1954). The cranial base and soft structures in cleft palate speech and breathing. *Plastic and Reconstructive Surgery* 14: 47–61.

Riley, R., Guilleminault, C., Herran, J. et al. (1983). Cephalometric analyses and flow-volume loops in obstructive sleep apnea patients. *Sleep* 6(4): 303–311.

Roberts, J.L., Reed, W.R., Mathew, O.P. et al. (1985). Assessment of pharyngeal airway stability in normal and micrognathic infants. *Journal of Applied Physiology* 58: 290–299.

Roberts, J.L., Reed, W.R., Mathew, O.P. et al. (1986). Control of respiratory activity of the genioglossus muscle in micrognathic infants. *Journal of Applied Physiology* 61(4): 1523–1533.

Russell, M.B., Kristiansen, H.A., and Kværner, K.J. (2014). Headache in sleep apnea syndrome: Epidemiology and pathophysiology. *Cephalalgia* 34(10): 752–755.

Saboisky, J.P., Butler, J.E., Gandevia, S.C. et al. (2012). Functional role of neural injury in obstructive sleep apnea. *Frontiers in Neurology* 15(3): 95.

Savini, S., Ciorba, A., Bianchini, C. et al. (2019). Assessment of obstructive sleep apnoea (OSA) in children: An update. *Acta Otorhinolaryngologica Italica* 39(5): 289–297.

Sawunyavisuth, B., Ngamjarus, C., and Sawanyawisuth, K. (2021). Any effective intervention to improve CPAP adherence in children with obstructive sleep apnea: A systematic review. *Global Pediatric Health* 8: 2333794X211019884.

Scammon, R. (1930). The measurement of the body in childhood. In: J.A. Harris, C.M. Jackson, D.G. Paterson et al. (eds.), *The Measurement of Man*. Minneapolis, MN: University of Minnesota Press, pp. 173–215.

Schmidt-Nowara, W., Lowe, A.A., Wiegand, L. et al. (1995). Oral appliances for the treatment of snoring and obstructive sleep apnea: A review. *Sleep* 18(6): 501–510.

Schulof, R.J. (1978). Consideration of airway in orthodontics. *Journal of Clinical Orthodontics* 12: 440–444.

Schwab, R.J. (2003). Pro: Sleep apnea is an anatomic disorder. *American Journal of Respiratory and Critical Care Medicine* 168(3): 270–271.

Schwab, R.J., Gefter, W.B., Hoffman, E.A. et al. (1993). Dynamic upper airway imaging during awake respiration in normal subjects and patients with sleep disordered breathing. *American Review of Respiratory Disease* 148: 1385–1400.

Schwab, R.J., Kuna, S.T., and Remmers, J.E. (2005). Anatomy and physiology of upper airway obstruction. In: M.H. Kryger, T. Roth, and W.C. Dement (eds.), *Principles and Practice of Sleep Medicine*, 4th ed. Philadelphia, PA: Elsevier/W.B. Saunders, pp. 983–1000.

Schwab, R.J., Pasirstein, M., Pierson, R. et al. (2003). Identification of upper airway anatomic risk factors for obstructive sleep apnea

with volumetric magnetic resonance imaging. *American Journal of Respiratory and Critical Care Medicine* 168: 522–530.

Seif-Eldin, N.F., Elkordy, S.A., Fayed, M.S. et al. (2019). Transverse skeletal effects of rapid maxillary expansion in pre and post pubertal subjects: A systematic review. *Macedonian Journal of Medical Sciences* 7(3): 467–477.

Sériès, F. (2002). Upper airway muscles awake and asleep. *Sleep Medicine Review* 6(3): 229–242.

Shah, F., and Stål, P. (2022). Myopathy of the upper airway in snoring and obstructive sleep apnea. *Laryngoscope Investigative Otolaryngology* 7(2):636–645.

Shakespeare, W. (1987) *The Tempest*, ed. S. Orgel. Oxford: Oxford University Press, first published c. 1611.

Shepard, J.W., Jr., and Thawley, S.E. (1989). Evaluation of the upper airway by computerized tomography in patients undergoing uvulopalatopharyngoplasty for obstructive sleep apnea. *American Review of Respiratory Disease* 140: 711–716.

Silvestri, J.M., Weese-Mayer, D.E., Bass, M.T. et al. (1993). Polysomnography in obese children with a history of sleep-associated breathing disorders. *Pediatric Pulmonology* 16: 124–129.

Smith, D.L., Gozal, D., Hunter, S.J. et al. (2017). Frequency of snoring, rather than apnea-hypopnea index, predicts both cognitive and behavioral problems in young children. *Sleep Medicine* 34:170–178.

Strauss, R.A., and Burgoyne, C.C. (2008). Diagnostic imaging and sleep medicine. *Dental Clinics of North America* 52(4): 891–915.

Suto, Y., Matsuo, T., Kato, T. et al. (1993). Evaluation of the pharyngeal airway in patients with sleep apnea: Value of ultrafast MR imaging. *American Journal of Roentgenology* 160: 311–314.

Suzuki, M., and Kirchner, J.A. (1969). The posterior cricoarytenoid as an inspiratory muscle. *Annals of Otology, Rhinology and*

Laryngology 78: 849–864.

Tan, Y.H., How, C.H., Chan, Y.H. et al. (2020). Approach to the snoring child. *Singapore Medical Journal* 61(4): 170–175.

Teculescu, D., Hannhart, B., Cornette, A. et al. (2001). Prevalence of habitual snoring in a sample of French males. Role of "minor" nose-throat abnormalities. *Respiration* 68(4): 365–370.

Tishler, P.V., Larkin, E.K., Schluchter, M.D. et al. (2003). Incidence of sleep-disordered breathing in an urban adult population: The relative importance of risk factors in the development of sleep-disordered breathing. *Journal of the American Medical Academy* 289(17): 2230–2237.

Trosman, I. (2013). Childhood obstructive sleep apnea syndrome: A review of the 2012 American Academy of Pediatrics guidelines. *Pediatric Annals* 42(10):195–199.

Trudo, F.J., Gefter, W.B., Welch, K.C. et al. (1998). State-related changes in upper airway caliber and surrounding soft tissue structures in normal subjects. *American Journal of Respiratory and Critical Care Medicine* 158: 1259–1270.

Tveit, R.L., Lehmann, S., and Bjorvatn, B. (2018) Prevalence of several somatic diseases depends on the presence and severity of obstructive sleep apnea. *PLoS One* 13(2): e0192671.

van Bunningen, R.H., Dijkstra, P.U., Dieters, A. et al. (2022). Precision of orthodontic cephalometric measurements on ultra-low low-dose CBCT reconstructed cephalograms. *Clinical Oral Investigations* 26(2): 1543–1550.

Vargervik, K., Miller, A.J., Chierici, G. et al. (1984). Morphologic response to changes in neuromuscular patterns experimentally induced by altered modes of respiration. *American Journal of Orthodontics* 85: 115–124.

Venekamp, R.P., Hearne, B.J., Chandrasekharan, D. et al. (2015). Tonsillectomy or adenotonsillectomy versus non-surgical management for obstructive sleep-disordered breathing in

children. *Cochrane Database of Systematic Reviews* 14(10): CD011165. doi: 10.1002/14651858.CD011165.pub2.

Verhulst, S.L., van Gaal, L., de Backer, W. et al. (2008). The prevalence, anatomical correlates and treatment of sleep-disordered breathing in obese children and adolescents. *Sleep Medicine Review* 12: 339–346.

Villa, M.P., Bernkopf, E., Pagani, J. et al. (2002). Randomized controlled study of an oral jaw-positioning appliance for the treatment of obstructive sleep apnea in children with malocclusion. *American Journal of Respiratory and Critical Care Medicine* 165(1): 123–127.

Villa, M.P., Malagola, C., Pagani, J. et al. (2007). Rapid maxillary expansion in children with obstructive sleep apnea syndrome: 12-month follow-up. *Sleep Medicine* 8: 128–134.

Viva, E., Stefini, S., Annibale, G. et al. (1992). Aspects of prevention of obstructive sleep apnea syndrome in developing children. *Advances in Otorhinolaryngology* 47: 284–289.

Weaver, T.E., and Grunstein, R.R. (2008). Adherence to continuous positive airway pressure therapy: The challenge to effective treatment. *Proceedings of the American Thoracic Society* 5(2): 173–178.

Weitzman, E.D., Pollak, C.P., Borowiecki, B. et al. (1978). The hypersomnia-sleep apnea syndrome: Site and mechanism of upper airway obstruction. In: C. Guilleminault and W.D. Dement (eds.), *Sleep Apnea Syndromes*. New York: Alan R. Liss, pp. 235–248.

Wellman, A., Genta, P.R., Owens, R.L. et al. (2014). Test of the Starling resistor model in the human upper airway during sleep. *Journal of Applied Physiology* 117(12): 1478–1485.

White, D.P., Lombard, R.M., Cadieux, R.J. et al. (1985). Pharyngeal resistance in normal humans: Influence of gender, age, and obesity. *Journal of Applied Physiology* 58: 365–371.

White, S.C., and Pharoah, M.J. (2008). The evolution and application of dental maxillofacial imaging modalities. *Dental Clinics of North America* 52(4): 689–705.

WHO Expert Consultation (2004). Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet* 363(9403): 157–163.

Wyke, B. (1974). Respiratory activity of intrinsic laryngeal muscles. An experimental study. In: B.D. Wyke (ed.), *Ventilatory and Phonatory Control Systems*. London: Oxford University Press, pp. 408–421.

Young, T., Plata, M., Dempsey, J. et al. (1993). The occurrence of sleep-disordered breathing among middle-aged adults. *New England Journal of Medicine* 328: 1230–1235.

Yow, M. (2009). An overview of oral appliances and management of the airway in obstructive sleep apnea. *Seminars in Orthodontics* 15(2): 88–93.

Yu, M.S., Ibrahim, B., Riley, R.W. et al. (2020). Maxillomandibular advancement and upper airway stimulation: Extrapharyngeal surgery for obstructive sleep apnea. *Clinical and Experimental Otorhinolaryngology* 13(3): 225–233.

Zaghi, S., Holty, J.E., Certal, V. et al. (2016). Maxillomandibular advancement for treatment of obstructive sleep apnea: A meta-analysis. *JAMA Otolaryngology & Head and Neck Surgery* 142(1): 58–66.

12
Interaction between the Orthodontist and Medical Airway Specialists on Respiratory and Nonrespiratory Disturbances

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Summary

The mouth is anatomically at the center of the region in which medical airway specialists (otolaryngologists, pulmonologists, maxillofacial and sleep surgeons) operate, thus their interacting with the orthodontist on diverse conditions is natural and often necessary. In this chapter, we focus on the main areas of collaboration by teams engaging the different specialists at various stages of intervention. The topics include (i) impaired nasal breathing, its consequences on craniofacial morphology, and the prevention or treatment of associated dysmorphologies; (ii) sleep-disordered breathing, concentrating on the use of mandibular advancement devices in the treatment of obstructive sleep apnea (OSA); (iii) nonrespiratory areas of interaction with ear, nose, and throat specialists such as otitis media and craniofacial anomalies; and (iv) the association between voice and speech. Specifically, the anatomical relations between mouth, nose, ear, and throat are reviewed. Most prominent among conditions requiring collaboration with the otorhinolaryngologist is airway obstruction. The evidence for early adenoidectomy and/or tonsillectomy to avoid the harmful effects of blocked airways on facial morphology and function yielded applicable guidelines, some of which require further exploration. The potential and limitations of the orthodontist's role in OSA treatment are exposed. Conductive hearing loss may be improved by maxillary expansion, but further research should validate this potential. Ear pain is a ground for cooperation, particularly when the temporomandibular joint is affected. Novel findings on the interface between voice and speech are presented. The integration of orthodontics into medical airway specialties is further recognized because of the necessary multidisciplinary treatment realized through advances in knowledge, diagnosis, research, and education.

For breath is life, so if you breathe well you will live long on earth.

(Sanskrit proverb)

Breathing is taken for granted as a common behavior essential for life, yet it is seamless, discreet, nonintrusive, and nonscheduled. It has been equated with life itself: it connects the living person to existence by providing oxygen to the body. Breathing also reflects present body status, expressions, and emotions, its tempo changing with relaxation, effort, mood, joy, anger, fear, exercise, and every other beat of life. This core function requires a properly operating inhalation–exhalation system, from nose to lung. Structural interferences, mechanical (e.g. nasal obstruction) or pathological (e.g. cold), compromise the normal air flow, requiring the body to adjust, typically by switching to oral breathing, with variable consequences on local maxillofacial anatomy and general health.

In this chapter, respiratory impairments and their consequences on oral morphology and functions are presented within the perspective of integrated therapy requiring the input of orthodontists and medical airway specialists. The obvious reason for the important interaction between the orthodontist, otolaryngologist, and pulmonary specialist is the critical position of the mouth between the nose, throat, and lungs.

The mouth in relation to the nasopharyngeal airway: Anatomy overview

The posterior boundary of the oral cavity comprises two pairs of folds of mucous membrane that cover two palatal muscles, the palatoglossus and the palatopharyngeus (Figure 12.1). The tonsils lie between these folds, which provide the contour of an opening, the exit from the oral cavity (fauces) to the pharyngeal area. Located in the roof of the nasopharynx, anterior to the basiocciput and inferior to the sphenoid, the adenoids are a mass of lymphoid tissue that merges with the lymphoid tissue of the fossa of Rosenmuller near the opening of the Eustachian tube, which connects to the ear. The tonsils (palatine or faucial tonsils) and the adenoids (pharyngeal tonsils) are part of Waldeyer's tonsillar ring (or pharyngeal lymphoid ring), which also includes the tubal tonsil where the Eustachian tube opens in the nasopharynx and the lingual tonsils.

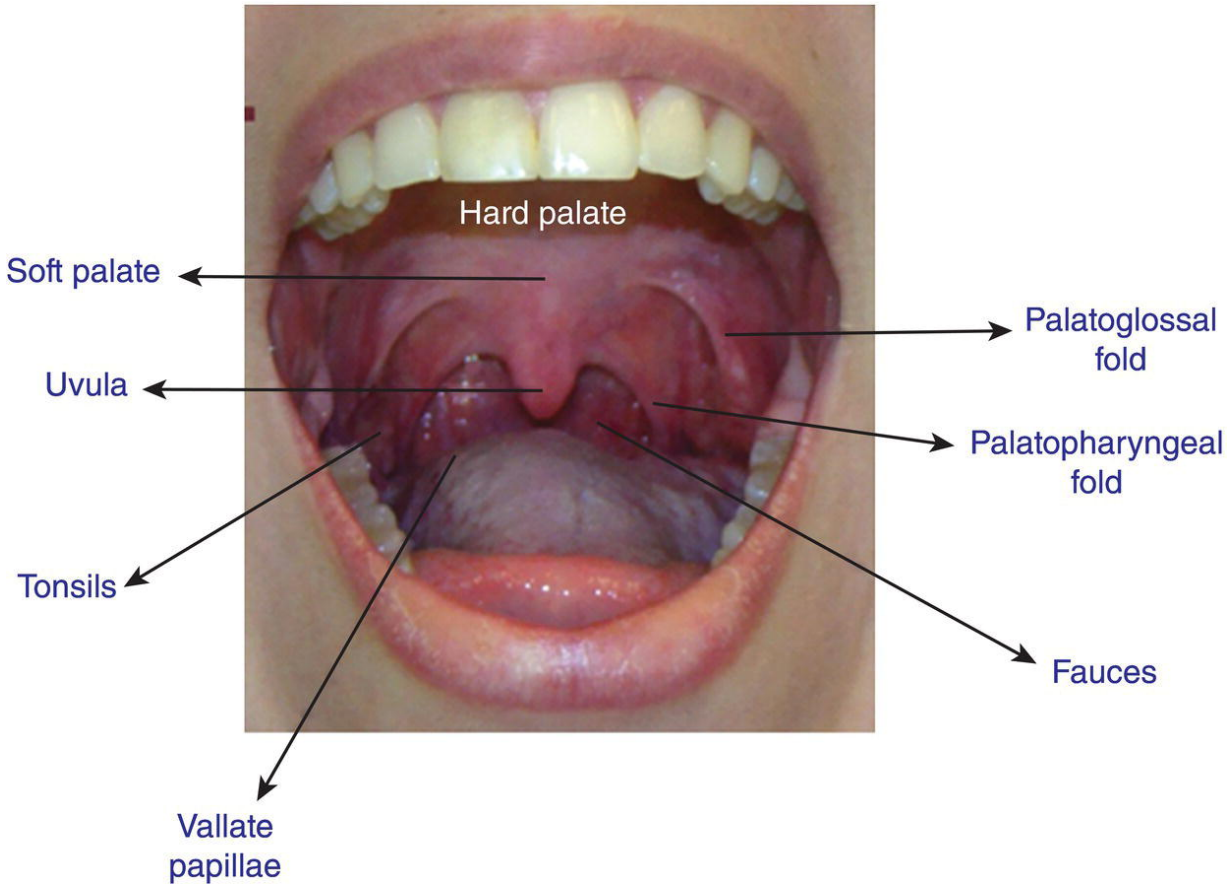


Figure 12.1 Anatomical structures in the mouth: oral and pharyngeal soft tissues.

At the gate of the upper respiratory and alimentary tracts where they are constantly exposed to antigens, the tonsils and adenoids are mostly composed of immunologically reactive lymphoid tissue, which contains antibody-producing lymphocytes, and are related to sounder immune status and the general health of patients, carrying out the functions of humoral and cellular immunity (Hata et al., 1996; Valtonen et al., 2000; Kaygusuz et al., 2009). Inflammation or hypertrophy of the adenoids and tonsils is caused by hypofunction of local and systemic immunity. Although still debated, particularly regarding the timing of surgery relative to the patient's age, findings indicate that removal of the lymphoid tissues has no adverse effect on immunity (Marcano-Acuña et al., 2019). Research is not available to support the theory that the adenoids and tonsils initially developed in nonurban, somewhat isolated environments to combat relatively uncommon types of infections, and that these tissues

become a health liability because they may not cope with the various viral infections attacking children in urban areas.

The development of the adenoids is unique among major tissues of the body: they increase in size to a peak of approximately twice the adult size around puberty, then decrease to near total regression in most adults (Figure 12.2; Scammon et al., 1930; Linder-Aronson and Leighton, 1983). The nasopharynx enlarges to accommodate the growing adenoids, thus maintaining a patent nasopharyngeal airway (Macari and Haddad, 2016). Any imbalance between the developing airway and the concomitant adenoid growth may result in nasopharyngeal obstruction or reduced potency. Some reports indicate that the lymphoid tissues do not follow a specific growth curve, but respond individually to different environmental factors (Macari and Haddad, 2016).

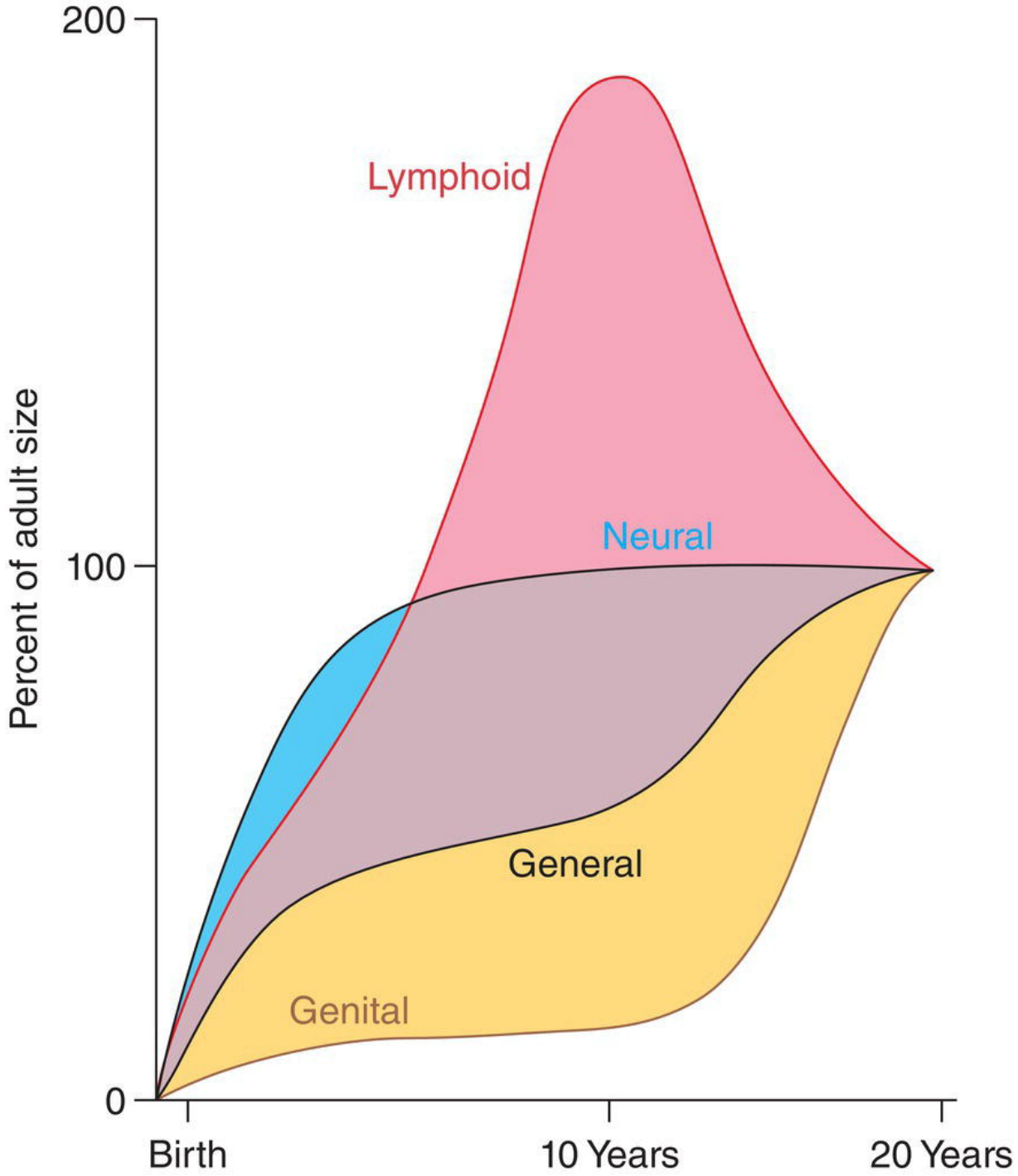


Figure 12.2 Scammon's curves: percentile of adult size of the neural, general, genital, and lymphoid tissues against age.

The nasal cavity extends from the nostrils anteriorly and the choanae posteriorly and is divided into halves by the septum, which is formed by the perpendicular plate of the ethmoid bone above, the vomer

bone posteriorly, and an extensive cartilage anteriorly (Figure 12.3). The roof of the nasal cavity is constituted by the ethmoidal cribriform plate, through which olfactory nerves enter the nasal cavity. The lateral walls comprise three bony shelf-like conchae or turbinates, which are covered with highly vascular mucous membranes (Figure 12.3). Air is heated and humidified past the conchae during breathing.

Beneath each concha is a meatus that opens the nasal cavity to the bilateral paranasal sinuses, which are membrane-lined cavities within the frontal, maxillary, ethmoid, and sphenoid bones (Figure 12.3). The ethmoid sinus contains a series of small, interconnected air cells instead of a single hollow space. The sinuses communicate with the nasal cavity at the level of the superior and middle meatuses and lateral walls of the cavity. Whereas none of the paranasal sinuses opens into the inferior meatus, the nasolacrimal duct does. Thus, tears produced in the eye by the lacrimal (and other) glands are collected into this duct and enter the nasal cavities.

The function of the paranasal sinuses has been subject to various hypotheses: lightening the housing bones, acting as resonance chambers during speaking, or, as we suggest, being part of the adaptation process to the oropharyngeal capsular matrix, as defined by Moss (Moss and Salentijn, 1969; Macari et al., 2012; see the later section on impaired nasal breathing).

Common sources of airway dysfunction

Tonsils and adenoids present a health problem when they become the nest of continuous infections. Particularly in children, hypertrophy of these tissues is a primary cause of nasal airway obstruction, leading to mouth breathing that in turn may affect facial morphology. Other consequences include nasal voice, snoring, and restless sleep (and associated learning problems if chronic). Considering their critical anatomical position, hypertrophied adenoids may affect nasal function and obstruct the Eustachian tubes, participating in the formation of middle ear effusions. In the rare condition when hypertrophied tonsils touch or meet in the midline, they are called “kissing tonsils.”

Impaired nasal breathing

Enlarged adenoids and tonsils are the most common obstructive agents of the posterior pharyngeal airway. Other causes that raise nasal resistance involve hard tissues, such as a deviated septum; turbinate irregularities; and congenital, traumatic, or therapeutic asymmetries of the nasal cavity; and soft tissues, such as catarrhal and allergic rhinitis and nasal polyps (Figure 12.4; Macari and Haddad, 2016).

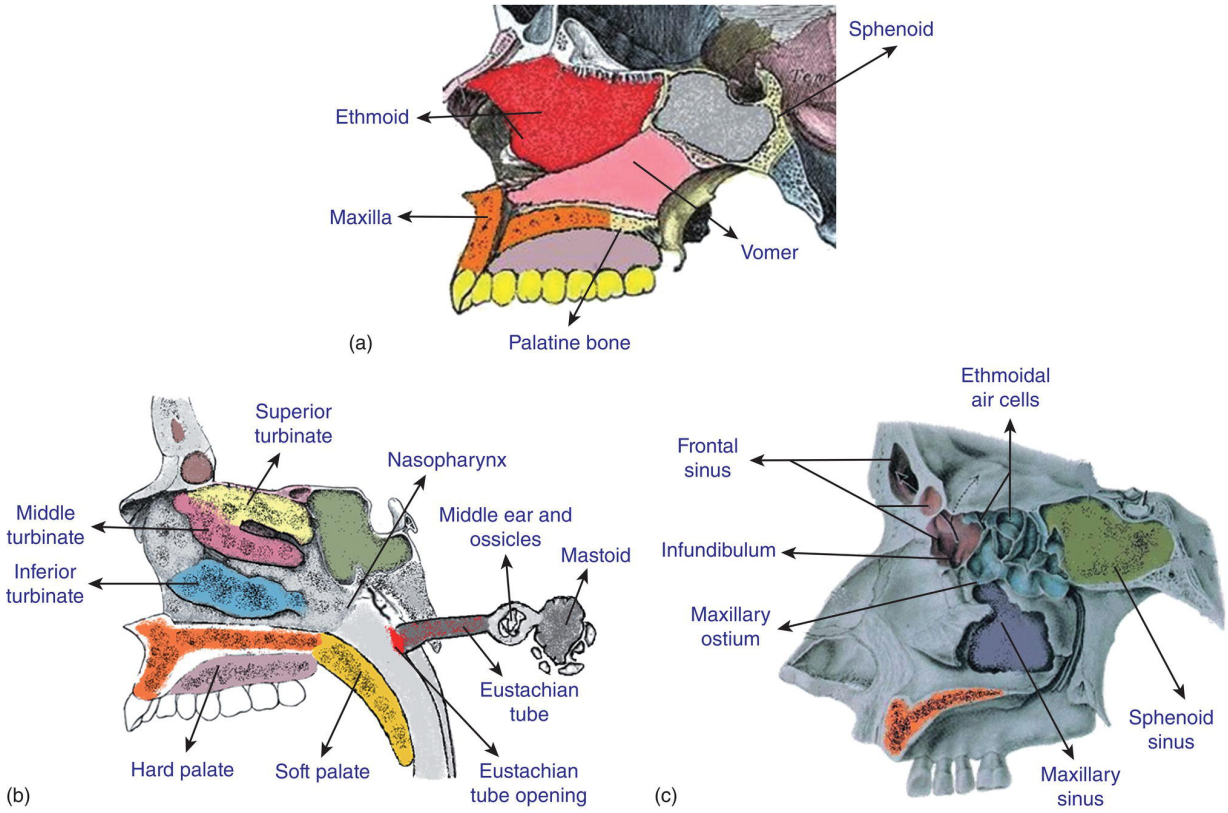


Figure 12.3 Anatomical structures in the face. (a) Sagittal near-midline; (b) lateral; and (c) cross-sections through oral and nasal hard tissues.

Source: (c) Adapted from Moore (1992), Figure 7, with permission of Lippincott, Williams and Wilkins.

Methods of evaluating airway obstruction

Airway assessment

Tonsillar hypertrophy is readily diagnosed clinically, and its cephalometric determination is only corroborative (Figure 12.4). Cephalometric imaging and the more intrusive endoscopic examination are more common in diagnosing adenoid hypertrophy. Cephalometric assessment of the nasopharyngeal airway may be through subjective rating or direct measurement of defined distances. In one of the various grading systems based on direct observation of the adenoid within the pharyngeal space, three grades were defined by estimating the space that the adenoid occupies between the posterior cranial base and the soft palate:

- Grade 1: less than 50% of the airway is obstructed (Figure 12.5a–c).
- Grade 2: more than 50% but less than 100% of the airway is blocked (Figure 12.5d–f)
- Grade 3: Near total to total obstruction is observed (Figure 12.5g–i).

The adenoids have been evaluated from two-dimensional (2D) cephalographs that simplify the imaging of three-dimensional (3D) structures. Moderate to high correlations ($0.60 < r < 0.88$) were reported between cephalometric assessment and the endoscopic evaluation of actual obstruction or the actual size of excised lymphoid tissue (Major et al., 2006). Cephalometric measurements of the shortest distance between adenoid and soft palate (SAD) and the distance between the maximum convexity point and soft palate (CAD) correlated best with actual size (Figure 12.6). A high correlation was reported between SAD and CAD ($r = 0.915$; Bitar et al., 2010). Moderate to high correlations between the airway grading and SAD and CAD measurements ($r = -0.73$ and $r = -0.79$, respectively) account for the correspondence of evaluation in half to two-thirds of the studied population (Bitar et al., 2010).

The 3D imaging of the nasopharyngeal space and structures yields more accurate information (Major et al., 2014). Visualization and volumetric quantification of the airway are achieved through specialized software applied on computed tomography (CT) and cone

beam computed tomography (CBCT) 3D images of the pharyngeal airway space in multiple planes (axial, coronal, and sagittal; Figure 12.7; Major et al., 2014; Brunetto et al., 2014; Tikku et al., 2016; Alsufyani et al., 2017). However, controversies persist, because defining the 3D volume may only be relevant at the "bottle neck," the narrowest bridge between adenoids and soft palate, corresponding to the most constricted region at the base of the tongue (El and Palomo, 2013). Extending measurements to the limits of the larynx in CBCT studies (Kim et al., 2010; El and Palomo, 2013) may also be clinically impractical, because no statistically significant differences were found between the 3D CBCT and 2D cephalometric groups in the cross-sectional area (Major et al., 2014). Further research is warranted to correlate diagnostic 3D findings with treatment outcome.

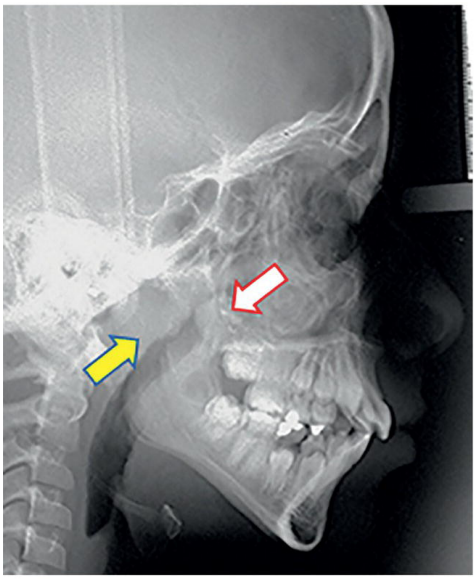
When cephalometric adenoid rating is negative, the ear, nose, and throat (ENT) specialist may resort to other means of assessment (endoscopy) to investigate other obstructive causes (e.g. enlarged turbinates), which is shown more in detail in Chapter 11. In all instances, the decision on the removal of adenoids and tonsils is based on clinical symptoms, not only the assessment of hypertrophy.

Assessment of mouth breathing

Unless it is obvious to the orthodontist or the ENT specialist in the clinical setting, the appraisal of mouth breathing often is based on subjective reporting by the patient or parents, usually figuring on the health history questionnaire, with inquiry on its occurrence during the day, night, or both. The association between mouth breathing and cephalometric measurement of airway clearance (SAD, CAD) indicates the significance of the radiographic record, but does not meet the requirement of validated quantitative evaluation of respiration. Means to generate objective evidence, such as rhinometry, nasal flow, and nasal resistance, have yet to be proven effective or practical for determining mouth breathing (Fujimoto et al., 2009; Ovsenik, 2009). The variation in frequency, duration, and intensity of oral breathing probably accounts for differing outcomes of these quantitative measurements.

Effect of airway obstruction on facial and occlusal morphology

The impact of airway impairment on dentofacial morphology has been evaluated extensively (Linder-Aronson et al., 1986, 1993; Kerr et al., 1989; Behlfelt et al., 1990; Woodside et al., 1991; Valera et al., 2003; Mattar et al., 2004). In the pioneering days of orthodontics, Edward H. Angle (1907) emphasized the consideration of not only the peculiarities of the occlusion and the relations of the jaws, but also the "condition of the throat and nose [and] habits of the patient." Angle accounted for mouth breathing in classifying the Class II Division 1 malocclusion as "always accompanied and, at least in its early stages, aggravated, if not indeed caused by mouth breathing due to some form of nasal obstruction," and the deformities under Class III beginning "at about the age of the eruption of the first permanent molars, or even much earlier, and always associated at this age with enlarged tonsils and the habit of protruding the mandible, the latter probably affording relief in breathing." Yet the nature of these associations requires further definition.



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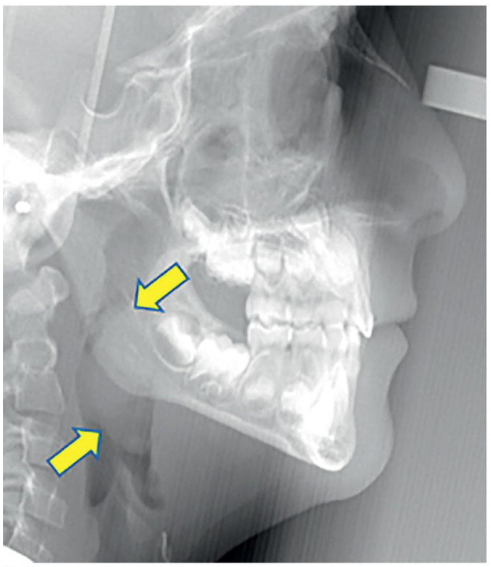

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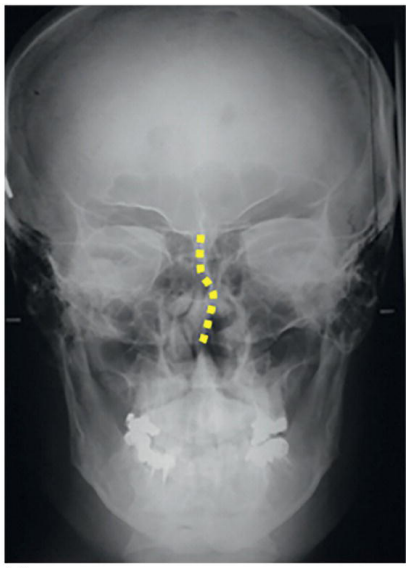

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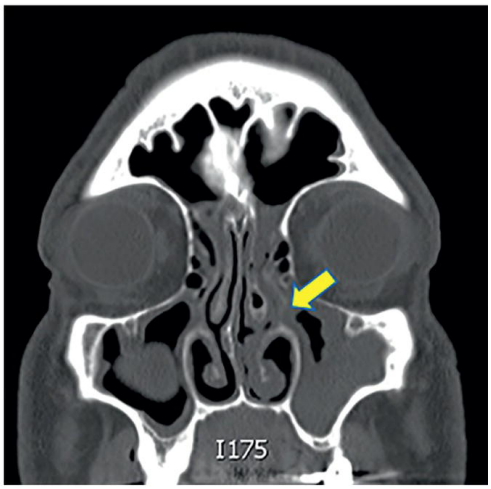

(f)

Figure 12.4 (a) Lateral cephalometric radiograph of a patient 10 years 7 months old, showing the hypertrophied adenoid (yellow arrow) and the posterior extension of the inferior turbinate toward the posterior wall of the nasopharynx (white arrow), causing obstruction of the airway. (b) Bilateral obstruction of the airway by the hypertrophied inferior turbinates (right and left, arrows) shown on a postero-anterior cephalogram. On endoscopic otolaryngological examination, the diagnosis of inferior turbinate hypertrophy was confirmed, and medication (nasal topical steroids) improved breathing. (c) Hypertrophied tonsils (arrows) in a boy 5 years 6 months old whose adenoids had been removed two years earlier. (d) Septal deviation: S-shaped deviation of the nasal septum shown on a postero-anterior cephalograph. (e, f) Cephalometric radiograph (e) of a 14-year-old chronic mouth-breathing patient with hyperdivergent vertical pattern but positive clinical overbite (30%). Note the hypertrophic adenoids, and a unilateral nasal polyp (yellow circle) that contributed to nasal obstruction. A computed tomography scan (f) revealed the extension of the polyp (arrow) from the sinus.

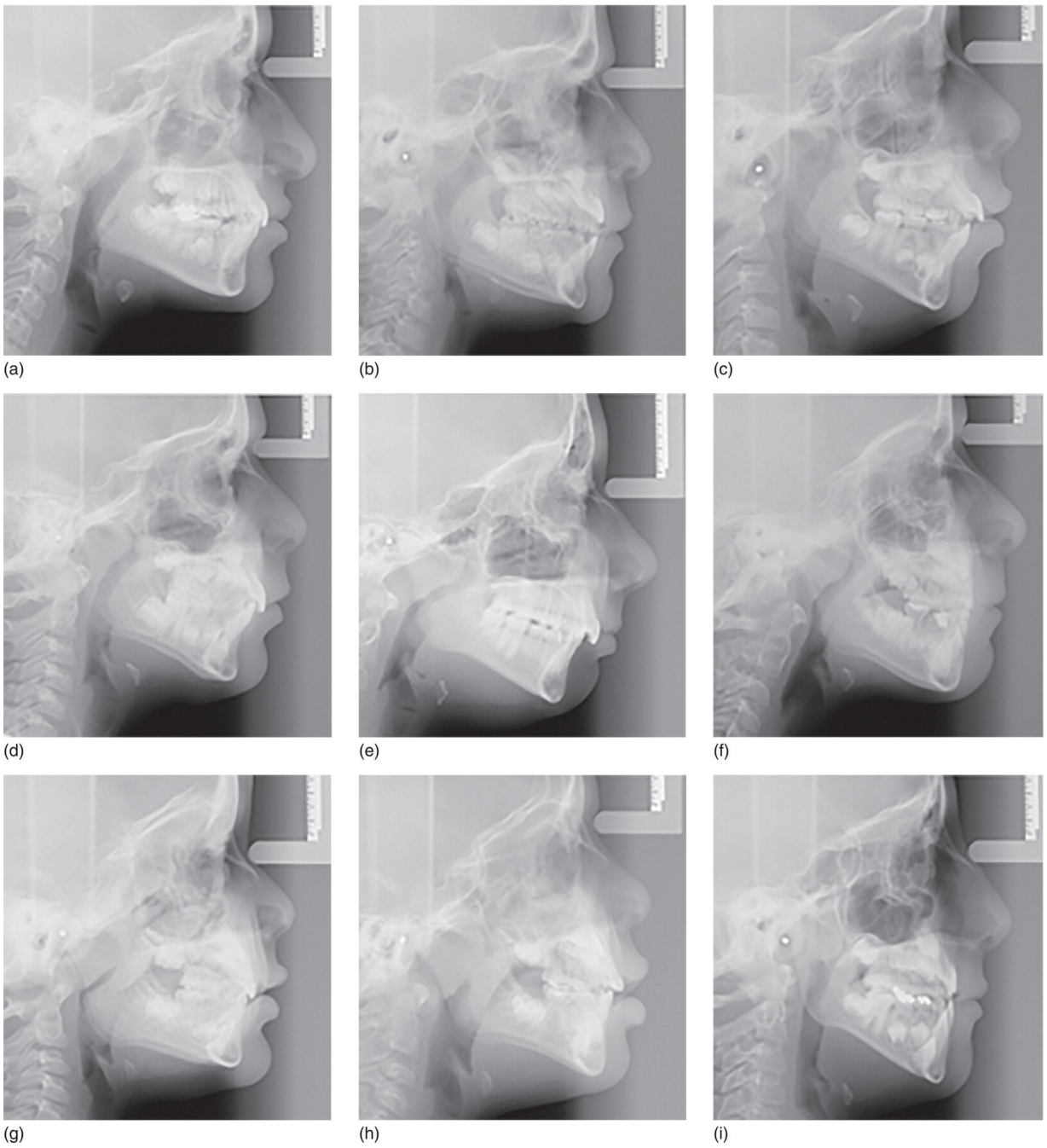

Figure 12.5 Grades of adenoid hypertrophy from less severe (Grade 1) to most severe (Grade 3) are illustrated along with various corresponding types of malocclusion. (a–c) Grade 1; (d–f) Grade 2; (g–i) Grade 3. This variation reflects the individual potentials for adaptation documented in animal (Harvold et al., 1981) and human (Macari et al., 2012) research.

The facial dysmorphology resulting from airway obstruction by

adenoid hypertrophy has been termed “adenoid facies” (Angle, 1907), synonymous with “long face syndrome” (LFS; Angle, 1907; Proffit, 2007) and a “high angle” facial pattern. Children who need adenoidectomy have been reported to have a longer facial height, a steeper mandibular plane angle, and a more retrognathic mandible than corresponding controls (Linder-Aronson et al., 1986; Kerr et al., 1989; Behlfelt et al., 1990; Woodside et al., 1991). Likewise, children with enlarged tonsils were reported to have more retrognathic and superior-posteriorly inclined mandibles, greater anterior total and lower facial heights, and increased mandibular plane angles (Behlfelt et al., 1990).

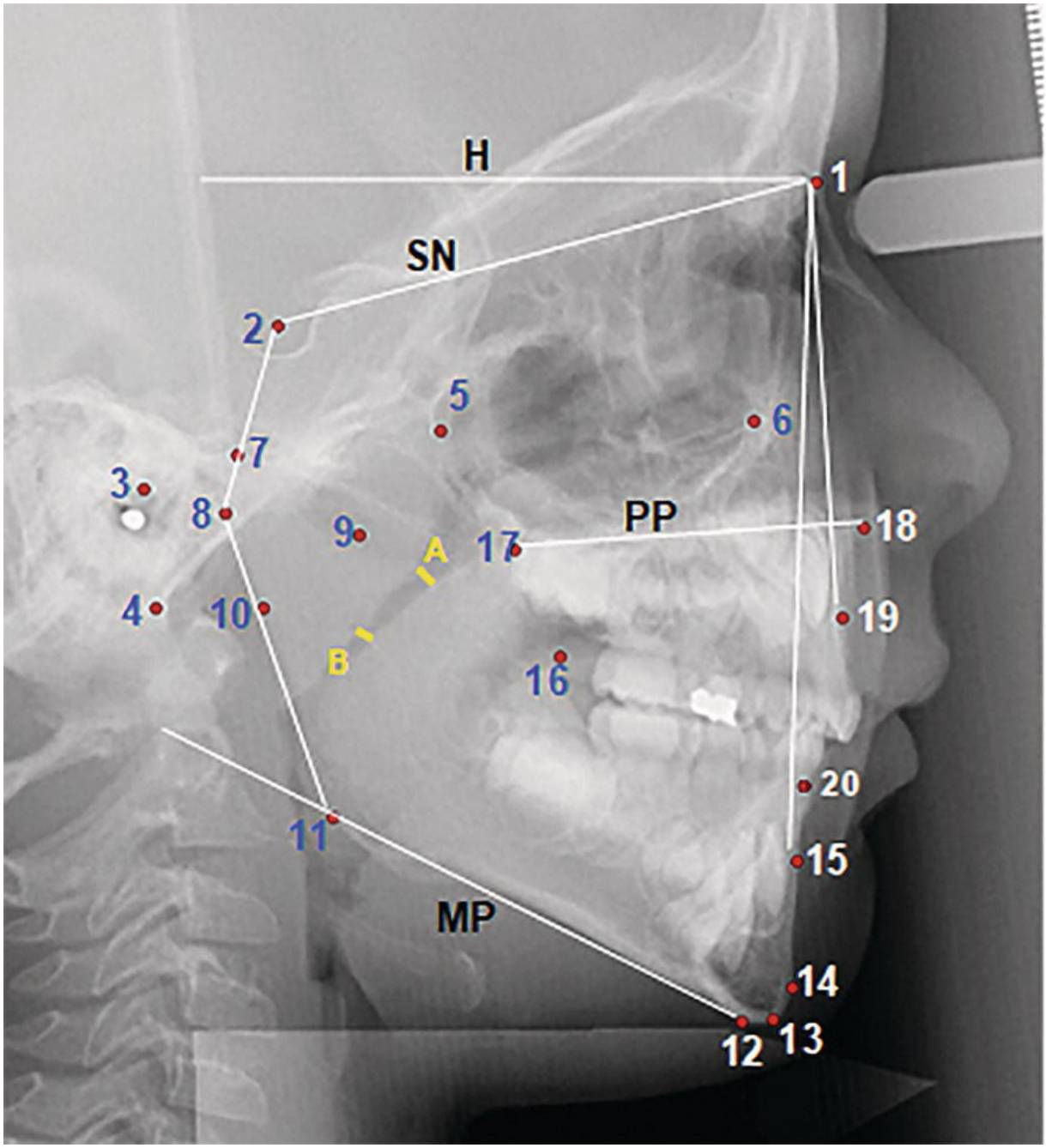
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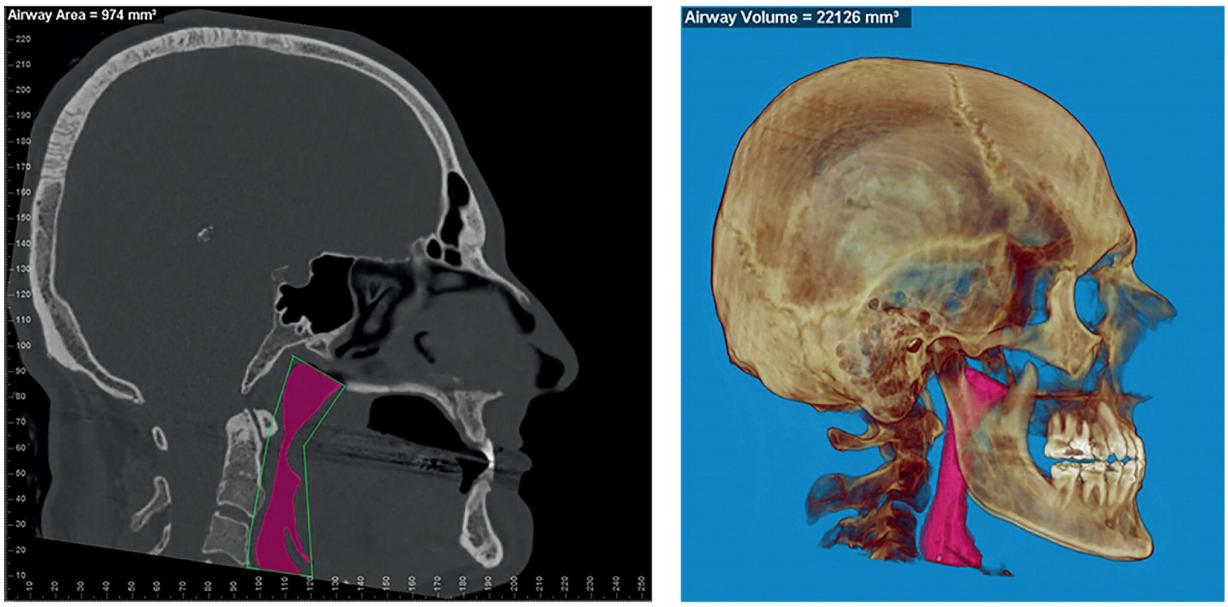
Figure 12.6 Cephalometric landmarks, planes, and measurements in the study of craniofacial morphology related to adenoid hypertrophy. Linear measurements of the palatal airway (between the adenoids and soft palate): A is the distance between the most convex contour of the adenoid and soft palate (CAD), and B is the shortest distance between the adenoid and soft palate (SAD). Various hard tissue landmarks (1–20) are used for linear and angular measurements. Key findings included the increased posteroinferior inclination of the palatal plane (PP) relative to the horizontal (H) oriented on natural head position, augmented hyperdivergence between PP and MP (mandibular plane through menton [Me 12] and gonion [Go 11]), as well as increased angle between MP and SN (sella [#2]-nasion [#1]).

The underlying theory is that chronic mouth breathing leads to narrow maxillary dental arches, anterior open bite, usually through excessive eruption of posterior teeth, and a hyperdivergent skeletal pattern. These symptoms are related primarily to low posturing of the tongue and the subsequent adaptation of other facial muscles. The lips, in repose, have been described as parting, although nasal breathing is possible with incompetent lips if the tongue provides an anterior seal (Macari and Haddad, 2016).

Time and sequence of facial alterations from airway obstruction

Macari et al. (2012) analyzed the cephalographs of 200 Caucasian children who had been diagnosed as chronic mouth breathers by the pediatric otolaryngologist who referred them for cephalometric appraisal of adenoid hypertrophy. Their mean age was 6.00 ± 2.62 years and nearly 50% of them were younger than 5 years. The authors reported posterior-inferior tilt of the maxilla (average inclination of palatal plane to horizontal −7.68° + 3.44°; norm 0° + 2.5°), apparently the initial response to functional alteration, occurring separately or together with one or all of the following modifications compatible with a hyperdivergent vertical pattern: increased palatal to mandibular plane angle, increased lower face height, steep mandibular plane, mandibular antegonial notching, increased gonial angle, and elongated and thinner symphysis (Figure 12.8). The palatal tilt reached severe levels (8–9°) between the ages

of 4 and 5 years. The occlusion ranged from normal with adequate overjet/overbite to malocclusions that contained one or more of these characteristics: posterior crossbite, overjet, Class II, open bite, anterior crossbite (Figure 12.5).



(a) (b)

Figure 12.7 (a) Cone beam computed tomography image and (b) three-dimensional rendition of the skull in which the nasopharyngeal space is mapped in red, illustrating the area (a) and volume (b) of the space.

(a) (b) (c)

Figure 12.8 Morphological characteristics of the "long face" syndrome in a girl 10 years, 10 months old with chronic mouth breathing. (a, b) Extraoral photographs reveal lip incompetence, increased lower facial height, narrow nose base width, and shadows under the eyes from chronic venous congestion. (c) Lateral cephalograph of the same patient shows characteristic findings of adenoid facies: palatal plane (ANS–PNS) tipped postero-inferiorly, steep mandibular plane (MP: menton [Me] to gonion [Go]), mandibular angular notching, reduced inclination of anterior slope of chin (horizontal arrow), and increased lower face height. The upper and lower curved arrows indicate the posterior-inferior tip of the palatal plane and anterior-inferior tip of the mandibular plane, respectively. PP, palatal plane.

Accordingly, the following conclusions are drawn regarding growth concepts on the association between airway status and craniofacial morphology:

- Facial dysmorphology related to nasal obstruction starts in structures closest to the obstruction, namely a posterior-inferior rotation of the maxilla.
- The array of malocclusions differs with the individual respiratory adjustment of the affected child. In this perspective, two observations are made. The occlusal variations join the experimental findings of Harvold et al. (1981) in monkeys at comparable ages. These authors obstructed inspiration, but allowed slight air escape during expiration in growing monkeys (age: 2–6 years), most of them (34/42) in the late deciduous and mixed dentitions (age: 2–4 years). Each animal found its own most convenient way to secure the oral flow, and then develop a dental occlusion in accordance with this new function. Thus, oral respiration induced mesioclusion, maxillary protrusion with distoclusion, open bite, dual bite, and some common cephalometric traits: increased face height, steeper mandibular inclination, and a larger gonial angle. Second, as suggested by Angle (1907) in his theory of Class III genesis and observed in many patients, including those treated for obstructive sleep apnea, forward positioning of the mandible enlarges the airway and enhances breathing through the consequent increase of

airflow (Liu et al., 2000). Ghafari (2004) suggested that if the anterior position is sustained in growing children, the ensuing anterior crossbite may induce maxillary retrognathism that otherwise would not exist. This phenomenon reflects intragrowth orthopedics (maxillary retrognathism) generated by the transfer of functional forces through a nontherapeutic occlusal "environmental induction" (anterior crossbite) (Ghafari and Macari, 2013).

- The findings qualify the variable relation between nasal obstruction and facial growth in line with Moss's functional matrix theory (Moss and Salentijn, 1969). The oropharyngeal space is a primary entity (capsular matrix related to respiration) that influences the position and behavior of the surrounding soft tissues, which in turn shape the associated skeletal units. Impingement on the oropharyngeal space leads to adaptive reorganization of the surrounding structures, beginning with and possibly restricted to the posterior-inferior maxillary tilt, probably because of its proximity to the obstructed pharynx. The greater amplitude of adaptation occurred at younger ages (<5 years). The adjustment may also start with mandibular remodeling favoring an increase in the gonial angle and mandibular plane inclination.
- As airway obstruction ranges from total to partial, and adaptation to either is an individual response (according to Moss to preserve the oropharyngeal matrix), the variation in malocclusions is not surprising. Conversely, any degree of adaptive morphological change may result in a level of restoration of nasal breathing.
- The association between the *amount* of blockage and *specific* signs of malocclusion remains unknown. The severity and extent of dysmorphology would depend on the timing, duration, and rate of oral breathing and associated functional changes, as a percentage of nasal breathing may coexist with mouth breathing (Fields et al., 1991).

Effect of the removal of lymphoid tissues on orofacial morphology

The critical clinical issue is determining the optimal time of lymphoid tissue removal to enhance nose breathing and prevent potential abnormal facial growth, or reverse/minimize developing long face features, possibly aided by orthodontic/orthopedic treatment. Posttreatment studies of adenoidectomy (Linder-Aronson et al., 1986; Woodside et al., 1991; Bahadir et al., 2006) reveal a more anterior direction of symphyseal growth, reversal of the tendency to posterior mandibular rotation, an increased amount of mandibular growth, and no difference in direction of maxillary growth. The latter is an indication that morphological alterations are not totally irreversible. Additionally, individual growth direction after adenoidectomy was more variable than in control children with clear airways matched for age and sex (Linder-Aronson et al., 1986). When Harvold et al. (1981) removed the nose plugs in their experimental animals two years after nasal obstruction, nasal breathing returned and some of the dentofacial changes were undone, but facial features and malocclusion were often retained. Research is needed on the extent, scope, and predictability of orofacial counter-adaptation in relation to age.

Through a recent study, Babakhanian et al. (2021) documented changes (12.92 ± 1.42 years; range 10.16–14.76 years) post adenoidectomy. Long-term normalization of dentofacial growth in bony bases was found, specifically in the mandible, enhancing more horizontal growth direction and chin projection in the surgical group. Surgery before the age of 6 years resulted in gonial angle closure and more anterior chin projection (Figure 12.9).

Clinical considerations

The findings on airway blockage and dentofacial dysmorphology emphasize the need for pediatricians and pediatric otolaryngologists to examine children for impaired nasal breathing in early childhood and ascertain their breathing mode at night from the parents. Otolaryngologists and orthodontists should appreciate the early impact of enlarged adenoids and tonsils.

From the perspective of *otorhinolaryngology*, reasons for adenoidectomy often include chronic and recurrent fluid or infections of the ears, chronic or recurrent sinus infections or "rhinosinusitis," and nasopharyngeal blockage. Tonsillar infection is rarely associated with ear infections and tonsillectomy is usually indicated when tonsils are enlarged. The prevailing practice among otolaryngologists is to delay removal of the pharyngeal lymphoid tissues because of their role in immunological defenses, and the increase in size of the adenoid in preschool and primary grade years followed by a decrease during pre- and early adolescence (Figure 12.2; (Linder-Aronson et al., 1983). Indications for adenotonsillectomy supported by the American Academy of Otolaryngology (2021) include statements related to infections, sleep disorders, malocclusion, and other infectious conditions (Table 12.1).

Adenoidectomy, often conducted using a small mirror and completed on average within 15–20 minutes, involves "shaving" or curetting the adenoid tissue from the back of the nose. Usually, low-grade bleeding is eliminated by cauterization. Although rare, surgical complications include infection of the surgical site (a source of bad breath), minor bleeding, and infrequently velopharyngeal insufficiency, possibly related to neglect of anatomical considerations. Postsurgical pain is more pronounced with tonsillectomy.

From the perspective of *orthodontics*, orthodontic correction may be needed to foster adequate tongue posture, such as widening the maxillary arch to maintain an upward position of the tongue at rest. Sometimes the palatal split improves respiration and helps reverse mouth breathing (habitual or from anterior obstruction) to nose breathing, or may even amelioate hearing (Kılıç et al., 2008a, 2008b). However, these responses cannot be predicted. When the mandible is thrust forward for better breathing, and an anterior crossbite follows possibly inducing maxillary retrognathism, early correction of the latter is recommended (Ghafari, 2004) along with the medical/surgical management of the respiratory problem.

Treatment combining orthodontics and orthognathic surgery to correct LFS reverses all characteristics observed in conjunction with sustained chronic mouth breathing during growth; namely, posterior impaction of the maxilla, mandibular advancement, and genioplasty

(Figure 12.10). These procedures validate the prior prevention of the symptoms by promoting nasal breathing through the earlier removal of lymphoid tissues.

Orthodontic intervention is confounded by several facts. First, a direct relation between mouth breathing and malocclusion is not established for all mouth breathers (Leiter and Baker, 1989), some of whom may exhibit normal occlusion, possibly because total nasal obstruction is rare. Second, the type and severity of malocclusion are determined by the individual pattern of adaptation to nasal obstruction (e.g. LFS occurring with and without anterior open bite). And last, clearing the nasal airway does not necessarily improve dentofacial relationships, particularly in older children (Ghafari and Macari, 2013).

(a)

(b)

(c)

(d)

Figure 12.9 (a) Lateral cephalograph of a boy 4 years 4 months old treated medically for airway obstruction and mouth breathing. (b) Cephalograph of the same subject 13 years later. Although the originally posterior caudal inclination of the palatal plane flattened, the hyperdivergent pattern remained with a very steep mandibular plane. (c) Cephalograph of another boy of a similar age (4 years 2 months) treated for the same conditions with adenoidectomy. Note the hyperdivergent pattern with a posterior-inferior tip of the palatal plane. (d) The cephalometric record of the second boy taken 14 years later reveals a shift of the morphological pattern to hypodivergence.

The early morphological changes observed with nasal airway obstruction support early surgical intervention (<5–6 years) to avoid a permanent setting of one or more characteristics of LFS that would be difficult to control orthodontically. Thus, adenoidectomy may be recommended in patients found at risk of LFS or based on the severity of some of its characteristics least affected by orthodontic treatment. Linder-Aronson advocates adenoidectomy in mouth breathers with a small nasopharynx (Linder-Aronson et al., 1986, 1993; Kerr et al., 1989; Woodside et al., 1991), but this recommendation is not yet supported by clinical trials. To develop operational guidelines, several considerations emerged:

Table 12.1 Summarized statements by the American Academy of Otolaryngology regarding guidelines for adenotonsillectomy.

Source: Adapted from American Academy of Otolaryngology Head and Neck Surgery, https://www.entnet.org/resource/clinical-indicators-tonsillectomy-adenoidectomy-adenotonsillectomy-in-childhood.

Related to infections	
1	Watchful waiting for recurrent throat infection if fewer than 7 episodes in the past year, or fewer than 5 episodes per year in the past 2 years, or fewer than 3 episodes per year in the past 3 years
2	Recurrent throat infection with a frequency of at least 7 episodes in the past year, or at least 5 episodes per year for 2 years, or at least 3 episodes per year for 3 years, with documentation for each episode of sore throat and one or more of the following: temperature >38.3 °C, cervical adenopathy, tonsillar exudates, or positive test for Group A β-hemolytic streptococci (GABHS)
3	Tonsillectomy for recurrent throat infection not meeting criteria in Statement 2 for modifying factors, which may include but are not limited to multiple antibiotic allergy/intolerance, PFAPA (periodic fever, aphthous stomatitis, pharyngitis, and adenitis), or history of peritonsillar abscess, parapharyngeal abscess, severe infection with dehydration requiring intravenous fluids, or severe infections that may aggravate comorbid conditions (e.g. seizure disorder). Children at risk for being held back in school due to excessive absences (e.g. over 10 school days per academic year) may also need consideration
Related to sleep disorders	
4	Tonsillectomy for sleep-disordered breathing (SDB) and tonsil hypertrophy considering comorbid conditions that might improve after tonsillectomy, including growth retardation, poor school performance, enuresis, and behavioral problems
5	Tonsillectomy to improve health in children with abnormal polysomnography who also have tonsil hypertrophy and SDB
Related to malocclusion and dysphagia	
6	Hypertrophy causing dental malocclusion or adversely affecting orofacial growth

7	Hypertrophy causing severe dysphagia (particularly when supported by swallow evaluation) or cardiopulmonary complications	
Related to recurrent, chronic, or unresponsive conditions		
8	Peritonsillar abscess unresponsive to medical management and drainage documented by surgeon, requiring surgery performed during acute stage	
9	Persistent foul taste or breath due to chronic tonsillitis not responsive to medical therapy and for which other causes have been eliminated or treated	
10	Unilateral tonsil hypertrophy presumed neoplastic	
11	Recurrent suppurative or chronic otitis media with effusion: adenoidectomy alone	Addition of tonsillectomy requires one of the indications listed above
12	Chronic sinusitis in pediatric population not responding to maximal medical therapy (e.g. antibiotic, topical nasal steroid sprays, saline irrigations): adenoidectomy alone	

- *Severity of dentofacial dysmorphology*. The irreversibility of set LFS characteristics, apparently a factor of age (beyond age 6; see earlier discussion), should be evaluated. Deviations within 1 standard deviation (SD) of the norm are usually accepted (within normal range), thus variations beyond this limit represent flags, particularly when observed in several LFS components.
- *Threshold of obstruction severity*. In the study by Macari et al. (2012), more children under age 5 (n = 35), but also children aged 5 or older (n = 22), had near complete obstruction (SAD <2 mm). In these patients, hyperdivergence (palatal and mandibular plane inclinations) and other LFS characteristics (increased lower face height) were of similar severity across ages (Table 12.2). The older children likely had sustained mouth breathing with the facial morphological changes being

irreversible. These observations would favor intervention when SAD <2 mm.

- *Potential variability*. The total number of patients with SAD <2 mm exhibiting LFS characteristics represents a minority of the studied "mouth breathing" population (in the referenced study 57/200 = 28.5%). However, many children with SAD >2 mm might exhibit severe dentofacial dysmorphology and should also be assessed for surgery based on irreversible traits and age.
- *Level of adaptation to the insult*. If compensation occurs within the dentition (absence of crossbite, open bite, or gummy smile) and morphological changes do not get worse at a later follow-up, early surgery may not be needed. Such compensations may reflect the lesser airway obstruction with increasing age (Figure 12.11) and the ensuing gradual adjustment to growth of the nasopharyngeal airway and face, as indicated by the decreased deviation of the palatal plane and other morphological features (Figure 12.12).

Reflecting these considerations, we developed guidelines for early adenoidectomy and/or tonsillectomy that account for the varied response to the obstruction and growth changes. They are based on a combination of the following:

- Persistent nasopharyngeal airway obstruction (SAD <2 mm or Grade 3) and mouth breathing, preferably supported by objective testing.
- Existing skeletal dysmorphology (palatal plane tip, steep mandibular plane, or increased lower face height) beyond one standard deviation from the norm.
- Signs of dental malocclusion (constricted maxillary arch, anterior open bite, or crossbite).

These guidelines need exploration in controlled longitudinal clinical trials and validation through prediction equations.

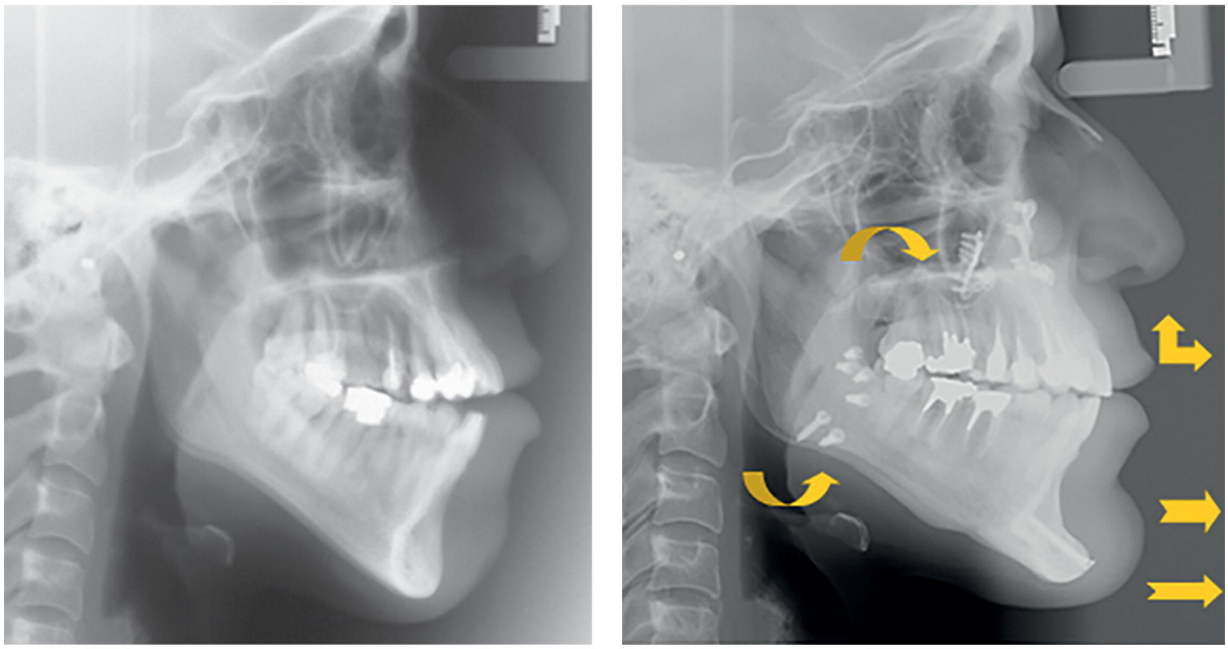


Figure 12.10 Normalization of long face syndrome involves surgical movements in a direction opposite to the description of its development following nasal obstruction and chronic mouth breathing. (a) Pretreatment and (b) postsurgical cephalographs of an adult female with long face syndrome treated with a combination of orthodontics and orthognathic surgery. The dentoskeletal dysmorphology was reversed (arrows) through orthodontic normalization of the inclinations of the incisors maxillary impaction, posterior rotation and advancement, mandibular anterior autorotation, mandibular advancement osteotomy, and further chin advancement genioplasty.

Table 12.2 Selected measurements for all patients exhibiting SAD <2 mm.

Age (mean)	SAD	n	PP–H (o)	MP–SN (o)	PP–MP (o)	LFH
<5 years (3.88)	0.99	35	−8.54	40.45	32.60	0.61
5–7 years (5.64)	1.46	14	−8.74	39.49	32.53	0.60
7–13 years (9.66)	0.58	8	−8.01	44.81	35.99	0.58

H, true horizontal; LFH, lower facial height; MP, mandibular plane; PP, palatal plane; SAD, shortest distance from adenoids to soft palate; SN, sella-nasion.

The interaction between specialists (orthodontist, ENT, pediatrician) involves a process of reciprocal education on evidence-based practice. Accordingly, parents become more receptive to surgical intervention to correct nasal respiratory impairment when indicated in younger children. A high rate of parent satisfaction was reported following improvement of preoperative symptoms in children post adenoidectomy (Bahadir et al., 2006).

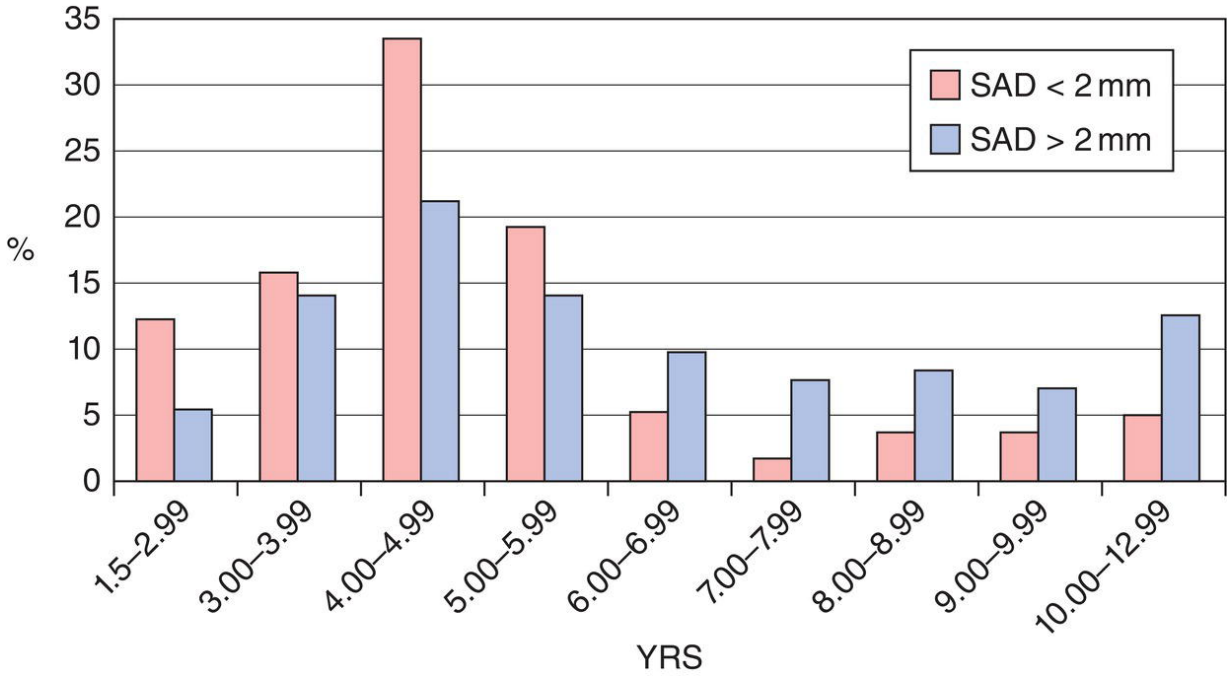


Figure 12.11 Percentage of children by age with the shortest distance between the adenoid and soft palate (SAD) less than and greater than 2 mm.

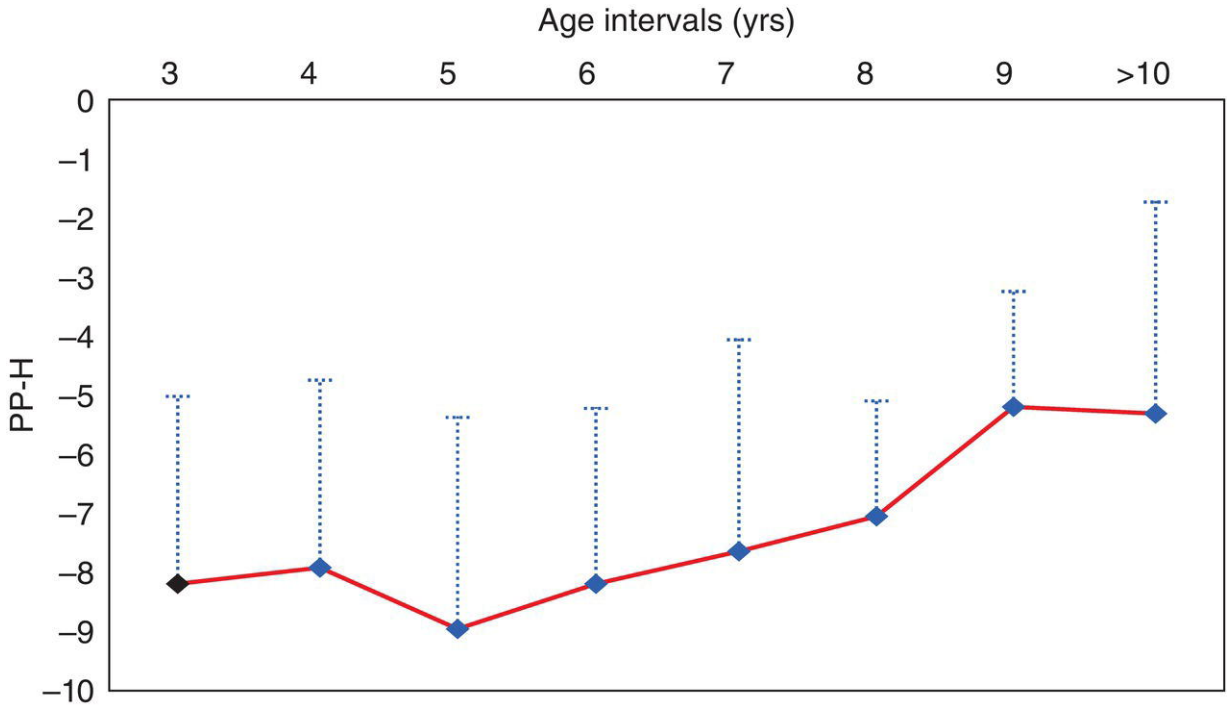


Figure 12.12 Palatal plane tip to horizontal (PP–H) with age. The inferior–superior inclination decreases in older children, progressing from –8.2° to –5.3° from the age brackets 1.7–2.9 years to 10–12.9 years.

Research considerations

Postnatal craniofacial skeletal growth is regulated by interacting genetic and environmental factors. Craniofacial components developing at various rates express different levels of susceptibility to epigenetic and environmental modifiers such as airway obstruction, thus variable response potentials or "growth maturity gradients," dependent on their respective growth rhythm (Buschang and Hinton, 2005). The cranial base and maxilla are earlier maturing structures, thus they respond to earlier stimuli than the later maturing structures (e.g. mandible). In addition to the differential maturity gradients, the concept of critical periods of growth, stipulating that dysmorphology depends on the timing of the insult, finds a critical application in the aforementioned variable responses to the oral breathing. These concepts are the basis for a research model that accounts for the environmental insult (mouth breathing) and the various growth interactions over time that would lead to adaptations or worsening dysmorphology toward the severe LFS (Figure 12.13).

Difficulties in the research of nasopharyngeal obstruction and mouth breathing include:

- Taking radiographs in cephalostats on younger children who must be still during exposure and keep the teeth in contact.
- The recruitment of control groups may be problematic because of the variability of malocclusion and underlying morphology, and the need for objective measures to define the presence or absence of mouth breathing, along with the assessment of airflow or nasal resistance, which do not always reflect the mode of breathing (Leiter and Baker, 1989).

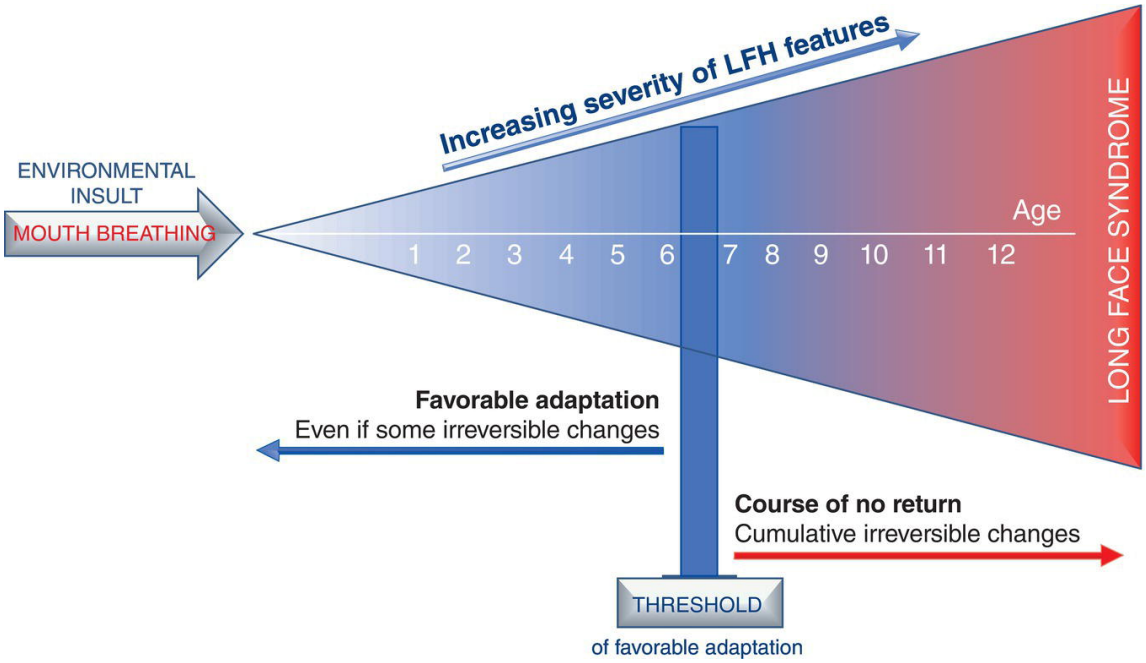


Figure 12.13 Schematic model of the effect of an environmental insult (mouth breathing) on craniofacial morphology through time. The diverging triangle and changing colors underscore the increasing severity of developing dysmorphology to the ultimate expression of long face syndrome. Available evidence suggests that favorable adaption would occur if the hypertrophied lymphoid tissues are removed before age 6. Beyond this threshold, a course of irreversible morphological changes would be underway. This scheme reflects a hypothesis that could be tested in focused research. LFH, lower facial height.

- The need for long-term follow-up post treatment.
- Sorting out the various sources of airway blockage that may coexist (e.g. adenoid and inferior turbinate hypertrophy).

Sleep-disordered breathing other than mouth breathing

Sleep disorders include abnormal behaviors associated with sleep, such as difficulty sleeping or staying asleep, falling asleep at unsuitable times, and excessive total sleep time. Sleep-disordered breathing such as snoring and obstructive sleep apnea (OSA) are

derangements in which the orthodontist is involved with medical airway specialists. OSA causes people to intermittently and temporarily halt or decrease breathing repeatedly during sleep because of partial or complete upper airway obstruction. Brief arousals from sleep restore optimal breathing. The diagnosis is confirmed through sleep studies (polysomnography). The apnea/hypopnea index (AHI) is a common gauge of the severity of the condition. A detailed study of OSA is presented in Chapter 11.

Sleep disturbances in children may influence the nocturnal secretion of the growth hormone (GH; Nieminen et al., 2002). Craniofacial characteristics of the "adenoid facies" resulting from mouth breathing were found in children with OSA (Zettergren-Wijk et al., 2006). The effects on jaw morphology and dentition were attributed to the long-term sustained altered position of the head, tongue, and mandible to ensure adequate air flow during sleep (Pirilä-Parkkinen et al., 2009; Stellzig-Eisenhauer and Meyer-Marcotty, 2010).

Treatment of OSA includes primarily the use of continuous or bilevel positive airway pressure (CPAP/BPAP), considered the standard most effective treatment in moderate to severe OSA to maintain airway patency, prevent breathing halts, and restore normal oxygen levels. Oral appliances are commonly recommended in patients with mostly mild (AHI<15) but also moderate (AHI 15-30), and, if sanctioned by the treating physician, in patients with severe apnea who cannot tolerate using CPAP. Mandibular anterior repositioning appliances clear the airway by pulling the tongue forward. Under specific indications, surgical approaches include the reduction or removal of tissue from the nasal passage, soft palate, uvula, tonsils, adenoids, or tongue, and maxillofacial surgery involving mandibular advancement. Behavioral approaches (e.g. halting smoking, weight loss) are supplementary or adjunctive rather than primary therapy for OSA.

Considering the serious medical consequences associated with OSA, the orthodontist should not provide an oral appliance without consultation with the physician treating the condition, usually the pulmonary specialist, but also other physicians specialized in OSA treatment (otolaryngologist, neurologist). The ENT specialist is a key member of the OSA team who manages underlying medical

conditions such as nasal allergies, which may be improved with a nasal steroid. In children, surgical removal of enlarged tonsils and adenoids often resolves the OSA. Following adenotonsillectomy, somatic growth returned toward normal levels (Bar et al., 1999; Nieminen et al., 2002), associated with the serum level increase of GH mediators, such as insulin-like growth factor 1 (IGF-1) and its binding protein. In some children, CPAP, further surgery, or specialized orthodontic treatment may be necessary.

Nonrespiratory areas of interaction with ENT specialists

Nonrespiratory issues that may be grounds for interaction with the orthodontist are considered in this section, notably conductive hearing loss, craniofacial anomalies, ear pain, and voice.

Conductive hearing loss

Otitis media

Otitis media is a frequent disease in childhood characterized by middle ear inflammation. The condition results, mainly, from the rupture of equilibrium between microbial load (viral and bacterial) and immune response (Rovers et al., 2004). Accumulation of fluid in the middle ear can follow because of the negative pressure produced by altered Eustachian tube function. If untreated, this fluid can induce conductive hearing impairment.

Otitis media is one of the prevailing causes of medical visits and the most common reason for antibiotic consumption and surgical intervention in children (Rovers et al., 2004). Several mechanisms have been reported to cause the infection, with possible multifactorial contributions. Bacterial pathogens and respiratory viruses (cold viruses) can cause otitis media. The most common bacterial pathogens causing otitis media in children are *Streptococcus pneumoniae*, *Moraxella catarrhalis*, and nontypable *Haemophilus influenzae* (Rovers et al., 2004), the latter being predominant among adolescents and young adults. The resulting congestion and ensuing malfunction of the Eustachian tube disturb

the pressure regulation of the middle ear, which in turn can be followed by aspiration of more pathogens from the oropharyngeal space into the middle ear, aggravating the original problem (Bluestone, 1996).

The adenoid provides local immune defenses against pathogen invasion through the upper respiratory tract and produces effector and memory lymphocytes that migrate to adjacent mucosal structures, strengthening local immune competence (Van Kempen et al., 2000). In addition, secretory immunoglobulin (Ig)A, generated by the nasopharyngeal mucosa, reinforces the defense mechanism by restraining bacterial and viral adherence and reducing bacterial colonization (Lim and Mogi, 1994).

Environmental risk factors include a family history of otitis media, parental smoking, pacifier usage, and outside daycare, which relates to the number of children in the facility (Dewey et al., 2000; Bowatte et al., 2015). Breastfeeding was reported to decrease the risk of otitis media, but more research is needed to determine the duration of protection (Bowatte et al., 2015). A strong genetic component of otitis media has been reported with higher concordance in monozygotic versus dizygotic twins (Kelly, 1993). Moreover, recurrent otitis media is associated with genetically determined Ig markers (Kelly, 1993).

The Eustachian tube connects the middle ear with the nasopharynx at the level of the inferior turbinate and measures 3–4 cm in adults. Narrow and formed by bone at its upper end, it becomes wider and cartilaginous at the pharyngeal end (Figure 12.14). The tube's opening and closing are physiologically and pathologically important, contributing to its significant functions (Rovers et al., 2004):

- *Ventilation*: the opening of the tube equilibrates the pressure between the middle ear and ambient air, preserving a healthy middle ear.
- *Protection*: the closure of the tube protects the middle ear against nasopharyngeal pressure fluctuations and ascending secretions or pathogens.

- *Clearance*: the mucus is drained away from the middle ear into the nasopharynx, preventing infection from ascending to the middle ear.

Normally the tube is closed in adults, but it opens on yawning, chewing, or swallowing to allow air flow in the middle ear.

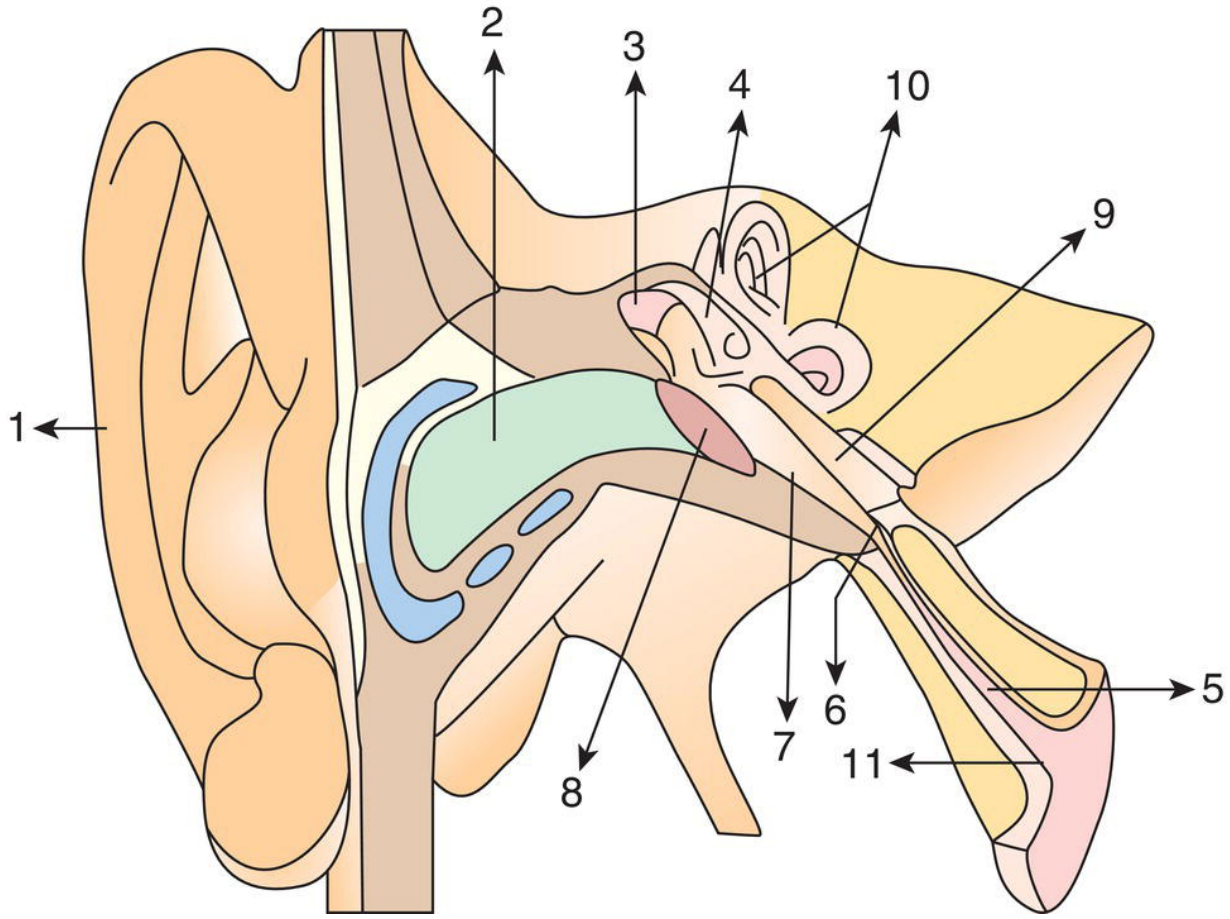


Figure 12.14 Schematic representation of the human ear. The ear is divided into three parts: external, middle, and internal. The external ear comprises 1 the auricule; and 2 the external acoustic meatus. The middle ear includes 3 the epitympanic recess; 4 the tympanic cavity; 5 the Eustachian tube; 6 the isthmus of the tube, where the bony and cartilaginous parts of the Eustachian tube merge; 7 the bony part of the Eustachian tube heading toward the tympanic cavity; 8 the tympanic membrane; and 9 the tensor tympani muscle. The inner ear has 10 the bony labyrinth. 11 The pharyngeal opening of the Eustachian tube.

Source: Adapted from Kahle (1993).

In children, the Eustachian tube's near horizontal position (10° compared to 45° in adults) and shape (shorter and wider) have been related to the higher occurrence of otitis media because the flatter inclination hinders mucus drainage (Cummings et al., 1998; Seibert and Danner, 2006). The tube's dysfunction has also been ascribed to

muscular problems (Mandel et al., 2016). The tensor veli palatine, levator veli palatine, salpingopharyngeus, and tensor tympani are the muscles responsible for opening and closing the Eustachian tube (Seibert and Danner, 2006). In children, the tensor palatine muscle operates less efficiently. In children with otitis media, the contraction of the levator veli palatine muscles closes the pharyngeal orifices and restrains the tensor veli palatine muscle from opening the Eustachian tube (Cozza et al., 2007).

When a disease or condition involves the outer or middle ear, as with otitis media, any decrease in hearing sensitivity is called conductive hearing loss. Normally, when sounds in the environment reach the ear, they propagate through the ear canal and impinge on the tympanic membrane, causing it to vibrate. These vibrations are transmitted through the middle ear via the ossicular chain (malleus, incus, and stapes) to the fluid-filled cochlea. The cochlea transduces the vibrations into nerve impulses that are carried into the brain for further processing. When the Eustachian tube malfunctions, the middle ear is not properly ventilated and air within its cavity stagnates. Part of the stagnant air is then absorbed by the tissues of the middle ear, resulting in a greater outer pressure at the level of the tympanic membrane than the air pressure in the middle ear; thus the membrane is pushed and restrained from proper vibration when hit by sound waves. Over time, the absorbed air from the middle ear is replaced with an accumulation of fluid, called effusion. The chronic presence of fluid in the middle ear induces muffled or dulled hearing because sound is not conducted efficiently through the middle ear system.

Diagnosis

Audiological tests are mandatory to confirm the presence of conductive hearing loss, including audiometry and tympanometry. Audiological test protocols vary according to the age of the child and often include a combination of behavioral and physiological tests (Table 12.3, Figure 12.15). For children under the age of 6 months, Behavioral Observation Audiometry (BOA), Visual Reinforcement Audiometry (VRA), Evoked Otoacoustic Emissions (EOAE), and Auditory Brainstem Response (ABR) are often used. VRA and EOAE

are also employed to assess the hearing of children aged 6–24 months. Above the age of 24 months, Play Audiometry can be used.

Tympanometry involves measuring the acoustic admittance of the ear using varying amounts of air pressure in a hermetically sealed ear canal. A probe is seated in the child's ear canal that introduces positive and negative air pressure on the tympanic membrane. The resulting movement of the eardrum is measured and depicted on a diagram called a tympanogram. Fluid in the middle ear leads to improper vibration of the tympanic membrane depicted by a flat tympanogram (Figure 12.16). In conjunction with the audiogram, tympanometry helps depict conductive hearing loss.

Table 12.3 Audiometry test descriptions and ages of testing.

Test	Description	Testing age
Behavioral tests		
Behavioral Observation Audiometry (BOA)	Survey of an infant's response to sudden and relatively intense sounds with different frequency and intensity composition	Under 6 months
Visual Reinforcement Audiometry (VRA)	Use of a conditioned localization response from the child and a visual reinforcer. Sounds of varying frequencies and intensities are presented through loudspeakers located off to the side of the child in a test room. The child is conditioned to turn his/her head toward the source of the presented sound. When the child turns to the source, the response is followed by the illumination of a visually appealing object (e.g. animated stuffed animal), which serves as a reward or reinforcement. The reinforcer increases the chances that the child will continue responding to subsequent sound presentations	Under 6 months to 24 months
Physiological tests		
Evoked Otoacoustic Emissions (EOAE)	Otoacoustic emissions are sounds emitted from the inner ear resulting from microscopic biomechanical activity associated with healthy cochlear outer hair cells. This activity is measured via a sensitive microphone seated in the ear canal, in response to an acoustic stimulus presented to the ear. EOAEs are present in 99+% of individuals with normal hearing sensitivity; their absence suggests the presence of hearing loss	Under 6 months to 24 months

Test	Description	Testing age
Auditory Brainstem Response (ABR)	The ABR measures change in the electrical activity of the nervous system when it reacts to a sound stimulus presented through earphones to an ear. This change can be picked up by electrodes placed on a child's head and then displayed as waves on the screen of a recording device. Sound levels are progressively lowered until a replicable waveform is no longer observed. This level indirectly suggests the child's threshold of hearing	Under 6 months
Play Audiometry	Training the child to listen for sounds and then make a specific motor response (e.g. throw a ball into a bucket, add a block to a stack of blocks, or place a peg into a pegboard). Sounds (pure tones and speech) are presented to the child via earphones (known as air conduction, AC) and through a bone vibrator positioned behind the child's ear on the mastoid process (known as bone conduction, BC). When a child hears a sound, he/she makes the motor response. Testing by AC assesses the entire auditory system. Testing by BC assesses the auditory system at the level of the cochlear and beyond (i.e. the status of the sensori-neural component of the hearing is evaluated). A comparison of hearing sensitivity as measured by AC and BC helps determine the nature of the hearing impairment: conductive, sensori-neural, or mixed (Figure 12.15). The presence of an "air bone gap" (i.e. hearing sensitivity is better by BC compared to sensitivity by	Above 24 months

Test	Description	Testing age
	AC) suggests the presence of a conductive or mixed hearing loss	

Treatment

Treatment of otitis media ranges from watchful waiting to antibiotics prescription to surgical intervention aiming to restore pressure equilibrium between the middle ear and the nasopharynx. Treatment modalities are related to the severity of the condition and timing of the intervention in relation to the original onset period. Guidelines on antibacterial treatment have been set by the American Academy of Pediatrics and American Academy of Family Physicians (Lieberthal et al., 2013). After initial diagnosis, they recommend an observation period of 48 hours without usage of antibiotics. Prescription of an antibacterial agent is recommended (amoxicillin, 80–90 mg/kg/day) after failure of response to the initial management.

Conductive hearing loss and maxillary expansion

Rapid maxillary expansion (RME) causes orthopedic separation of the midpalatal suture that is filled with immature bone around 4–6 weeks post expansion; bone matures within months, although reportedly not to full density by 6 months (Proffit et al., 2018). RME can be applied in the primary, mixed, or permanent dentition and is commonly used by orthodontists to correct maxillary transverse hypoplasia, often expressed in posterior crossbites, but also for space increase and improvement of smile esthetics to reduce the space between the maxillary buccal teeth and lip commissure, also known as the black corridor or “negative” space (Huertas and Ghafari, 2001). RME increases the width of the nasal cavity through a lateral move of its anterior walls (Haas, 1961; Wertz, 1968; Warren et al., 1987), but this widening does not necessarily translate into improved respiration or normalization of the mode of breathing (Warren et al., 1987). Improvement in nocturnal enuresis, also associated with mode of breathing, was observed after palatal splitting (Schütz-Fransson and Kurol, 2008).

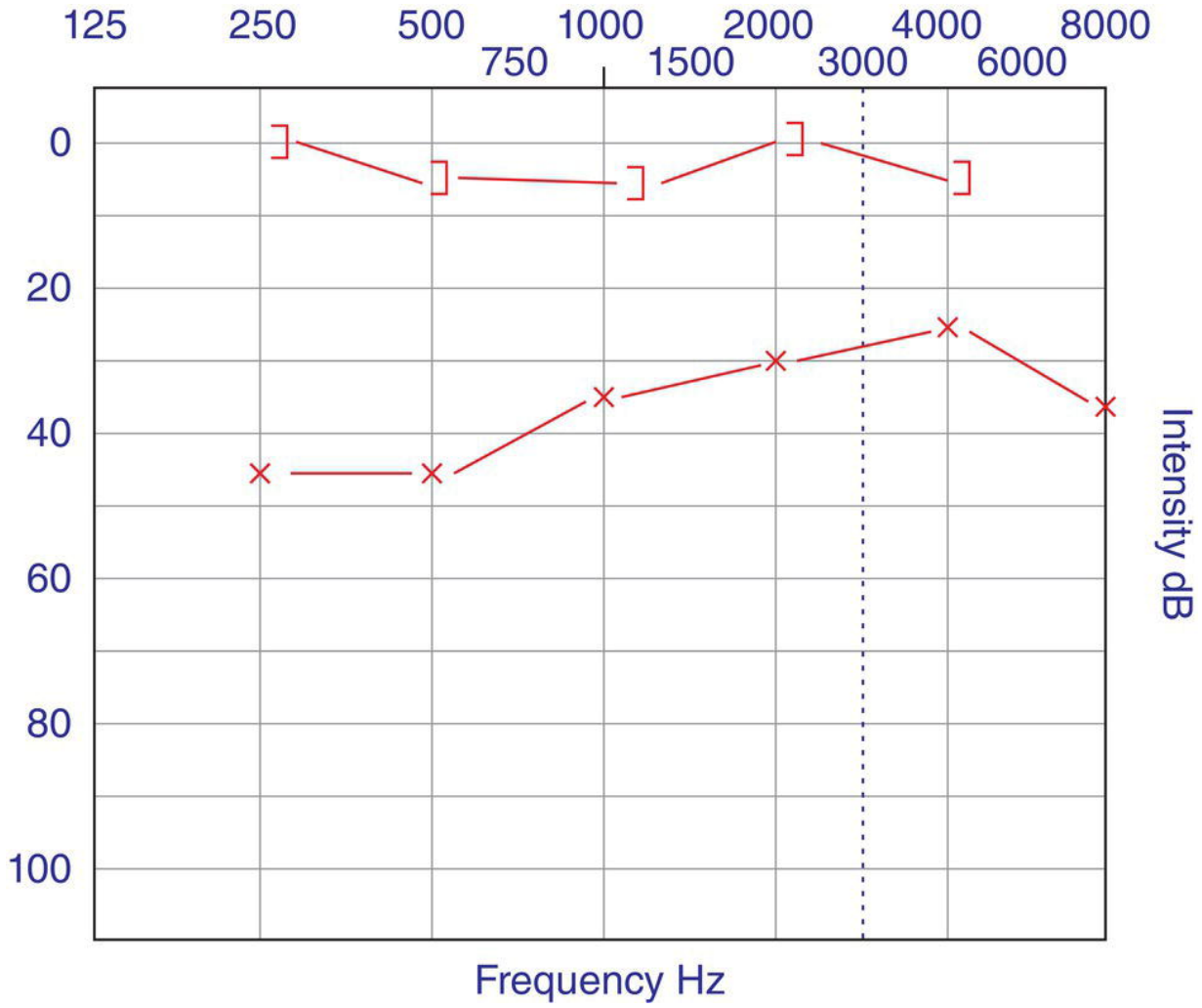


Figure 12.15 Audiogram depicting normal bone conduction hearing (top line) with a moderate rising (40 decibels) conductive hearing loss depicted by an air conduction test (bottom line). Note that severe hearing loss is present when the threshold moves to more than 70 decibels.

The link between palatal morphology and otitis media relates to the finding that Eustachian tube dysfunction was frequently observed in the presence of high palatal vault. A malfunction of the tensor and levator palatini muscles results in the inability of the tube to open in response to negative pressure in the middle ear (Fagundes et al., 2017). A possible explanation of the improvement of conductive hearing after maxillary expansion is the stretching of the tensor veli muscle, which opens the pharyngeal orifice of the Eustachian tube and allows air to enter and exit the middle ear. Thus, the pressures

on either side of the tympanic membrane are balanced and the vibration of the ossicular bones is normalized, inducing hearing improvement. Furthermore, a link between palatal morphology and otitis media is assumed because of the decrease of recurrent serous otitis media and the amelioration of symptoms a few weeks after RME (Villano et al., 2006; Lieberthal et al., 2013; Fagundes et al., 2017). Illustrated in Figure 12.17 is the improvement in a boy's pure audiometry and tympanometry measurements, reflecting better hearing sensitivity and middle ear function, one week after palatal expansion.

Lacking the rigor of randomized control trials, available evidence reveals improved hearing after RME in children and adolescents with hearing impairments (Fagundes et al., 2017). Kiliç et al. (2016) compared the effect of RME in children exhibiting maxillary constriction and resisting otitis media with effusion with the effect of ventilation tube placement in children who had no maxillary constriction. They concluded that otitis media release and improvement of hearing thresholds levels were similar between the two groups. Several authors showed the positive impact of RME on hearing and the middle ear function in noncleft and cleft lip and palate patients (Singh et al., 2021; Rosso et al., 2022). The outcomes were stable at six-month follow-up and significantly better when compared to a control group (Rosso et al., 2022). Sustenance of the initial improvements was reported in studies with longer-term assessments (two or more years; Taşpinar et al., 2003; Kılıç et al., 2008a, 2008b).

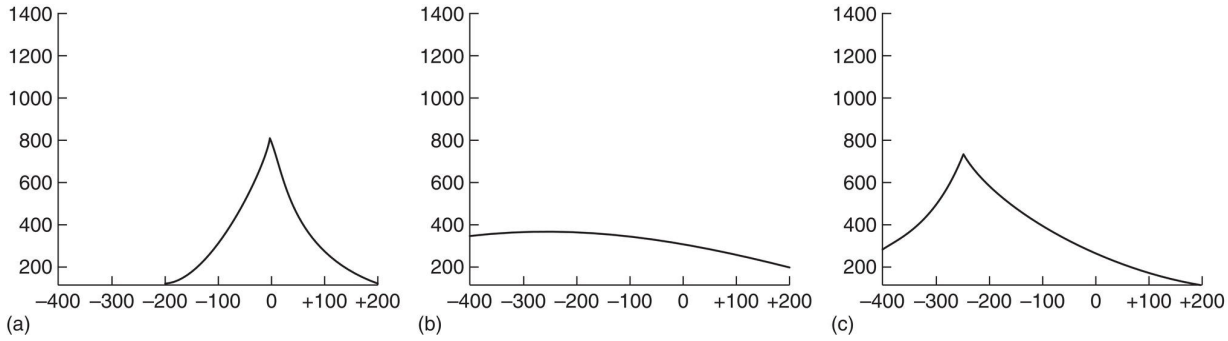


Figure 12.16 Three different types of tympanogram, plotting the pressure measured in decaPascals (daPa; x-axis) relative to the conductivity of sounds in mmho (y-axis). (a) Tympanogram indicating a normal middle ear system, free of fluid or physiological anomalies that would prevent the admittance of sound from the middle ear into the cochlea. (b) Tympanogram consistent with middle ear pathology, such as fluid or infection behind the ear drum. (c) Tympanogram indicating negative pressure in the middle ear space, often consistent with sinus or allergy congestion, or the end stages of a cold or ear infection.

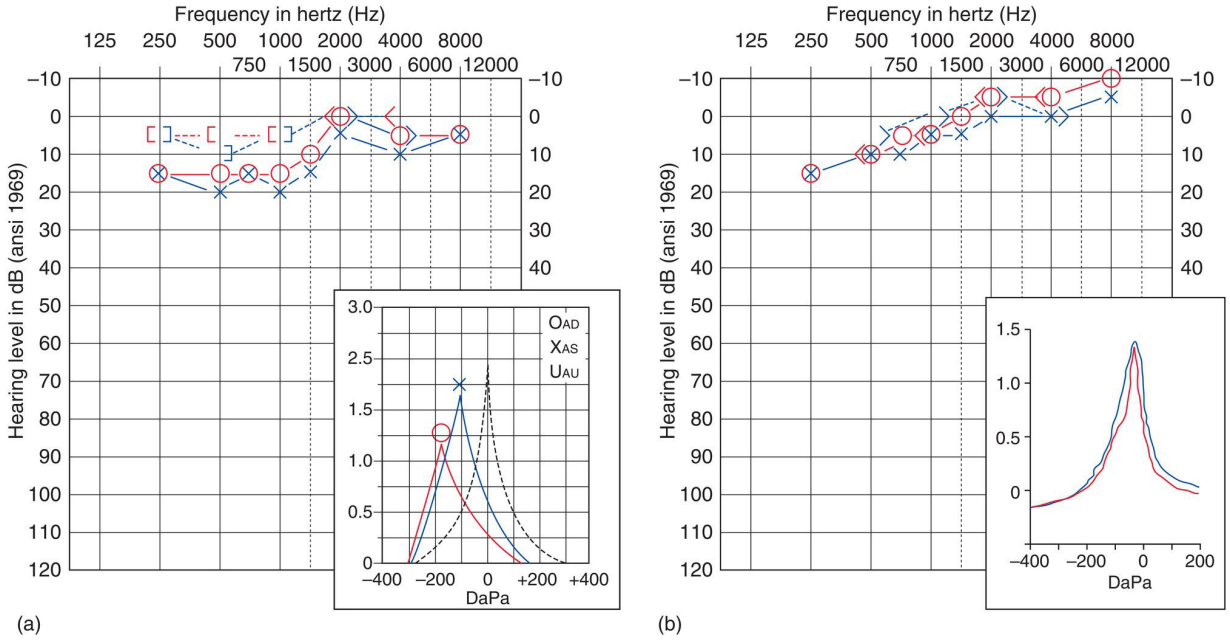


Figure 12.17 Audiograms and tympanograms of an 11-year-old boy before and after maxillary rapid expansion. (a) Preexpansion audiometric tests show mild conductive hearing loss and a type C tympanometry (see Figure 12.16c) denoting negative middle ear pressure bilaterally. (b) Postexpansion audiogram and tympanogram are within the normal limits.

Although these studies indicate that RME was an effective therapy in children who have poorly functioning Eustachian tubes along with maxillary constriction (Kılıç et al., 2021), outcomes do not seem to be predictable in the individual patient, notwithstanding the fact that variable methods have been used in the investigations. More controlled future long-term trials should determine whether RME may be a predictable alternative treatment to surgical options or at least tried before surgery in children with conductive hearing loss who also require palatal expansion.

Craniofacial anomalies

Craniofacial anomalies include mostly congenital conditions, such as syndromic and nonsyndromic cleft lip and/or palate, hemifacial microsomia, and plagiocephaly. Comprehensive planning and timely treatment of these developmental conditions require a multidisciplinary approach by a team of specialists capable of managing structural and functional problems in the craniofacial complex: pediatrician, pediatric dentist, nurse practitioner, otorhinolaryngologist, geneticist, speech therapist, orthodontist, maxillofacial surgeon, plastic surgeon, prosthodontist, social worker, and psychologist. Intervention is needed from birth to variable postpubertal times. If the intervention does not accompany key growth events (e.g. dental development, adolescent growth spurt), opportunities are lost and the outcome is at best the result of a series of compromises instead of optimal function of the orofacial structures, facial esthetics, hearing, and intelligible speech for some of the anomalies.

The epidemiology, diagnosis, and management of theses anomalies are discussed in Chapters 7 and 8. A brief summary is presented here in the context of interaction between orthodontist and ENT specialist within the multidisciplinary team as defined in specific centers,

whereby the ENT specialist may also assume the role of the maxillofacial or plastic surgeon in those anomalies here hearing and breathing may be impaired.

Clefting of the lip, alveolus, and palate is the most common craniofacial congenital malformation of the head and neck and the second most common congenital malformation of the entire body after clubfoot deformity (IPDTOC Working Group, 2011). In the absence of a universal approach to cleft management, the sequence, timing, and treatment modalities are specific to teams and centers. The specialists delineate and institute management options, continuously review progress, and when needed revise treatment. The general sequence of procedures is comparable in different centers, but timing is more variable. Treatment stages commonly include intervention in the neonatal period and ofen end in the later teenage years. The timing of certain procedures might overlap between periods (e.g. staged orthodontic interventions, restorative dental procedures), particularly those defined as adjunct procedures (i.e. speech therapy, psychotherapy). (See Chapter 7 for details.)

The ENT specialist deals with hearing problems, which increase between the ages of 6 months and 2.5 years (Sheahan and Blayney, 2003). The muscles responsible for opening the Eustachian tube do not function properly, resulting in more frequent fluid build-up, otitis media, and ear infections that can be very painful. The infant's hearing must be tested during the first few months of life, and if it is impaired by fluid build-up or unequal pressure, the otothinolaryngologist would place pressure-equalizing tubes, often at the time of the lip or palate surgery. Regular hearing tests are necessary to monitor middle ear problems that could alter the normal hearing and speech development. As the child grows, the frequency of ear infections seems to decrease (Sheahan and Blayney, 2003).

Ear pain

Otalgia, or ear pain, is discussed in this chapter in relation to temporomandibular dysfunction, a condition commonly seen by the dentist and/or the otorhinolaryngologist because of the proximity and similar innervation of the ear and promaxillary structures. The

sensory innervation of the ear derives from branches of cranial nerves V, VII, IX, and X.

Primary otalgia stems from pathologies affecting the ear itself, including local inflammation or infection such as in otitis externa or otitis media, Eustachian tube problems with pressure gradient disparities on both sides of the tympanic membrane, infections of the skull base (e.g. necrotizing otitis externa), or, less commonly, primary malignancies involving the ear. Associated symptoms of hearing loss, aural fullness, otorrhea (or ear drainage), and dizziness may occur.

Secondary, or referred, otalgia develops from pathologies affecting any of the structures innervated by the nerves mentioned, such as the temporomandibular joint (TMJ), mandible, teeth, gingiva, nose, paranasal sinuses, nasopharynx, and oropharynx, including the tonsils, tongue, parotid gland, larynx, and esophagus.

Evaluation

Most problems are properly diagnosed after history and physical examination. The history should gauge the pain location (in the ear only or radiating to surrounding structures), character (sharp, dull, or burning), and duration (acute, chronic, constant, or intermittent). The diurnal pattern of the pain, any association with chewing or swallowing, and the presence of associated hearing loss, discharge, or dizziness are recorded. The patient is asked about any obvious precipitating factors such as trauma to the head or local trauma to the ear. Difficulties or pain with swallowing, changes in voice or breathing, and blood in the sputum are serious symptoms that may relate to a malignancy of the head and neck. A history of smoking and/or alcohol intake increases the suspicion for malignancies.

On examination, the ear is carefully evaluated to rule out any primary otological etiology. The ENT specialist also focuses on the adjacent head and neck region, including the areas of the pinna and over the mastoid process for redness and swelling; the ear canal for redness, discharge, cerumen, foreign body, and lesions; the tympanic membrane for redness, perforation, and signs of middle ear fluid collection such as bulging, distortion, or change in normal light reflex; and hearing. It is often helpful to ask the patient to point to

the origin of the pain with one finger. A full head and neck examination includes flexible endoscopy to evaluate the pharynx and larynx. Clicking or grinding of the TMJ along with point tenderness and trismus likely indicates a nonotological etiology. As a nonotological cause, TMJ dysfunction is considered when examination of the ear yields normal findings. Depending on clinical findings, nonotological conditions may require further testing, such as CT scans or magnetic resonance imaging.

Key to the differential diagnosis on TMJ involvement are the findings of normal ear examination; absence of middle and external ear problems; absence of oropharyngeal cause (tonsillitis, peritonsillar abscess); and absence of potential red flags such as redness over the mastoid, immunocompromised condition, or chronic pain concomitant with other symptoms of the head and neck region. While in a case of neuralgia sharp pain occurs in brief severe episodes (seconds to 2 minutes), TMJ dysfunction (TMD) might be accompanied with chronic otalgia. Depending on the symptoms, the patientmay see the dentist or ENT specialist first. The orthodontist or dentist conducts a thorough examination to differentiate structural TMJ problems from neuromuscular conditions. The examination includes palpation of the joint area, oral examination covering the static and functional occlusion, and radiographs if needed. TMJ-related symptoms are caused by degeneration of joint structures (arthritis, fractures, congenital) or the effects of physical stress on the structures around the joint.

TMD symptoms include clicking, “cracking,” popping, fremitus, difficulty or discomfort when biting or chewing, pain in the jaw, ear, face, or head, limitation in mouth opening, and tenderness on palpation of cheek or temple areas. The etiology is multifactorial, including stress, tooth clenching or bruxism, malocclusion, orthodontic treatment, and even muscular strain from poor posture. A definitive relation between occlusion and TMD is not available.

Treatment

When otological causes are diagnosed, treatment targets the underlying disorder, including oral analgesics, topical analgesics, local manipulation (e.g. suction of debris, ear drops), and surgery.

With nonotological causes, treatment has ranged from addressing clicking to minimizing the occlusal impact and pain management. When TMD is confirmed, ideally it should be addressed before the start or resumption of orthodontic treatment. Details on pathogenesis, diagnosis, and controversies on treatment of TMJ disorders are presented in Chapter 21.

Voice and speech

General knowledge on voice

The voice is an integral part of ENT practice and is not usually linked to orthodontic studies or practice. Yet voice changes are part of pubertal events that the orthodontist accounts for in regular early and adolescent treatment, and have been associated with malocclusion, particularly Class III malocclusion. As such, the study of the voice deserves attention.

The voice is produced through a cascade of physiological events, and vocal characteristics such as pitch and timbre are considered acoustic signals to human personality and morphology. When the air is exhaled, the laryngeal muscles pulsate the vocal folds, inducing air vibration. The fundamental frequency (f0_sustained) or pitch is defined as the number of cycles of vibration (opening–closing) of vocal folds per second. The average f0 for a person is calculated when pronouncing a lengthy steady vowel, whereas the average f0 calculated while the subject is counting to 10 is referred to as the habitual frequency or f0_count.

The sound produced in the larynx is amplified and modified by oral and nasal cavities as well as sinuses, which are considered resonating cavities. Extending from the laryngeal vocal folds to the lips, the vocal tract is not uniform in size and shape and can resonate at different frequencies, inducing what is termed the formants. Among the formant frequencies (the resonant frequencies of air in the vocal tract that vary with the size and form of the vocal tract and work together to identify the sound being made), the third, fourth, and fifth are the most important in defining the speaker's voice timbre (Titze, 2008).

The association between formant frequencies and body size and morphology is debatable (Evans et al., 2006). However, as a significant component of the phonatory apparatus, the dentofacial skeleton, including jaws and dental arches, should play a major role in shaping the voice timbre. Accordingly, voice parameters have been investigated in relation to craniofacial morphology and dentofacial orthopedic treatment.

Craniofacial morphology and voice parameters

Investigations on the association between formant frequencies and dentofacial morphology and malocclusions are scarce. In a study on 46 consecutive orthodontic patients who presented with Class I (51%), Class II (40.5%), and Class III (8.5%) malocclusions, Macari et al. (2015) evaluated the association between the sagittal projection and length of the maxilla and mandible and formant frequencies F1, F2, F3, and F4 of vowels /α/, /i/, /o/ and /u/. Skeletal relations were determined through cephalometric measurements and acoustic analysis by real-time spectrography. Moderate negative correlations were observed between the tested vowels and maxillary and mandibular lengths. The longer the jaws, the lower the position of formants, and the narrower the interspace of these formants. Similar findings were reported on the association between fundamental frequency and jaw length (Figure 12.18; Macari et al., 2014), facial length, and facial width (Macari et al., 2017). Reported differences in voice characteristics between Class III and Class I malocclusions have been attributed mainly to the high position of the hyoid bone in Class III subjects (Viegas et al., 2021), who are also unable to protrude their lips during the production of the vowel /u/ (Niemi et al., 2006).

Marunick and Menaldi (2000) demonstrated that maxillary dental arch form, dimensions, and volume may be predictors of the different voice types (soprano, mezzo, alto). None of the measured arch parameters was a predictor for voice classification, but palatal volume and depth related to the singer's category, sopranos having a shallow palate, mezzo-sopranos a medium palate, and altos a deep palate. In 35 prepubertal patients whose maxillary arch measurements and voices were analyzed while sustaining four vowels, /α/, /i/. /o/, and /u/, Hamdan et al. (2018) found significant

negative correlations between arch depth and F3 for the vowels /ɑ/, /i/, and /u/, and between arch length and F4 for the vowels /ɑ/, /o/, and /u/. Notably, F3 correlated most consistently with all maxillary arch measurements. The authors concluded that maxillary arch length and depth play an important role in setting the voice timbre in the prepubertal period. At puberty, the sexual difference in the descent of the larynx is partially responsible for vocal dimorphism (Sataloff, 2017).

Effect of palatal expansion and orthognathic surgery on voice parameters

Considering these findings, alterations in the configuration of the vocal tract are expected to influence voice quality and timbre. Macari et al. (2016) investigated the effect of RME in 14 consecutive patients aged 8–15 years. Acoustic analysis and maxillary arch variables were recorded before and two weeks after expansion. RME resulted in a significant drop in F1/ɑ/ and F2/ɑ/.

Acoustic parameters have been evaluated following maxillary and mandibular osteotomies, distraction osteogenesis, and repair of cleft palate (Jorge et al., 2009). Surgically assisted RME resulted in significant changes in the F1 frequency of the /a/ sound, the F2 frequency of the /e/ sound, and the jitter value of the /i/ (Erdur and Yilmaz, 2022). Mishima et al. (2013) compared voice characteristics in 16 patients whose Class III malocclusion was treated with mandibular setback, and a control group (n = 50). They reported significantly lower F0 preoperatively for the vowels /ɑ/, /i/, /u/, and /o/ in female subjects. Also, significant differences were found in the resonance characteristics between the treated and control groups. Significant changes in the acoustic analysis units (mLE1s, mean Lyapunov Exponent First) for /u/ in males, /o/ in females, and the F2s for /i/ and /u/ in males were observed postsurgically.

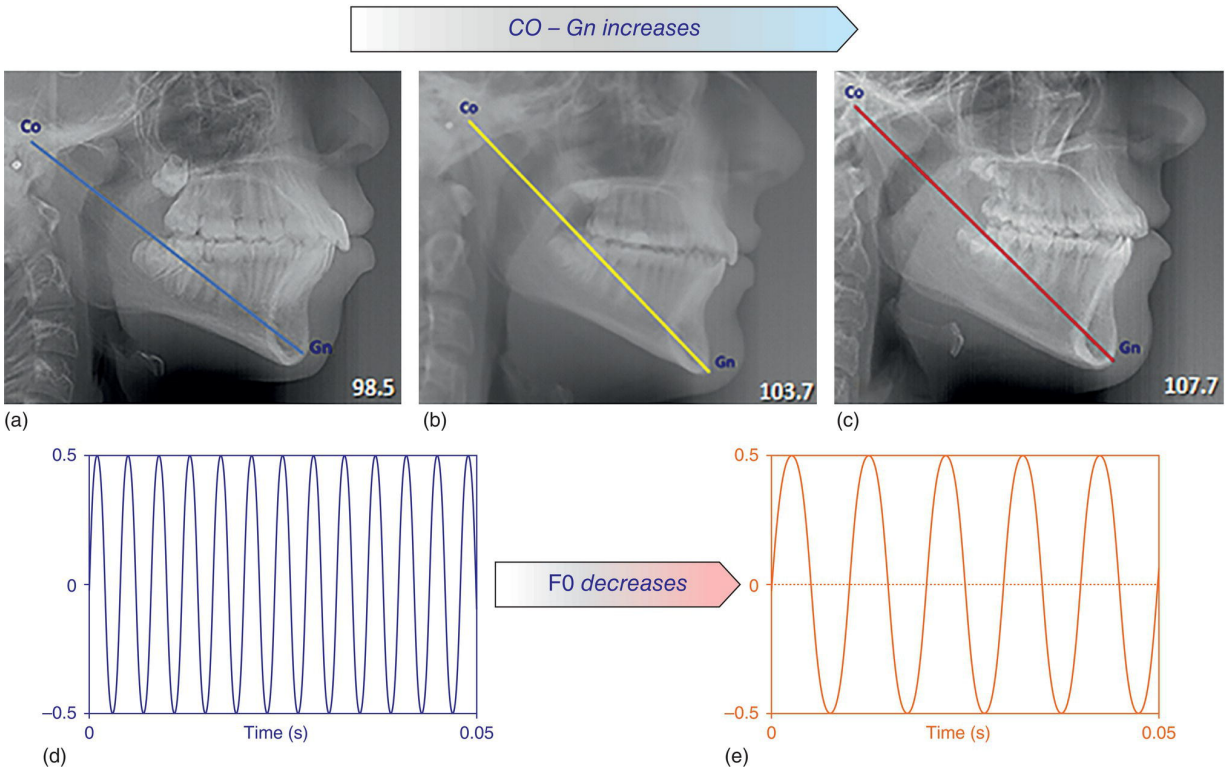


Figure 12.18 (a–c) Cephalometric radiographs of three individuals with increasing mandibular length (condylion–gnathion, Co–Gn). Research data revealed an inverse correlation between mandibular length and voice frequency at statistically significant levels. (d) High fundamental frequency (F0) was observed when Co–Gn was shorter and (e) decreased frequency when Co–Gn was longer.

Whereas knowledge about the potential effects of surgical and orthopedic procedures on the phonatory apparatus is important, the clinical perceptibility of these alterations and accordingly the definition of a traceable threshold may be difficult. Nevertheless, clinicians should provide the necessary information to patients who are candidates for surgical or orthopedic procedures, particularly individuals using their voices professionally.

The intersection between orthodontics and speech problems

Speech directly relates to oral and airway structures and involves precise coordination of muscular movements in the head and neck regions, extending to the chest and abdomen. Throughout growth, humans learn to regulate the muscles in these regions to produce comprehensible speech.

Problems with speech may develop early in life (about 5% of children), including stuttering (National Institute on Deafness and Other Communication Disorders, n.d.). In this chapter we focus on problems that may be related to malocclusion, notably Class III malocclusion, anterior crossbite, posterior crossbite, and open bite, which have been associated with misarticulation of medio-alveolar consonants, usually produced too anteriorly (Laine, 1992). Notable among the incorrectly pronounced sounds is the /s/ phoneme (occurring in different languages). Errors in the production of sounds /s/ and /t/ were associated with the Orthodontic Treatment Priority Index, whereby open bite >2 mm constituted a key malocclusal factor in underlying speech sound errors (Leavy et al., 2016). Misarticulations apparently are associated with occlusal problems affecting the position of the tongue and hyoid bone through a decrease of the posterior intermaxillary space, or a modification of the size and shape of the resonating cavity in the anterior part of the oral cavity. Risk ratios for producing consonants too far anteriorly in the oral cavity were reported to be greater in subjects with Class III (4.5 times), incisal open bite (3.4 times), and lateral cross-bite (1.7 times) compared to subjects who had no occlusal anomalies.

Improvement in the /s/ sound has been reported following treatment (orthodontic and/or orthognathic surgery) to correct Class III malocclusion and close open bite (Hassan et al., 2007). However, such corrections are not documented in children who have developmental disabilities (e.g. cleft lip and palate, neuromuscular disease). Speech therapy may be beneficial particularly if implemented at an early age; however, in various situations the speech therapist requests an orthodontic intervention (e.g. maxillary expansion) prior to the therapy. Often the speech problem is diagnosed by the orthodontist or ENT specialist, who brings the speech therapist into the multidisciplinary approach. Communication and mutual education are essential among these practitioners as early as the speech problem is recognized.

State of interaction between orthodontists and medical airway specialists

Unlike general dentists or other dental specialists, the orthodontist may be the dental practitioner with the least need to interact with physicians for the regular treatment of patients. The most common dealings of an orthodontist are with the surgeon involved in orthognathic surgery and, in a lower percentage of orthodontists, with the physicians engaged in the treatment of craniofacial anomalies and obstructive sleep apnea. Research and developing practice trends indicate that more regular communication between orthodontist and medical airway specialists should take place in various conditions. These conclusions may be formulated on such interactions:

- Children with chronic oral respiration must be examined by the ENT specialist at an early age, because of the potential progressive impact on craniofacial morphology. The orthodontist and pediatric ENT specialist must engage in a process of reciprocal education on evidence-based removal of lymphoid tissues obstructing nasal respiration, or medical clearance of obstacles to nasal respiration. Collaborative work is still needed to avoid maintaining nasal obstruction or performing unnecessary excision of adenoids or tonsils.
- The orthodontist (and ENT specialist) should be familiar with the recognition of hypertrophic adenoids on a cephalogram, and with the appearance of other structures (hypertrophied inferior turbinate, tonsils, septal deviation) on lateral and postero-anterior cephalograms, even if definitive diagnosis is confirmed with other tests (e.g. endoscopy for enlarged turbinates).
- The involvement of the orthodontist in OSA treatment with oral appliances must be in consultation and agreement with the treating physician (commonly a pulmonologist, but also a neurologist or otorhinolaryngologist).
- The potential of RME to improve conductive hearing loss should be further explored for possible beneficial applications.

- The role of the ENT specialist as an otolaryngologist and/or a facial surgeon in the treatment of cleft lip/palate and other craniofacial anomalies is asserted as part of the team handling these conditions.
- Collaboration is needed in the presence of ear pain caused by temporomandibular dysfunction to rule out otological reasons that cause the otalgia.

References

Alsufyani, N.A., Noga, M.L., Witmans, M. et al. (2017). Upper airway imaging in sleep-disordered breathing: Role of cone-beam computed tomography. *Oral Radiology* 33:161–169.

American Academy of Otolaryngology–Head and Neck Surgery (2021). Clinical indicators: Tonsillectomy, adenoidectomy, adenotonsillectomy in childhood. https://www.entnet.org/resource/clinical-indicators-tonsillectomy-adenoidectomy-adenotonsillectomy-in-childhood.

Angle, E.H. (1907). *Treatment of Malocclusion of the Teeth*, 7th ed. Philadelphia, PA: S.S. White.

Babakhanian, A., Karam, I., Ghafari, J.G. et al. (2021). Long term (>10 years) effects of airway obstruction treatment on dento-facial morphology. Thesis, American University of Beirut.

Bahadir, O., Caylan, R., Bektas, D. et al. (2006). Effects of adenoidectomy in children with symptoms of adenoidal hypertrophy. *European Archives of Oto-rhino-laryngology* 263(2): 156–159. doi: 10.1007/s00405-005-0962-x.

Bar, A., Tarasiuk, A., Segev, Y. et al. (1999). The effect of adenotonsillectomy on serum insulin-like growth factor-I and growth in children with obstructive sleep apnea syndrome. *Journal of Pediatrics* 135(1): 76–80. doi: 10.1016/s0022-3476(99)70331-8.

Behlfelt, K., Linder-Aronson, S., McWilliam, J. et al. (1990). Cranio-facial morphology in children with and without enlarged tonsils.

European Journal of Orthodontics 12(3): 233–243. doi: 10.1093/ejo/12.3.233.

Bitar, M.A., Macari, A.T., and Ghafari, J.G. (2010). Correspondence between subjective and linear measurements of the palatal airway on lateral cephalometric radiographs. *Archives of Otolaryngology —Head & Neck Surgery* 136(1)L 43–47. doi: 10.1001/archoto.2009.198.

Bluestone, C.D. (1996). Pathogenesis of otitis media: Role of eustachian tube. *Pediatric Infectious Disease Journal* 15(4): 281–291. doi: 10.1097/00006454-199604000-00002.

Bowatte, G., Tham, R., Allen, K.J. et al. (2015). Breastfeeding and childhood acute otitis media: A systematic review and meta-analysis. *Acta Paediatrica* 104(467): 85–95. doi: 10.1111/apa.13151.

Brunetto, D.P., Velasco, L., Koerich, L. et al. (2014). Prediction of 3-dimensional pharyngeal airway changes after orthognathic surgery: A preliminary study. *American Journal of Orthodontics and Dentofacial Orthopedics* 146(3): 299–309. doi: 10.1016/j.ajodo.2014.05.024.

Buschang, P., and Hinton, R. (2005). A gradient of potential for modifying craniofacial growth. *Seminars in Orthodontics* 11: 219–226.

Cozza, P., Di Girolamo, S., Ballanti, F. et al. (2007). Orthodontist-otorhinolaryngologist: An interdisciplinary approach to solve otitis media. *European Journal of Paediatric Dentistry* 8(2): 83–88.

Cummings, B.J., Fredrickson, J.M., Harker, L.A. et al. (1998). *Anatomy and Physiology of the Eustachian Tube*, vol. 4, 3rd ed. St. Louis, MO: Mosby-Yearbook.

Dewey, C., Midgeley, E., and Maw, R. (2000). The relationship between otitis media with effusion and contact with other children in a British cohort studied from 8 months to 3 1/2 years. The ALSPAC Study Team. Avon Longitudinal Study of Pregnancy and

Childhood. *International Journal of Pediatric Otorhinolaryngology* 55(1): 33–45. doi: 10.1016/s0165-5876(00)00377-3.

El, H., and Palomo, J.M. (2013). An airway study of different maxillary and mandibular sagittal positions. *European Journal of Orthodontics* 35(2): 262–270.

Erdur, O.E., and Yilmaz, B.S. (2022). Voice changes after surgically assisted rapid maxillary expansion. *American Journal of Orthodontics and Dentofacial Orthopedics* 161(1): 125–132. doi: 10.1016/j.ajodo.2020.06.055.

Evans, S., Neave, N., and Wakelin, D. (2006). Relationships between vocal characteristics and body size and shape in human males: An evolutionary explanation for a deep male voice. *Biological Psychology* 72(2): 160–163. doi: 10.1016/j.biopsycho.2005.09.003.

Fagundes, N., Rabello, N.M., Maia, L.C. et al. (2017). Can rapid maxillary expansion cause auditory improvement in children and adolescents with hearing loss? *A systematic review*. *Angle Orthodontist* 87(6): 886–896. doi: 10.2319/021517-111.1.

Fields, H.W., Warren, D.W., Black, K. et al. (1991). Relationship between vertical dentofacial morphology and respiration in adolescents. *American Journal of Orthodontics and Dentofacial Orthopedics* 99(2): 147–154. doi: 10.1016/0889-5406(91)70117-F.

Fujimoto, S., Yamaguchi, K., and Gunjigake, K. (2009). Clinical estimation of mouth breathing. *American Journal of Orthodontics and Dentofacial Orthopedics* 136(5): 630.e1–631. doi: 10.1016/j.ajodo.2009.03.034.

Ghafari, J. (2004). Therapeutic and developmental maxillary orthopedics: Evaluation of effects and limitations. In: Z. Davidovitch and J. Mah (eds.), *Biological Mechanisms of Tooth Movement and Craniofacial Adaptation*. Boston, MA: Harvard Society for the Advancement of Orthodontics, pp. 167–181.

Ghafari, J.G., and Macari, A.T. (2013). Component analysis of predominantly vertical occlusal problems. *Seminars in Orthodontics* 4: 227–238.

Haas, A.J. (1961). Rapid expansion of the maxillary dental arch and nasal cavity by opening the midpalatal suture. *Angle Orthodontist* 31: 73–90.

Hamdan, A.L., Khandakji, M., and Macari, A.T. (2018). Maxillary arch dimensions associated with acoustic parameters in prepubertal children. *Angle Orthodontist* 88(4): 410–415. doi: 10.2319/111617-792.1.

Harvold, E.P., Tomer, B.S., Vargervik, K. et al. (1981). Primate experiments on oral respiration. *American Journal of Orthodontics* 79(4): 359–372. doi: 10.1016/0002-9416(81)90379-1.

Hassan, T., Naini, F.B., and Gill, D.S. (2007). The effects of orthognathic surgery on speech: A review. *Journal of Oral and Maxillofacial Surgery* 65(12): 2536–2543. doi: 10.1016/j.joms.2007.05.018.

Hata, M., Asakura, K., Saito, H. et al. (1996). Profile of immunoglobulin production in adenoid and tonsil lymphocytes. *ActaOoto-laryngologica Supplementum* 523: 84–86.

Huertas, D., and Ghafari, J. (2001). New posteroanterior cephalometric norms: A comparison with craniofacial measures of children treated with palatal expansion. *Angle Orthodontist* 71(4): 285–292. doi: 10.1043/0003-3219(2001)071<0285:NPCNAC>2.0.CO;2.

IPDTOC Working Group (2011). Prevalence at birth of cleft lip with or without cleft palate: Data from the International Perinatal Database of Typical Oral Clefts (IPDTOC). *Cleft Palate-Craniofacial Journal* 48(1): 66–81. doi: 10.1597/09-217.

Jorge, T.M., Brasolotto, A.G., Gonçales, E.S. et al. (2009). Influence of orthognathic surgery on voice fundamental frequency. *Journal*

of Craniofacial Surgery 20(1): 161–164. doi: 10.1097/SCS.0b013e3181945a64.

Kahle, W. (1993). *Nervous System and Sensory Organs*, vol. 3, 3rd ed. New York: Thieme Medical Publishers.

Kaygusuz, I., Alpay, H.C., Gödekmerdan, A. et al. (2009). Evaluation of long-term impacts of tonsillectomy on immune functions of children: A follow-up study. *International Journal of Pediatric Otorhinolaryngology* 73(3): 445–449. doi: 10.1016/j.ijporl.2008.11.014.

Kelly, K.M. (1993). Recurrent otitis media: Genetic immunoglobulin markers in children and their parents. *International Journal of Pediatric Otorhinolaryngology* 25(1–3): 279–280. doi: 10.1016/0165-5876(93)90066-c.

Kerr, W.J., McWilliam, J.S., and Linder-Aronson, S. (1989). Mandibular form and position related to changed mode of breathing—a five-year longitudinal study. *Angle Orthodontist* 59(2): 91–96. doi: 10.1043/0003-3219(1989)059<0091:MFAPRT>2.0.CO;2.

Kılıç, N., Kiki, A., Oktay, H. et al. (2008a). Effects of rapid maxillary expansion on conductive hearing loss. *Angle Orthodontist* 78(3): 409–414. doi: 10.2319/050407-217.1.

Kılıç, N., Oktay, H., Selimoğlu, E. et al. (2008b). Effects of semirapid maxillary expansion on conductive hearing loss. *American Journal of Orthodontics and Dentofacial Orthopedics* 133(6): 846–851. doi: 10.1016/j.ajodo.2006.05.047.

Kılıç, N., Yörük, Ö., and Kılıç, S.C. (2021). An alternative treatment approach for patients with resistant otitis media with effusion and dysfunctional Eustachian tube. *Angle Orthodontist* 91(6): 772–777. doi: 10.2319/021421-127.1.

Kılıç, N., Yörük, Ö., Kılıç, S.C. et al. (2016). Rapid maxillary expansion versus middle ear tube placement: Comparison of hearing improvements in children with resistance otitis media

with effusion. *Angle Orthodontist* 86(5): 761–767. doi: 10.2319/101515-693.1.

Kim, Y.J., Hong, J.S., Hwang, Y.I. et al. (2010). Three-dimensional analysis of pharyngeal airway in preadolescent children with different anteroposterior skeletal patterns. *American Journal of Orthodontics and Dentofacial Orthopedics* 137(3): 306.e1–307. doi: 10.1016/j.ajodo.2009.10.025.

Laine, T. (1992). Malocclusion traits and articulatory components of speech. *European Journal of Orthodontics* 14(4): 302–309. doi: 10.1093/ejo/14.4.302.

Leavy, K.M., Cisneros, G.J., and LeBlanc, E.M. (2016). Malocclusion and its relationship to speech sound production: Redefining the effect of malocclusal traits on sound production. *American Journal of Orthodontics and Dentofacial Orthopedics* 150(1): 116–123. doi: 10.1016/j.ajodo.2015.12.015.

Leiter, J.C., and Baker, G.L. (1989). Partitioning of ventilation between nose and mouth: The role of nasal resistance. *American Journal of Orthodontics and Dentofacial Orthopedics* 95(5): 432–438. doi: 10.1016/0889-5406(89)90305-3.

Lieberthal, A.S., Carroll, A.E., Chonmaitree, T. et al. (2013). The diagnosis and management of acute otitis media. *Pediatrics* 131(3): e964–e999. doi: 10.1542/peds.2012-3488.

Lim, D.J., and Mogi, G. (1994). Mucosal immunology of the middle ear and Eustachian tube. In: P.L. Ogra, J. Mestechy, M.E. Lamen et al. (eds.), *Handbook of Mucosal Immunology*. San Diego, CA: Academic Press, pp. 599–606.

Linder-Aronson, S., and Leighton, B.C. (1983). A longitudinal study of the development of the posterior nasopharyngeal wall between 3 and 16 years of age. *European Journal of Orthodontics* 5(1): 47–58. doi: 10.1093/ejo/5.1.47.

Linder-Aronson, S., Woodside, D.G., Hellsing, E. et al. (1993). Normalization of incisor position after adenoidectomy. *American*

Journal of Orthodontics and Dentofacial Orthopedics 103(5): 412–427. doi: 10.1016/S0889-5406(05)81792-5.

Linder-Aronson, S., Woodside, D.G., and Lundström, A. (1986). Mandibular growth direction following adenoidectomy. *American Journal of Orthodontics* 89(4)L 273–284. doi: 10.1016/0002-9416(86)90049-7.

Liu, Y., Zeng, X., Fu, M. et al. (2000). Effects of a mandibular repositioner on obstructive sleep apnea. *American Journal of Orthodontics and Dentofacial Orthopedics* 118(3): 248–256. doi: 10.1067/mod.2000.104831.

Macari, A.T., Bitar, M.A., and Ghafari, J.G. (2012). New insights on age-related association between nasopharyngeal airway clearance and facial morphology. *Orthodontics & Craniofacial Research* 15(3): 188–197. doi: 10.1111/j.1601-6343.2012.01540.x.

Macari, A.T., and Haddad, R.V. (2016). The case for environmental etiology of malocclusion in modern civilizations: Airway morphology and facial growth. *Seminars in Orthodontics* 22(3): 223–233.

Macari, A.T., Karam, I.A., Tabri, D. et al. (2014). Correlation between the length and sagittal projection of the upper and lower jaw and the fundamental frequency. *Journal of Voice* 28(3): 291–296. doi: 10.1016/j.jvoice.2013.10.003.

Macari, A.T., Karam, I.A., Tabri, D. et al. (2015). Formants frequency and dispersion in relation to the length and projection of the upper and lower jaws. *Journal of Voice* 29(1): 83–90. doi: 10.1016/j.jvoice.2014.05.011.

Macari, A.T., Karam, I.A., Ziade, G. et al. (2017). Association between facial length and width and fundamental frequency. *Journal of Voice* 31(4): 410–415. doi: 10.1016/j.jvoice.2016.12.001.

Macari, A.T., Ziade, G., Khandakji, M. et al. (2016). Effect of rapid maxillary expansion on voice. *Journal of Voice* 30(6): 760.e1–760.e6. doi: 10.1016/j.jvoice.2015.09.013.

Major, M.P., Flores-Mir, C., and Major, P.W. (2006). Assessment of lateral cephalometric diagnosis of adenoid hypertrophy and posterior upper airway obstruction: A systematic review. *American Journal of Orthodontics and Dentofacial Orthopedics* 130(6): 700–708. doi: 10.1016/j.ajodo.2005.05.050.

Major, M.P., Witmans, M., El-Hakim, H. et al. (2014). Agreement between cone-beam computed tomography and nasoendoscopy evaluations of adenoid hypertrophy. *American Journal of Orthodontics and Dentofacial Orthopedics* 146(4): 451–459. doi: 10.1016/j.ajodo.2014.06.013.

Mandel, E.M., Casselbrant, M.L., Richert, B.C. et al. (2016). Eustachian tube function in 6-year-old children with and without a history of middle ear disease. *Otolaryngology—Head and Neck Surgery* 154(3): 502–507. doi: 10.1177/0194599815620149.

Marcano-Acuña, M.E., Carrasco-Llatas, M., Tortajada-Girbés, M. et al. (2019). Impact of adenotonsillectomy on the evolution of inflammatory markers. *Clinical Otolaryngology* 44(6): 983–988. doi: 10.1111/coa.13423.

Marunick, M.T., and Menaldi, C.J. (2000). Maxillary dental arch form related to voice classification: A pilot study. *Journal of Voice* 14(1): 82–91. doi: 10.1016/s0892-1997(00)80097-1.

Mattar, S.E., Anselmo-Lima, W.T., Valera, F.C. et al. (2004). Skeletal and occlusal characteristics in mouth-breathing pre-school children. *Journal of Clinical Pediatric Dentistry* 28(4): 315–318. doi: 10.17796/jcpd.28.4.hg0k800564031787.

Mishima, K., Moritani, N., Nakano, H. et al. (2013). Voice characteristics before versus after mandibular setback surgery in patients with mandibular prognathism using nonlinear dynamics and conventional acoustic analyses. *Journal of Cranio-maxillofacial Surgery* 41(8): 706–709. doi: 10.1016/j.jcms.2012.01.021.

Moore, K. (1992). The head. In K.L. Moore (ed.), *Clinically Oriented Anatomy*, 3rd ed. Philadelphia, PA: Lippincott, Williams and Wilkins, ch. 7.

Moss, M.L., and Salentijn, L. (1969). The primary role of functional matrices in facial growth. *American Journal of Orthodontics* 55(6): 566–577. doi: 10.1016/0002-9416(69)90034-7.

National Institute on Deafness and Other Communication Disorders (n.d.). Voice, speech, and language. https://www.nidcd.nih.gov/health/what-is-voice-speech-language.

Niemi, M., Laaksonen, J.P., Peltomäki, T., et al. (2006). Acoustic comparison of vowel sounds produced before and after orthognathic surgery for mandibular advancement. *Journal of Oral and Maxillofacial Surgery* 64(6): 910–916. doi: 10.1016/j.joms.2006.02.009.

Nieminen, P., Löppönen, T., Tolonen, U. et al. (2002). Growth and biochemical markers of growth in children with snoring and obstructive sleep apnea. *Pediatrics* 109(4): e55. doi: 10.1542/peds.109.4.e55.

Ovsenik, M. (2009). Incorrect orofacial functions until 5 years of age and their association with posterior crossbite. *American Journal of Orthodontics and Dentofacial Orthopedics* 136(3): 375–381. doi: 10.1016/j.ajodo.2008.03.018.

Pirilä-Parkkinen, K., Pirttiniemi, P., Nieminen, P. et al. (2009). Dental arch morphology in children with sleep-disordered breathing. *European Journal of Orthodontics* 31(2): 160–167. doi: 10.1093/ejo/cjn061.

Proffit, W.R. (2007). The etiology of orthodontic problems: Respiratory pattern. In: W.R. Proffit, H.W Fields, and D.M. Sarver (eds.), *Contemporary Orthodontics*, 4th ed. St. Louis, MO: Elsevier, pp. 154–158.

Proffit, W., Fields, H.W., Larson, B. et al. (2018) *Contemporary Orthodontics*, 6th ed. St. Louis, MO: Elsevier.

Rosso, C., Colletti, L., Foltran, M. et al. (2022). Effects of rapid maxillary expansion on hearing loss and otitis media in cleft

palate children. *European Archives of Oto-rhino-laryngology* 279(9): 4335–4343. doi: 10.1007/s00405-021-07187-5.

Rovers, M.M., Schilder, A.G., Zielhuis, G.A. et al. (2004). Otitis media. *Lancet* 363(9407): 465–473. doi: 10.1016/S0140-6736(04)15495-0.

Sataloff, R.T. (2017). Endocrine function. In: *R.T. Sataloff, Professional Voice: The Science and Art of Clinical Care*, 4th ed. San Diego, CA: Plural Publishing, pp. 665–671.

Scammon, R.E., Harris, J.A., Jackson, C.M. et al. (1930). *The Measurement of Man*. Minneapolis, MN: University of Minnesota Press.

Schütz-Fransson, U., and Kurol, J. (2008). Rapid maxillary expansion effects on nocturnal enuresis in children: A follow-up study. *Angle Orthodontist* 78(2): 201–208. doi: 10.2319/021407-71.1.

Seibert, J.W., and Danner, C.J. (2006). Eustachian tube function and the middle ear. *Otolaryngologic Clinics of North America* 39(6): 1221–1235. doi: 10.1016/j.otc.2006.08.011.

Sheahan, P., and Blayney, A.W. (2003). Cleft palate and otitis media with effusion: A review. *Revue de laryngologie – otologie – rhinologie* 124(3): 171–177.

Singh, H., Maurya, R.K., Sharma, P. et al. (2021). Effects of maxillary expansion on hearing and voice function in non-cleft lip palate and cleft lip palate patients with transverse maxillary deficiency: A multicentric randomized controlled trial. *Brazilian Journal of Otorhinolaryngology* 87(3): 315–325. doi: 10.1016/j.bjorl.2019.09.010.

Stellzig-Eisenhauer, A., and Meyer-Marcotty, P. (2010). Interaktion von Hals-Nasen-Ohren-Heilkunde und Kieferorthopädie: Die Beziehung zwischen dem nasopharyngealen Luftraum und den kraniofazialen Strukturen [Interaction between otorhinolaryngology and orthodontics: Correlation between the nasopharyngeal airway and the craniofacial complex]. *Laryngo-*

rhino-otologie 89(Suppl 1): S72–S78. doi: 10.1055/s-0029-1246163.

Taşpinar, F., Uçüncü, H., and Bishara, S.E. (2003). Rapid maxillary expansion and conductive hearing loss. *Angle Orthodontist* 73(6): 669–673. doi: 10.1043/0003-3219(2003)073<0669:RMEACH>2.0.CO;2.

Tikku, T., Khanna, R., Sachan, K. et al. (2016). Dimensional and volumetric analysis of the oropharyngeal region in obstructive sleep apnea patients: A cone beam computed tomography study. *Dental Research Journal* 13(5): 396–404. doi: 10.4103/1735-3327.192273.

Titze. I.R. (2008). Nonlinear source-filter coupling in phonation: Theory. *Journal of the Acoustical Society of America* 123(5), 2733–2749. doi: 10.1121/1.2832337.

Valera, F.C., Travitzki, L.V., Mattar, S.E. et al. (2003). Muscular, functional and orthodontic changes in pre school children with enlarged adenoids and tonsils. *International Journal of Pediatric Otorhinolaryngology* 67(7): 761–770. doi: 10.1016/s0165-5876(03)00095-8.

Valtonen, H.J., Blomgren, K.E., and Qvarnberg, Y.H. (2000). Consequences of adenoidectomy in conjunction with tonsillectomy in children. *International Journal of Pediatric Otorhinolaryngology* 53(2): 105–109. doi: 10.1016/s0165-5876(00)00312-8.

van Kempen, M.J., Rijkers, G.T., and Van Cauwenberge, P.B. (2000). The immune response in adenoids and tonsils. *International Archives of Allergy and Immunology* 122(1): 8–19. doi: 10.1159/000024354.

Viegas, F., Viegas, D., Serra Guimarães, G. et al. (2021). Acoustic analysis of voice and speech in men with skeletal Class III malocclusion: A pilot study. *Folia Phoniatrica et Logopaedica* 73(2): 117–125. doi: 10.1159/000505186.

Villano, A., Grampi, B., Fiorentini, R. et al. (2006). Correlations between rapid maxillary expansion (RME) and the auditory apparatus. *Angle Orthodontist* 76(5): 752–758. doi: 10.1043/0003-3219(2006)076[0752:CBRMER]2.0.CO;2.

Warren, D.W., Hershey, H.G., Turvey, T.A. et al. (1987). The nasal airway following maxillary expansion. *American Journal of Orthodontics and Dentofacial Orthopedics* 91(2): 111–116. doi: 10.1016/0889-5406(87)90467-7.

Wertz, R.A. (1968). Changes in nasal airflow incident to rapid maxillary expansion. *Angle Orthodontist* 38(1): 1–11. doi: 10.1043/0003-3219(1968)038<0001:CINAIT>2.0.CO;2.

Woodside, D.G., Linder-Aronson, S., Lundstrom, A. et al. (1991). Mandibular and maxillary growth after changed mode of breathing. *American Journal of Orthodontics and Dentofacial Orthopedics* 100(1): 1–18. doi: 10.1016/0889-5406(91)70044-W.

Zettergren-Wijk, L., Forsberg, C.M., and Linder-Aronson, S. (2006). Changes in dentofacial morphology after adeno-/tonsillectomy in young children with obstructive sleep apnoea—a 5-year follow-up study. *European Journal of Orthodontics* 28(4): 319–326. doi: 10.1093/ejo/cji119.

13
Neuromuscular Diseases and the Orthodontist

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Summary

Neuromuscular diseases, a heterogeneous group of rare disorders affecting the neuromuscular system, can lead to muscle weakness, degeneration, and atrophy. If the orofacial muscles are affected by the disease, dentofacial development and craniofacial growth may be altered, which can have important implications for the orthodontist. A look at individuals with two of the less rare myopathies, namely myotonic dystrophy and Duchenne muscular dystrophy, highlight that a high prevalence of malocclusions is present. Patients with myotonic dystrophy may develop dentofacial aberrations early in childhood, while those with Duchenne muscular dystrophy develop serious dentofacial malocclusions during the pubertal and postpubertal periods. When proposing orthodontic treatment with or without orthognathic surgery to treat malocclusions and dentofacial deformities caused by neuromuscular disorders, one must be aware that such treatments are inherently prone to be unstable due to the nature of the diseases in question. Treatment planning in these cases needs to consider the severity and progression of the disease in consultation with the neurologist and other specialists involved. Interceptive orthodontic measures may be a more reasonable approach in these individuals to impede the development of dentofacial aberrations. Interceptive approaches must however be adapted to the specific type of neuromuscular disease in question. One example of such an approach is in patients with Duchenne muscular dystrophy, where the use of rigid lingual arches may help for some years in this respect.

Neuromuscular diseases are a heterogeneous group of rare disorders, either hereditary or acquired, affecting the neuromuscular system. Different diseases affect different parts of the neuromuscular system, including the peripheral nervous system, the neuromuscular junction, or the muscle fibers themselves, all of which are components of the motor unit. Muscle weakness, degeneration, and atrophy may be the consequences of damage to these structures. It is known that masticatory muscles and their function can influence dentofacial development and craniofacial growth (Kiliaridis, 1995), and thus if the muscles of the craniofacial system are affected this may have important implications for the orthodontist, which will be illustrated in this chapter.

There have been numerous attempts at classifying neuromuscular diseases, with a myriad of classification systems existing and being used in different academic textbooks and by different authors. These are based on clinical, pathological, clinicopathological, neuroanatomical, or etiological systems, although there is not one that is considered superior to the others (Gaspar et al., 2019a). One relatively simple neuroanatomical classification of diseases affecting the neuromuscular system, used in recent reviews on neuromuscular disease (Askanas and King Engel, 2015; Bhatt, 2016), will be adopted and used in this chapter, which is the distinction into four main groups, namely:

- *Motor neurone/anterior horn diseases*, including diseases such as spinal muscular atrophy and amyotrophic lateral sclerosis.
- *Peripheral neuropathies*, including diseases such as Charcot-Marie-Tooth disease and chronic inflammatory demyelinating neuropathy.
- *Neuromuscular junction disorders*, including diseases such as myasthenia gravis.
- *Myopathies*, including muscular dystrophies: diseases such as Duchenne muscular dystrophy, Becker muscular dystrophy, and myotonic dystrophy.

The number of individuals with each specific neuromuscular disease is small, making these relatively rare disorders. However, the disease burden is often severe and the management required is multidisciplinary, with a neurologist, respiratory physician, orthopedic specialist, and orthodontist involved in the follow-up and treatment of these individuals. With regard to genetic diagnosis, characteristic muscle biopsy abnormalities, specific biomarkers, and disease-specific targeted therapy, this is a rapidly developing field (Askanas and King Engel, 2015), with gene therapy approaches already making headway for some diseases.

The influence of neuromuscular diseases on craniofacial growth and the development of malocclusions has not received much attention in the orthodontic literature, owing probably to the fact that each of these diseases affects a very small percentage of the population. Even more scarce is literature on the orthodontic management of individuals with neuromuscular diseases. In this chapter, we will focus on the two neuromuscular diseases that have received the most attention in orthodontics: myotonic dystrophy (DM) and Duchenne muscular dystrophy (DMD). These myopathies are less rare, making them easier to study than other neuromuscular diseases. We will discuss the influence of these myopathies on the orofacial muscles and craniofacial growth and morphology, which illustrates that not all muscular diseases present similar dentofacial morphology. We also discuss approaches to orthodontic prevention and management of the malocclusions and growth aberrations typical in these diseases. Some other neuromuscular diseases will also briefly be touched on.

Myotonic dystrophy

DM (type 1; OMIM #160900) is a neuromuscular multisystem disease characterized by progressive muscular weakness, and a delayed relaxation of muscles after contraction referred to as myotonia (Bird, 1993). The most common form of muscular dystrophy, it affects approximately 1 in 8000 to 1 in 20,000 individuals (Bird, 1993; Soltanzadeh, 2022). The inheritance of DM is autosomal dominant, with variable expressivity but complete penetrance. Two distinct forms of DM have been defined, type 1 and type 2, based on different unstable nucleotide repeat expansions in untranslated DNA, with type 1 being the most commonly occurring and caused by the expansion of an unstable trinucleotide (CTG) repeat sequence in a region of the myotonic dystrophy kinase gene (Turner and Hilton-Jones, 2014). DM type 1 consists of five clinically distinct phenotypes based on the age of onset and CTG repeat size, namely congenital, childhood onset, classical (adult onset), mild, and permutation (Turner and Hilton-Jones, 2014). DM has a primary distal distribution, the principal affliction being of the hands, forearms, lower legs, and the muscles of the jaws, neck, face, and eyelids. One of the earliest and most constant features of DM is facial weakness. The course of the disease varies from individual to individual. The disease may involve the muscles very early in life, but the development of severe muscle weakness can appear much later, entailing a late diagnosis.

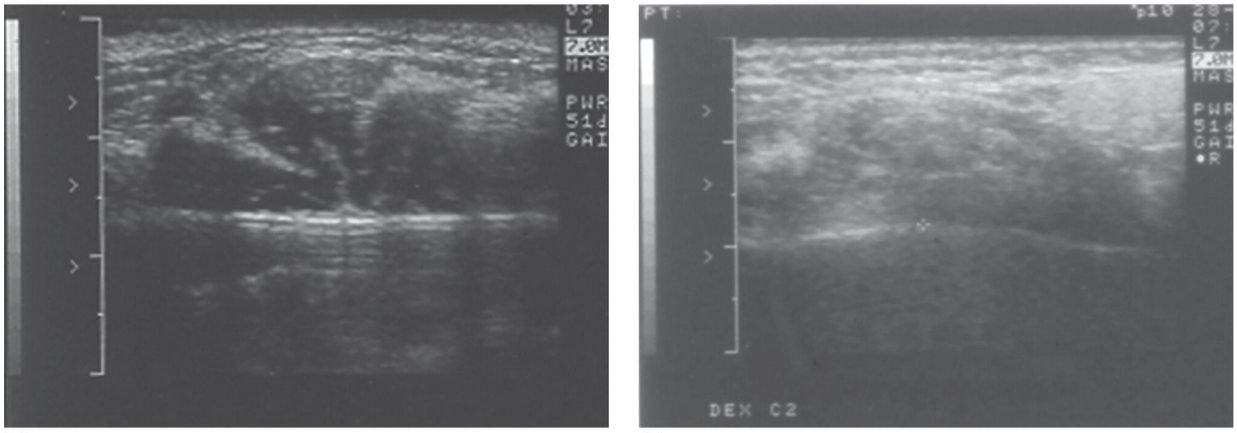
Orofacial muscles

The functional capacity of the masticatory muscles in adult individuals with DM is weaker than that of healthy subjects of the same sex and age. Adult subjects with DM in western Sweden were found to have a low maximal bite force level, on average less than half of the mean value of matched healthy control subjects, 138 N (standard deviation [SD] 79 N) in 16 females with DM compared with 383 N (SD 130 N) in healthy females; 205 N (SD 59 N) in 8 males with DM compared with 540 N (SD 137 N) in healthy males ($p < 0.001$; Kiliaridis et al., 1989). This has been confirmed by another study in Brazil on 37 subjects (Guimaraes et al., 2007). When looking at masticatory muscle activity, it seems that the disease influences the muscles involved in closing the mandible, as measured by the electromyographic (EMG) activity of the temporal and masseter muscles of adults with DM during maximal clenching and while chewing five peanuts until swallowing when compared to healthy matched subjects (Odman and Kiliaridis, 1996). It was found that the patients with DM had approximately three times less EMG activity in the masticatory muscles during maximal clenching. During chewing, patients with DM had approximately half the activity in the anterior temporal and the masseter muscles. DM thus influences the masticatory muscles, reducing their activity both at a maximal and a functional level.

Ultrasonography has also been applied to measure the thickness and examine the internal structure of the masseter muscle in 16 adult patients with DM compared to healthy individuals matched for age, sex, and number of occluding teeth (Kiliaridis et al., 1995a). The masseter thickness was measured bilaterally both under relaxed conditions and during maximal clenching. The imaging characteristics of the

masseter in most DM patients revealed thin muscles with obvious atrophy, increased echo intensity of the intramuscular tissue, and visual loss of the internal structure concerning tendons and fasciae (Figure 13.1). The mean masseter muscle thickness in the DM group was 10.4 mm (SD 2.2 mm) under relaxed conditions and 11.1 mm (SD 2.4 mm) during maximal clenching, compared with 13.3 mm (SD 2.2 mm) and 14.1 mm (SD 2.4 mm), respectively, in the healthy group ($p < 0.001$). Ultrasonography is considered a valuable method for both qualitative and quantitative evaluation of the condition of the masseter muscles. These findings indicate that, in most patients with DM, the masseter muscle is atrophic with obvious signs of degeneration (Kiliaridis et al., 1995a).

In children and adolescents with DM, the characteristics and prevalence of oral motor dysfunction have also been studied and different aspects of oral motor function have been correlated with the type of DM and sex (Sjögreen et al., 2007). In this study, 56 individuals with DM (30 males, 26 females) with a median age of 13 y 2 mo (range 2 y 6 mo–21 y 5 mo) were compared with healthy controls. They were divided into four subgroups: congenital DM (n = 18), mild congenital DM (n = 18), childhood DM (n = 18), and classical DM (n = 2). A speech-language pathologist assessed different variables of oral motor function, intelligibility, and lip force. The families used a questionnaire to report on eating difficulties and drooling. All individuals with DM had impaired facial expressions. Intelligibility was moderately or severely reduced in 30 patients (60%), excluding 6 patients without speech. Most of the children had moderate or severe impairment of lip motility (76.0%), tongue motility (52%), and lip force (69%), causing deviant production of bilabial and dental consonants. The families reported problems with eating (52%) and drooling (37%). Oral motor dysfunction was most prominent in congenital DM, and males were more affected than females (Sjögreen et al., 2007). In addition to the published findings, most patients were characterized by a downward-hanging mandibular position and a big free-way space.



(a) (b)

Figure 13.1 Ultrasonographic images of masseter muscle echogenicity and thickness. (a) Normal internal muscle structure in a healthy subject; (b) altered internal structure in a patient with myotonic dystrophy.

Dentofacial morphology

Occlusal traits and dentofacial morphology have been studied in 24 adult patients with DM and compared with a matched group of healthy individuals (Kiliaridis et al., 1989). A high prevalence of malocclusions was found among the patients with DM, who presented a higher frequency of malocclusions in the sagittal, vertical, and transversal planes, characterized often by Angle Class II malocclusion, anterior open bite, lateral crossbite, and notable space discrepancies (Figure 13.2). This patient group's craniofacial morphology showed a vertical aberration, characterized by a large angle between the mandibular and palatal planes and a steep mandible (Figure 13.3). These findings seem to be most pronounced in patients with early onset of the disease (Kiliaridis et al., 1989).

Interpretation of these data helps one conclude that the weak masticatory muscles are the likely etiological factor creating the aberration in the dentofacial morphology in adults with DM. To be able to develop and implement possible interceptive measures and to inhibit the development of the detected dentofacial anomalies, knowledge about the functional situation of these patients during childhood and adolescence and the extent and progress of the observed dentofacial aberrations during growth in these

individuals is necessary. Therefore, a cohort study of a group of children and adolescents with DM was necessary to reveal their functional and dentofacial characteristics, as well as a longitudinal study to follow up a cohort of young patients with DM and observe the development of their dentofacial anomalies.

The craniofacial morphology of 26 young individuals with congenital or childhood-onset DM was studied on lateral cephalograms in a cross-sectional manner and compared with normal standards obtained from healthy individuals from the Michigan Growth Study, according to their age and sex (Fontinha et al., 2018). Subsequently, the growth changes that occurred in the facial morphology of the children with DM over five years were recorded longitudinally and compared to the growth changes observed in healthy children (Fontinha et al., 2021). On examination of initial radiographic measurements, patients with DM showed a more retruded mandible sagitally, with larger ANB and smaller SNPg angles. Analysis of the vertical plane showed the mandibular plane angle and the intermaxillary angle to be larger. It was interesting to notice that during the five-year follow-up period, the intermaxillary angle remained the same in the children with DM, whereas this angle decreased in healthy individuals. Thus, it is important to stress that the young patients with DM already had a more retrognathic profile and hyperdivergent skeletal aberration with a steep mandibular plane and large intermaxillary angle at a young age, compared with healthy individuals. Their facial morphology seems to be established early and does not deteriorate during growth. With regard to different growth patterns, in children with DM the intermaxillary angle did not seem to decrease during the observation period, contrary to what was observed in healthy individuals (Fontinha et al., 2018).

Figure 13.2 A 32-year-old female patient with myotonic dystrophy. (a) Extraoral photographs showing a severely hyperdivergent facial pattern; (b) intraoral photographs presenting a Class II division 1 malocclusion, with a large overjet, space deficiency, and a narrow and deep palate.

Source: Kiliaridis and Katsaros (1998) / with permission from Taylor & Francis Group.

The malocclusions of 36 children and adolescents with DM were studied on dental casts and compared with a control group of 50 healthy growing individuals (Fontinha et al., 2021). The changes that had occurred in the sagittal, vertical, and transversal planes of occlusion of 26 of these patients over a median time of nine years during their growth were then traced longitudinally and compared to the changes observed in healthy growing individuals. It was found that the children and adolescents with DM had a higher prevalence of anterior open bite and posterior crossbite. When compared to controls, patients with DM presented smaller upper and lower intermolar as well as intercanine widths. In both groups, the individuals revealed longitudinal changes with a decrease in both upper and lower arch lengths and an increase in palatal vault height. During the follow-up period, the prevalence of malocclusions remained almost the same, only significantly differing with regard to the maxillary intermolar width, which decreased in individuals with DM. Similar to what was found in the craniofacial morphology of children and adolescents with DM, it has been shown that a higher prevalence of both anterior open bite and posterior crossbite is found already at an early age, compared to healthy control

individuals. These occlusal traits do not change with time except for the maxillary narrow intermolar width, which further decrease over time (Fontinha et al., 2021).

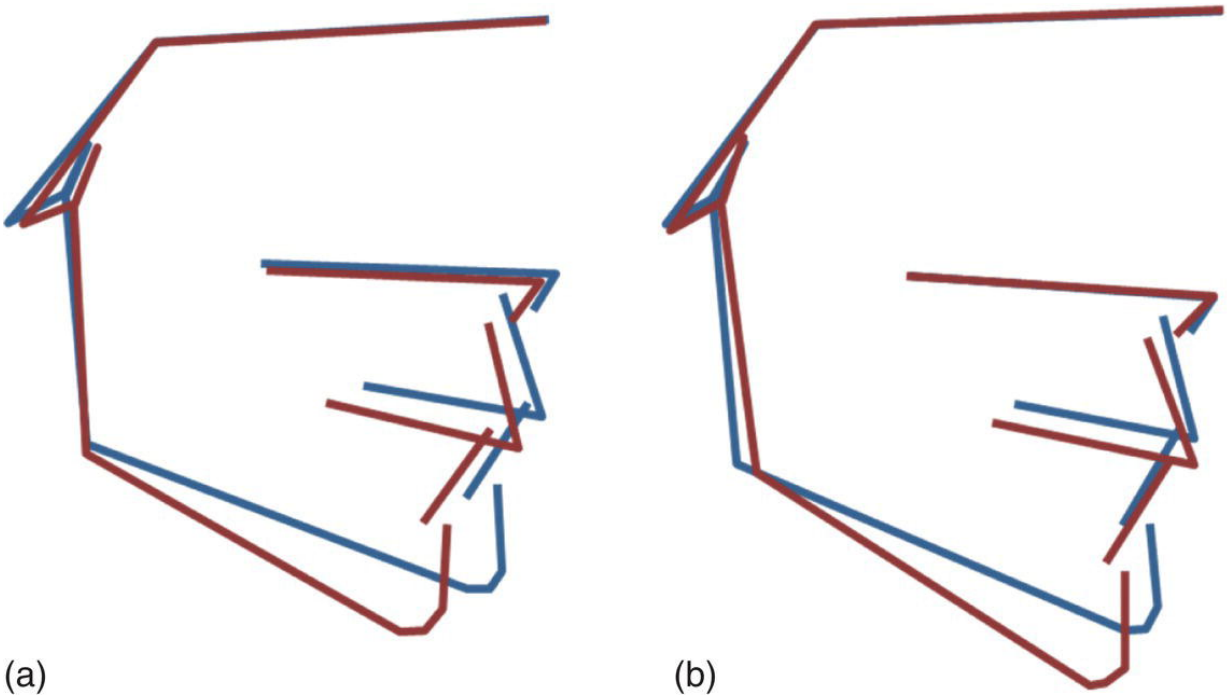


Figure 13.3 Average cephalometric tracings of healthy individuals (blue tracing) versus those with myotonic dystrophy (red tracing) of (a) males (average age 40.5 years; standard deviation [SD] 9.0 years); (b) females (average age 42.3 years; SD 10.1 years).

Source: Adapted from Kiliaridis et al. (1989).

Thus, concerning the dentofacial characteristics of patients with DM, it is important to stress that contrary to what one would expect, young patients with DM already have a more retrognathic profile and hyperdivergent skeletal aberration with a higher prevalence of anterior open bite and posterior crossbite from an early age, compared with healthy individuals. It seems that these characteristics have been established early and do not dramatically deteriorate during growth.

Orthodontic treatment

Due to the severity of the malocclusion and dentofacial deformity present, as well as possible functional limitations resulting in impairments in daily living, orthognathic surgery may be the best option to be considered in some patients with DM (Bezak et al., 2016). Orthognathic surgery can play an important role in managing deformities of the facial skeleton due to DM (Manzon and Philbert, 2007), especially in cases where, due to the magnitude of the discrepancy, the aesthetic and functional goals of treatment are not achievable with conventional orthodontics alone.

However, patients with DM present certain particularities that may complicate the task of deciding whether orthognathic surgery will be proposed as a viable treatment option. One must consider both the benefits and risks of such a procedure. In this population, the potential risks of elective surgery and general anesthesia may outweigh such procedures' benefits (Manzon and Philbert, 2007). Moreover, the indication to propose orthodontic treatment and orthognathic surgery to improve esthetics and masticatory function is difficult to determine, since the progressive nature of MD implies that the prognosis with regard to the development of dentofacial abnormalities and the outcome and stability after a particular treatment remain unpredictable (Balasubramaniam et al., 2008).

Despite this, the psychosocial effect related to esthetics and facial appearance may also influence the treatment decision process (Bezak et al., 2016). The importance of esthetics cannot be overlooked for teenagers and young adults, who are often defined and limited by the physical manifestations of their disability (Phillips and Beal, 2009; Marik and Hoag, 2012). Considering that the treatment can result in

a significant improvement in facial esthetics, jaw function, self-esteem, and quality of life, these situations may lower the threshold in favor of orthognathic surgery in selected patients (Manzon and Philbert, 2007; Bezak et al., 2016). A treatment plan involving orthognathic surgery, coupled with multidisciplinary management, in patients with DM and associated dentofacial deformities can surely offer satisfactory esthetic and functional outcomes, but the question of whether this satisfactory result will remain stable in the long term is a question that is central to the treatment planning and decision-making process.

The body of the maxillofacial and orthodontic literature is relatively light with regard to orthodontic and orthognathic surgical management of patients with DM. A limited number of cases have been described in the literature over the past 40 years. To our knowledge, one case with camouflage orthodontic treatment (Thind and Turbill, 2015) and ten cases with combined orthodontic and orthognathic surgical treatment (Müller and Punt-van Manen, 1982; Kaufman et al., 1983; Manzon and Philbert, 2007; Bezak et al., 2016; Cacucci et al., 2017; Antonarakis et al., 2019) have been reported. These are presented in Table 13.1. However, among these cases only four refer to postsurgical follow-up (12 and 18 months in two cases, both of which refer to follow-up post surgery and not post orthodontics, while two cases present postorthodontic follow-up, one of 7 months and one of 13.5 years). Moreover, all of these cases were treated at a relatively young age, either in late adolescence or in early adulthood.

In cases where postsurgical follow-up is reported (Manzon and Philbert, 2007; Kaufman et al., 1983), it is not clear when orthodontic treatment was terminated, since the authors refer to postoperative and not posttreatment follow-up and it could well be that the postoperative orthodontic phase lasted for the greatest part of this postoperative follow-up period. In addition, records shown in these cases are incomplete without a lateral cephalometric radiograph immediately postoperatively and after the 12–18-month follow-up to assess skeletal and dental stability. In the two cases where postorthodontic follow-up is discussed (Cacucci et al., 2017; Antonarakis et al., 2019), both discuss relapse and the difficulties in maintaining long-term stability. The case showing the longest follow-up (13.5 years) presents a case with significant relapse of the anterior open bite within these years of follow-up (Antonarakis et al., 2019), which brings to light the difficulties in maintaining stability given the muscular weakness (Figure 13.4). One major contributing factor to the relapse of the open bite was the overeruption of posterior teeth, shown in the cephalometric superimpositions (Figure 13.5), which may be due to muscular weakness (Antonarakis et al., 2019).

With this in mind, the complexity of the disease, the perioperative morbidity that can accompany DM, and the unpredictability of long-term treatment results dictate the need for a thorough evaluation from the multidisciplinary team when planning a combined orthodontic and orthognathic surgical intervention (Manzon and Philbert, 2007). The orthodontist and maxillofacial surgeon involved must be knowledgeable about the disease process, the physical characteristics, and the concomitant systemic anomalies, which helps facilitate proper planning, timely interventions, and efficient postoperative care.

When carrying out orthognathic surgery in these individuals, rigid fixation must be used and maxillomandibular fixation avoided to maintain patency of the upper airway and promote early return to function (Manzon and Philbert, 2007). Orthognathic surgical movements must be designed to favor long-term skeletal stability because of the high relapse potential due to progressive weakness of the masticatory muscles (Manzon and Philbert, 2007). Weakness of the masticatory muscles may result in immediate relapse of surgical movements to correct the anterior open bite, or may present as a late complication due to the overeruption of both the maxillary and mandibular posterior dentition (Manzon and Philbert, 2007; Kaufman et al., 1983; Antonarakis et al., 2019; Kiliaridis et al., 2019). The abnormal patterns of vertical facial growth (Fontinha et al., 2018; Staley et al., 1992), linked with altered neuromuscular function, may present difficulties for orthodontists and maxillofacial surgeons treating these patients.

The high potential for instability following orthodontic and orthognathic correction of an anterior open bite in patients with DM raises the issue of long-term retention. There is a critical need for long-term retention in these patients, and the orthodontist must evaluate the most appropriate way to provide retention to avoid the reappearance of an open bite. This may be with a posterior bite block, through its positive effect on the maxillary and mandibular molars, or elastics attached to skeletal anchorage plates that act on the maxillary and mandibular molars. This was attempted by the authors of one case that asked the patient to wear elastics from their removable retainers to skeletal anchorage plates, and

subsequently elastics directly on the anterior teeth to decrease the relapse of the open bite (Cacucci et al., 2017).

As with any long-term retention protocol, patient compliance may be challenging. This highlights the importance of informed consent, which must be properly obtained from the individual in question. Suppose patients with DM choose to correct their dentofacial anomaly. In that case, they must be aware that the result may only be stable for a limited time due to the high relapse potential, perhaps even despite any long-term lifelong retention protocols. One must always keep in mind that not undergoing any treatment also remains an option.

Regardless of which retention protocol is chosen to favor long-term stability, chewing and mandibular exercises may also be of benefit. The adaptability of the healthy masticatory muscles to training, such as chewing exercises, has been demonstrated in healthy individuals (Kiliaridis et al., 1995b; Ingervall and Bitsanis, 1987; Georgiakaki and Kiliaridis, 1998; He et al., 2013). Whether this is the case in individuals with DM and whether it would help in maintaining stability is, however, unknown. No studies have been carried out on patients with DM, but some data exist on patients with other neuromuscular disorders where masticatory exercises are found to improve masticatory function and performance (Kawazoe et al., 1982; Nozaki et al., 2010; van Bruggen et al., 2015). Nevertheless, it is not known whether in individuals with DM, and if so in which types of DM, chewing exercises might help prevent severe molar overeruption and thus diminish the chance of anterior open bite development.

Table 13.1 Published case reports or case series of orthodontic treatment with or without orthognathic surgery in patients with myotonic dystrophy.

Year	Authors	Patient age	Sex	Type of DM	Malocclusion	Tooth extractions	Orthognathic surgery	Orthodont
1982	Müller and Punt-van Manen	19	M	Unspecified	AOB	–	Mandible	FA
		16	M	Unspecified	AOB	–	Bimaxillary	FA
		20	F	Unspecified	AOB	–	Bimaxillary	FA
		17	M	Unspecified	AOB	–	Mandible	FA
1983	Kaufman et al.	26	M	Unspecified	Class III; AOB tendency	4 premolars	Bimaxillary + genio	FA
2007	Manzon and Philbert	15	F	Type 1	AOB	–	Bimaxillary	FA
2015	Thind and Turbill	11	F	Type 1	Class II; AOB tendency	–	None	TB, HPHG;
2016	Bezak et al.	15	F	Type 1	Class III; AOB	–	Bimaxillary	FA
		18	M	Type 1	Class II; AOB	–	Bimaxillary	FA
		19	M	Type 1	Class III; AOB	–	Mandible	FA
2017	Cacucci et al.	15	M	Type 1	Class III; AOB	–	Bimaxillary	Mx expansi FA
2019	Antonarakis et al.	17	M	Type 1	Class III; AOB	–	Bimaxillary	FA

AOB, anterior open bite; DM, myotonic dystrophy; F, female; FA, fixed appliances; genio, genioplasty; HPHG, high-pull headgear; M, male; Mx, maxillary; postop, postoperative; postortho, after the completion of orthodontic treatment; TB, twin block.

Source: Adapted from Antonarakis et al. (2019).

A final point worth raising is that dentofacial deformities similar to the ones seen in patients with DM may also be seen in apparently healthy individuals. Relapse of anterior open bite in healthy individuals is also relatively common, with approximately 16% of those undergoing maxillary surgical procedures and 12% of those undergoing bimaxillary procedures presenting with long-term relapse (Solano-Hernandez et al., 2013). Care is advised in these individuals with regard to the potential for instability

for these reasons, and since some patients may seek orthodontic treatment for anterior open bite unaware that they are affected by DM (Mercier et al., 1995). Thus orthodontists, as well as maxillofacial surgeons, must be alert to this possibility. Postponing treatment in these individuals until a later age may decrease the risk of presenting with vertical relapse in the long term. Delayed treatment ensures that the overeruption capacity of the posterior teeth, though still present, may be decreased (Kiliaridis et al., 2000).

(a)

(b)

(c)

Figure 13.4 Intraoral photographs of a patient with myotonic dystrophy treated with orthodontics and orthognathic surgery, followed up for 13.5 years post orthodontic treatment. (a) Initial intraoral photographs (age 17-0 years); (b) post-treatment intraoral photographs (age 18-8 years); (c) intraoral photographs at 13.5 years after the end of the orthodontic treatment (age 32-2 years).

Source: Antonarakis et al. (2019) / with permission from European Journal of Paediatric Dentistry.

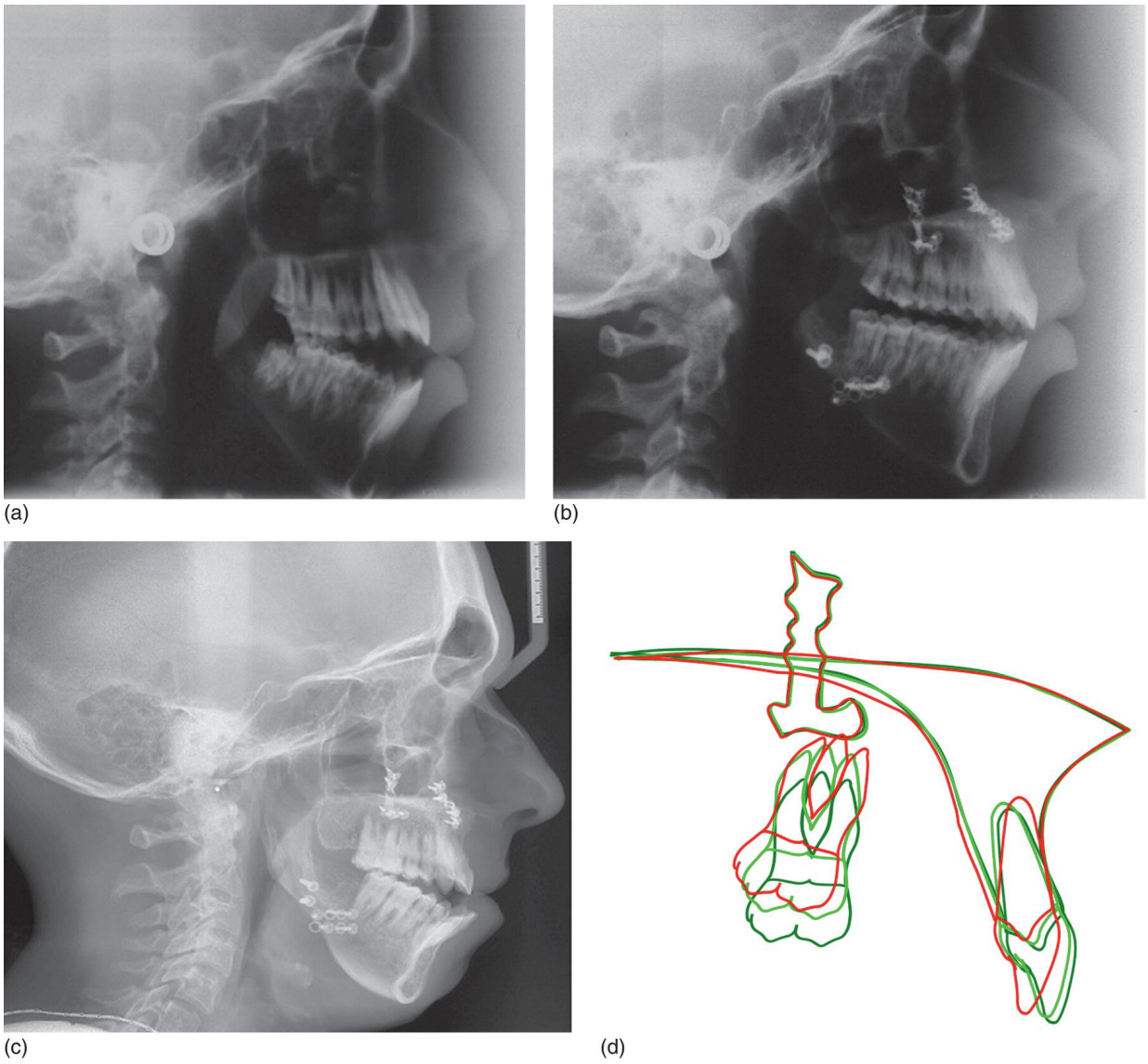


Figure 13.5 Lateral cephalometric radiographs of a patient with myotonic dystrophy, the same patient shown in Figure 13.4, treated with orthodontics and orthognathic surgery and followed up for 13.5 years post orthodontic treatment. (a) Initial lateral cephalometric radiograph (age 17-0 years); (b) post-treatment lateral cephalometric radiograph (age 18-8 years); (c) lateral cephalometric radiograph at 13.5 years after the end of the orthodontic treatment (age 32-2 years); (d) cephalometric maxillary superimposition on maxillary surgical rigid fixation plates of the immediate posttreatment (red), 4.5 years posttreatment (light green), and 13.5 years posttreatment (dark green) lateral cephalograms, showing changes in the position of the maxillary first molars.

Source: Antonarakis et al., 2019 / with permission from European Journal of Paediatric Dentistry.

Duchenne muscular dystrophy

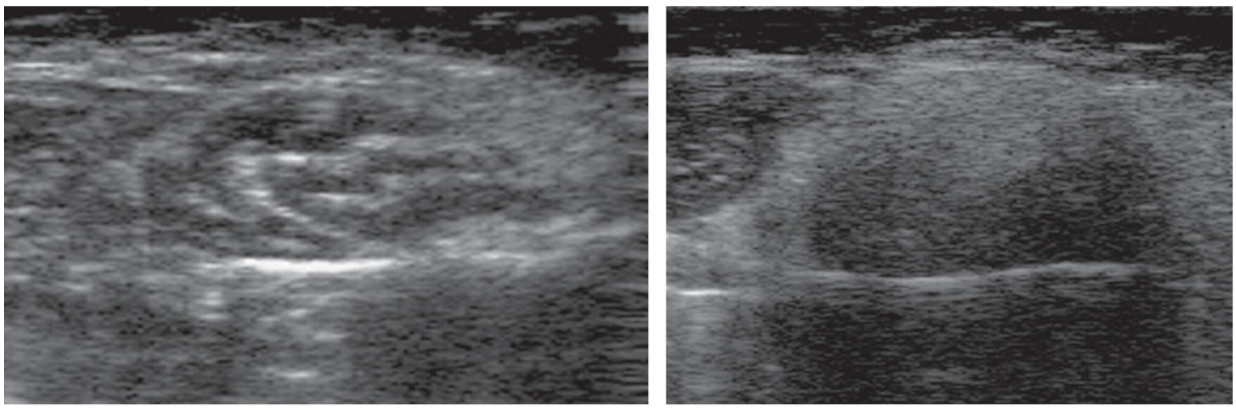
DMD (OMIM #310200) is a life-limiting X-linked recessive neuromuscular disorder characterized by progressive muscle degeneration and weakness, primarily affecting boys, with an incidence of 1 in 3500–5000 live male births, making it the most prevalent muscular dystrophy of childhood in boys (Mah et al., 2016). DMD is caused by mutations in the *dystrophin* gene, leading in most cases to the complete absence of the dystrophin protein, a cytoskeleton protein critical for the stability and normal function of the myofibers (Deconinck and Dan, 2007). DMD has a primarily distal distribution: it first

affects the hands, forearms, lower legs, and the muscles of the jaws, neck, face, and eyelids. It results in progressive muscle degeneration that manifests generally between 3 and 6 years of age, when the child's physical abilities such as walking, running, and climbing stairs begin to diverge from children of the same age, leading to frequent falls and then loss of independent ambulation in the second decade, the use of a wheelchair from around 10 years of age, pulmonary and cardiac complications, and ultimately premature death (Kieny et al., 2013; Bushby et al., 2010). The course of the disease and the development of severe muscle weakness vary among individuals.

Despite the recent advancement in novel therapeutic approaches (Verhaart and Aartsma-Rus, 2019), DMD remains a fatal condition requiring life-long multidisciplinary care, including symptomatic and rehabilitative management, surveillance, treatment of expected complications, and the use of corticosteroids (Yiu and Kornberg, 2015). With current specific and improved symptomatic treatment and advances in cardiac and respiratory care, including mechanical ventilatory support, life expectancy has shown a marked increase, with the median life expectancy now being 28 years (95% confidence interval [CI] 25–30 years; Broomfield et al., 2021).

Orofacial muscles

DMD has been seen to affect orofacial function. Certain characteristics of orofacial function in patients with DMD have been evaluated in an attempt to relate functional deteriorations to age and to the diminished internal structural quality of the masseter muscles. Bite force and finger force were measured in a cross-sectional study of 16 patients with DMD (6–20 years old) and 16 age-matched healthy control subjects (Botteron et al., 2009). The thickness and internal structural quality of the masseter muscles were evaluated ultrasonographically. No data, but only general trends, will be presented here due to the large heterogeneity in age. A reduced mouth opening was found, but there were no signs of masticatory muscle tenderness. Bite force values were lower in patients with DMD than in healthy control subjects. Masseter muscles showed no significant differences in thickness between the patients and the healthy subjects. Nevertheless, poorer internal muscle structural quality characterized the elder, nonambulatory patients with DMD (Figure 13.6), explaining their low bite force values. Based on this cross-sectional study, it was concluded that the masseter muscles, and by extension possibly all of the masticatory muscles, follow the general deterioration of the disease, which gradually affects the muscles after the first years of life, and becomes worse during the prepubertal, pubertal, and postpubertal periods (Botteron et al., 2009).



(a) (b)

Figure 13.6 Ultrasonographic images of masseter muscle echogenicity and thickness in (a) a healthy individual with normal internal muscle structure; (b) a patient with Duchenne muscular dystrophy showing altered internal muscle structure.

(a) (b) (c) (d)

Figure 13.7 Frontal photographs of patients with Duchenne muscular dystrophy at the ages of (a) 11.6 years; (b) 13.2 years; (c) 14.4 years; (d) 19.6 years. A progressively deteriorating malocclusion is seen in these images.

Source: Morel-Verdebout et al. (2007) / with permission from Oxford University Press.

Dentofacial morphology

The occlusal traits and craniofacial morphology of growing patients with DMD were studied and compared with healthy age-matched male individuals (Morel-Verdebout et al., 2007). The dental arches

and occlusal traits of both groups were analyzed on dental casts and compared with norms from healthy individuals from the literature. Lateral cephalograms of those with DMD and healthy individuals were compared by using scored values based on standard deviations in order to compensate for heterogeneity in the age of the subjects. A high prevalence of malocclusions was found in individuals with DMD, including posterior crossbites, anterior and lateral open bites, a tendency toward an Angle Class III malocclusion due to skeletal Class III relationships, and dental compensations of the Class III relationships by lingual retrusion of the lower incisors (Figure 13.7). Both upper and lower dental arches were wider posteriorly than those of the healthy controls (Figure 13.8). The lower arches were even wider than the upper arches, resulting frequently in posterior crossbites, with an excess of space in the dental arches of the patient group. No significant skeletal vertical deviations were observed in this group of patients with DMD, except for the maxillary plane angle that was larger than normal, while the anterior upper face height was smaller. Nevertheless, no difference was found in lower face height. The posterior enlargement of the dental arches and the dentoalveolar development toward an Angle Class III relationship were significantly related to the age of the patients, since they showed a higher prevalence in older adolescents than in younger children (Morel-Verdebout et al., 2007).

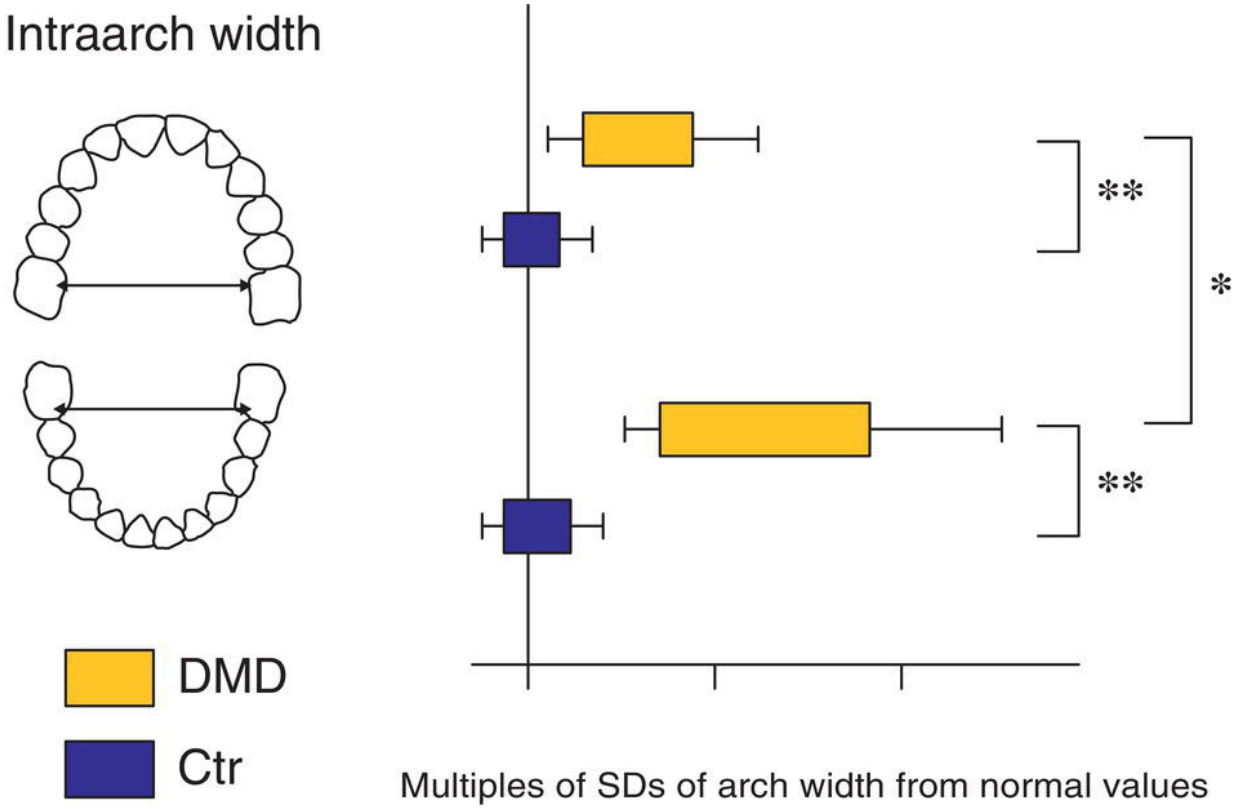


Figure 13.8 Arch width at the upper and lower first molars in patients with Duchenne muscular dystrophy (DMD) compared to healthy control subjects (Ctr), showing a statistically larger arch width in both upper and lower arches in patients with DMD compared with controls, and more so in the lower arch. Because of the heterogeneity in age, the units in the x axis express the deviation, in standard deviations (SDs), of the individuals from normal values.

To identify the effects of the progression of DMD on the oral function of growing patients and the impact it may have on the longitudinal changes in facial morphology and dental arch occlusal relationships, 12 patients with DMD (6.5–17.5 years of age) and 12 matched healthy controls were screened on two different occasions, two years apart (Egli et al., 2018). Dental casts, lateral cephalometric radiographs, maximal posterior bite force, and labial force were measured to determine changes in their functional capacities and dentofacial morphology. Furthermore, the thickness and echogenicity of the masseter muscle were measured during clenching. Within the two-year period, widening of the lower dental arch by 2.6 mm (SD 0.9 mm) for patients with DMD was observed, compared with a slight reduction of −0.1 mm (SD 0.8 mm) in the control group ($p = 0.001$). A statistically significant reduction of the sagittal

skeletal intermaxillary relationship (ANB angle) of 2.0° (SD 2.0°) was also found in the DMD group (p = 0.012). At both time points, the maximal posterior bite force and the labial force were lower for the patients with DMD compared to the healthy patients (p = 0.001), who presented an increase in these forces during the two years.

These findings indicate that DMD influences facial morphology, dental arch dimensions, and oral functional capacities (Egli et al., 2018). The longitudinal perspective of this study revealed that the worsening of most of the measured parameters was associated with the progression of the disease. Apart from the expected deterioration of the functional measurements, a tendency toward a skeletal Class III relationship was also found, as well as a marked transverse increase of the posterior part of the dental arches, more so in the lower than in the upper arch (Figure 13.9), resulting in posterior crossbites. The development of Class III skeletal relationships could be due to accelerated mandibular growth because of the enlarging tongue, or to a restriction of maxillary growth through the use of a continued positive airway pressure device. The transverse increase of the posterior part of the dental arches seems to be related to the progressive increase in tongue volume linked to the degenerative process of the muscle fibers and their replacement by adipose and connective tissue (Egli et al., 2018).

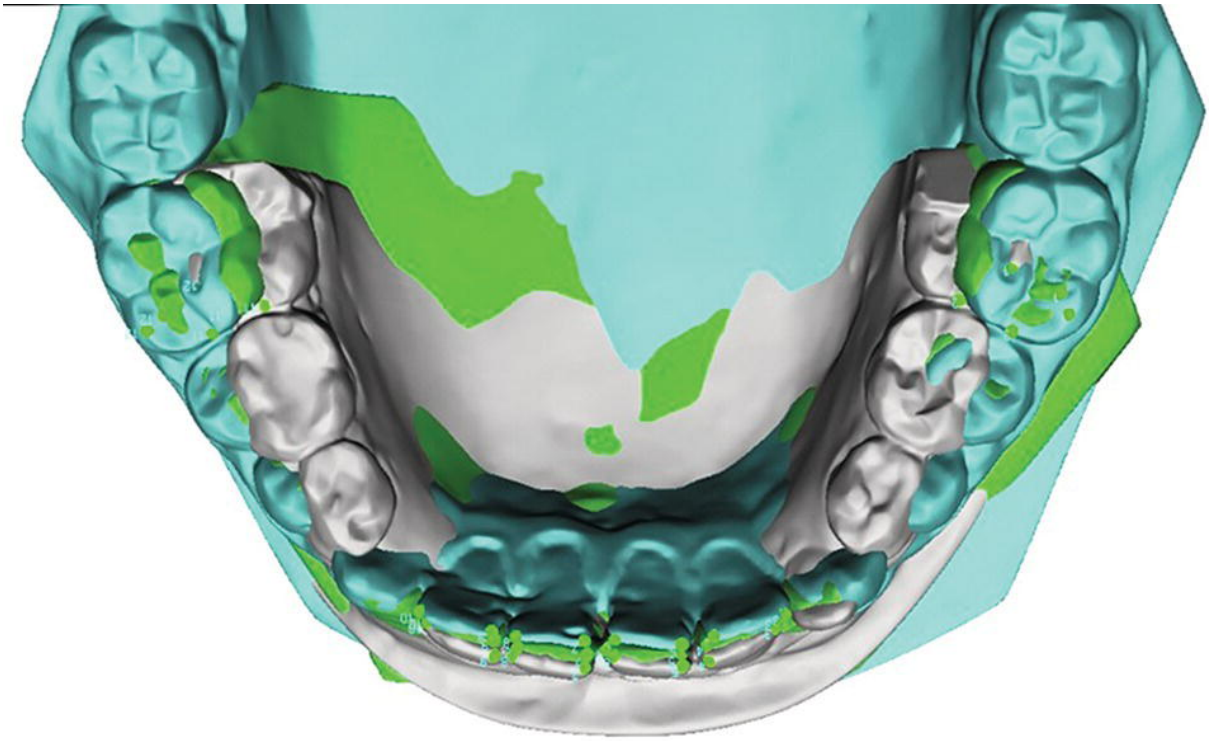


Figure 13.9 Superimpositions of dental casts from a patient with Duchenne muscular dystrophy at the age of 10.3 years (white), 12.4 years (green), and 14.8 years (blue), showing the large increase in the intermolar distance with time.

Orthodontic treatment

Only one case has been reported in the literature of comprehensive orthodontic treatment in a male patient with DMD (Miller, 2013). The author presented a young adult with severe anterior and lateral open bites with a proclined and spaced lower dentition, treated with glossectomy, extractions, fixed appliances, and elastics, to an excellent and commendable outcome. The treatment was also stable 13 months after removal of orthodontic appliances. Whether the result remained stable in the long term is not known. No other reports of similarly treated cases are available in the literature, and this is perhaps due to concerns about long-term stability given the nature of the disease itself. However, one may attempt to concentrate treatment efforts on prevention rather than trying to correct already developed and severe malocclusion.

Maintaining acceptable occlusal contacts despite the progression of the disease, for as long as possible, may preserve a better quality of life for subjects affected with DMD. One recent prospective pilot study (Antonarakis et al., 2020) proposed the use of a rigid mandibular lingual holding arch placed in boys with DMD to help prevent or at least slow down the rapid deterioration of the developing malocclusions in these children that accompanies the progressive deterioration of the disease. The mandibular lingual holding arch was laboratory constructed and soldered onto bands placed on the mandibular first molars. The arch was semicircular in cross-section, with 2 mm height and 1 mm depth and made of stainless steel (Figure 13.10). The semicircle's flat end faced the lingual aspects of the mandibular teeth while the circular end faced the tongue.

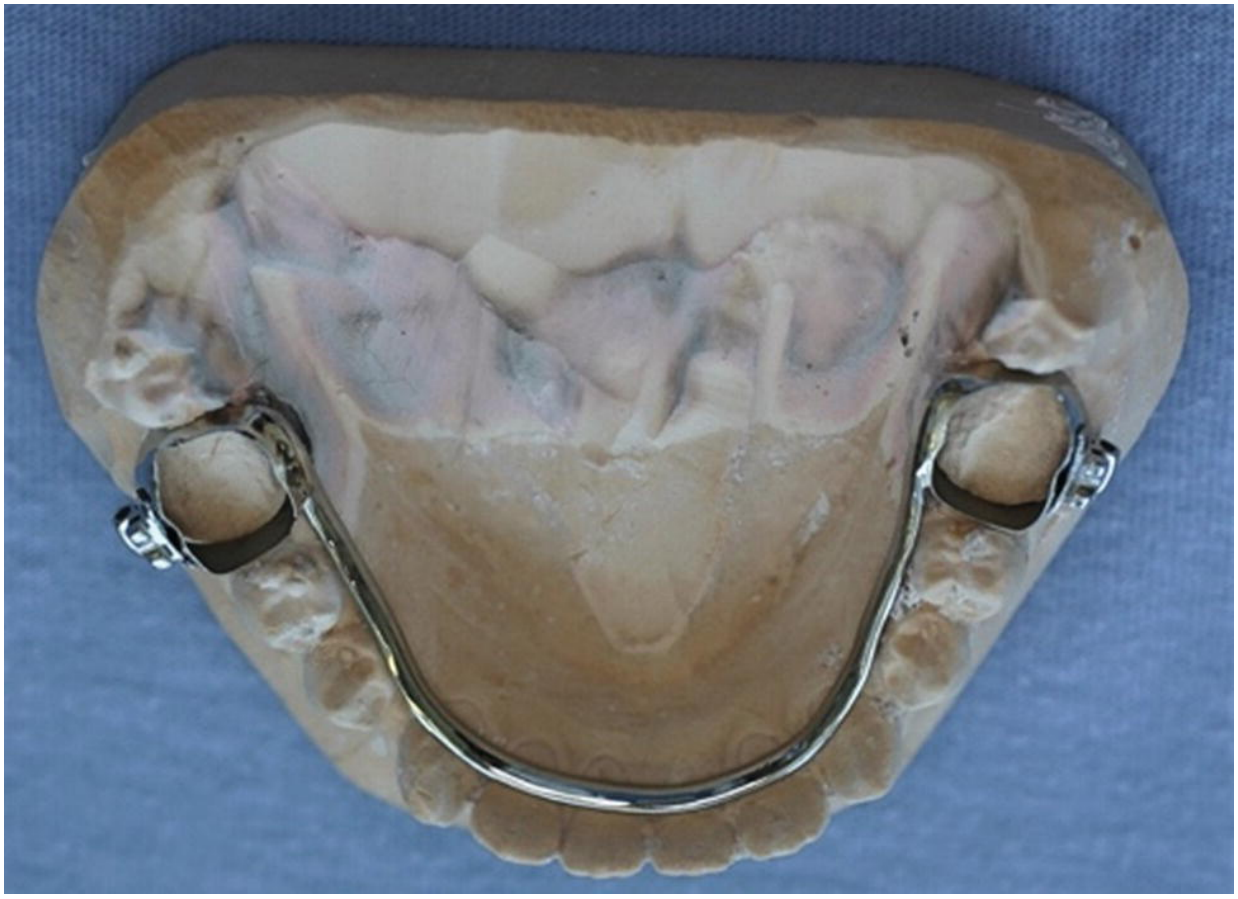


Figure 13.10 The mandibular lingual holding arch used in patients with Duchenne muscular dystrophy, with a semi-circular cross-sectional area 2 mm in height and 1 mm in depth, which is laboratory constructed in stainless steel and soldered onto bands placed on the mandibular first molars. The flat end of the semicircle is facing the lingual aspects of the mandibular teeth, while the circular end faces the tongue.

The success of this lingual arch is not only in the transverse dimension, where the mandibular intermolar width stays relatively stable, but also in the vertical dimension. The overbite does not decrease rapidly; thus, an open bite is not created, and this may be due to blocking of the force of the tongue, which can otherwise create this problem due to its enlargement (Eckardt and Harzer, 1996). We should keep in mind that boys and young men with DMD have a relatively stable lip force during growth, which is lower than in healthy individuals but at least does not decrease with time (Botteron et al., 2009; van den Engel-Hoek et al., 2016). Figure 13.11 shows two boys with DMD, one treated in an interceptive manner with a lingual arch and one untreated, where the deterioration in the malocclusion can be seen in the untreated boy, whereas the boy with the lingual arch shows the preservation of a more favorable occlusion.

The outcomes observed in the pilot study (Antonarakis et al., 2020) were very promising and make us believe that this interceptive treatment could be a useful alternative to more complex and lengthy

treatments, or treatment abstention, in this population. As prevention is preferable to treatment, if the development of a severe malocclusion can be prevented with the placement of a mandibular lingual arch, this would be able to negate the need for more complex, lengthy, and potentially risky treatment. It might be maximally beneficial in this group of children to place the rigid mandibular holding arch early on to prevent to some extent the development of more severe malocclusions. The best time to begin this interceptive treatment seems to be around the time of loss of ambulation, since this age corresponds to the time when malocclusions begin to occur. The lingual arch should perhaps be started at a point where the child has the most normal occlusion possible. This would ensure the preservation of an acceptable masticatory function, which is essential to these individuals.

The inconveniences of such a treatment, however, would mean that the children would have to wear the appliance for numerous years. This would create an unfavorable environment for oral hygiene maintenance and caries risk, requiring regular and frequent dental and hygiene follow-up. Several authors have observed that individuals with DMD often have a severe accumulation of plaque and calculus and a high prevalence of caries and periodontal disease, with these problems tending to increase with age (Morinushi and Mastumoto, 1986; Ertürk and Doğan, 1991; Symons et al., 2002; Mielnik-Błaszczak and Małgorzata, 2007; Balasubramaniam et al., 2008). Moreover, there is a characteristic decline in oral hygiene related to the loss of muscle function of the arms and hands in these patients (Symons et al., 2002), which worsens matters. Despite the inconveniences of performing this interceptive treatment, the benefits most likely outweigh the risks, provided that a sufficient dental follow-up protocol is implemented. A reasonable alternative suggestion could be to replace the lingual arch once the child is in their full permanent dentition, by splints or removable appliances so that the mandibular arch could remain stable without overexpanding, but at the same time providing for a healthier oral environment. It remains to be seen what effect such a treatment would have on the tendency of these children to develop a skeletal Class III relationship.

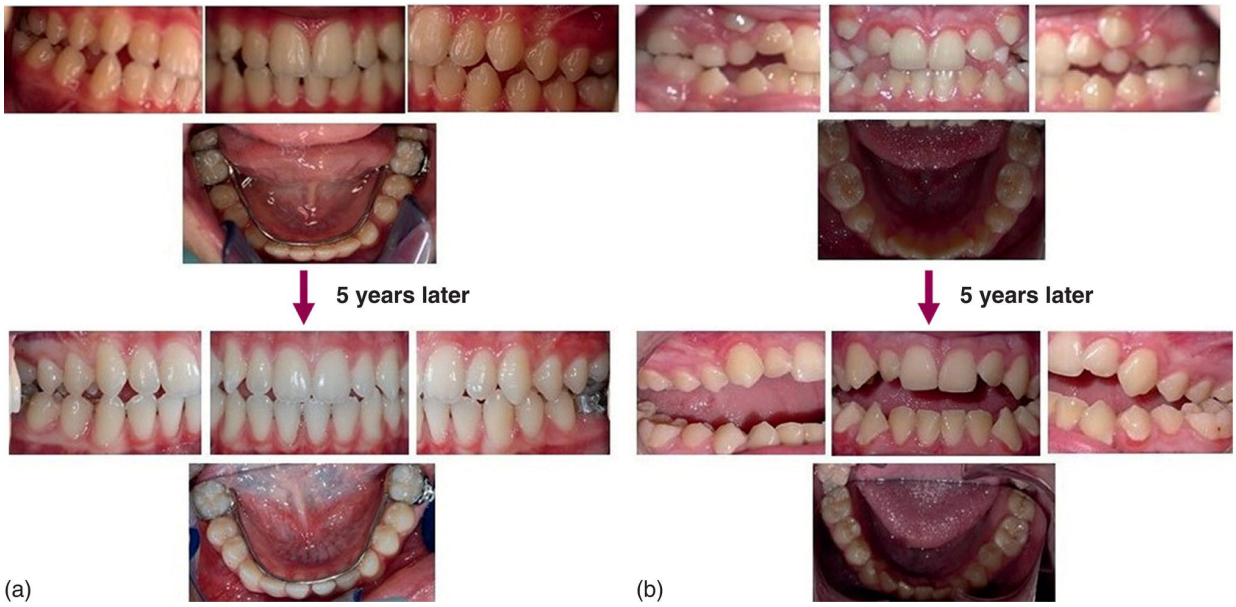


Figure 13.11 Two boys with Duchenne muscular dystrophy showing the intraoral photographs and the evolution of the malocclusion over a five-year period. (a) A boy with interceptive treatment using only a lingual arch where the preservation of a favorable occlusion can be seen; (b) an orthodontically untreated boy where the deterioration in the malocclusion can be seen.

Source: Antonarakis et al. (2020) / with permission from ELSEVIER.

Another proposed method to improve the masticatory system's disuse and potentially help prevent the development of severe malocclusions is by masticatory exercises. This was proposed as long as almost 40 years ago by Kawazoe et al. (1982), who suggested the use of therapeutic exercises for masticatory function. Nozaki et al. (2010) more recently used range of motion exercises with hot packs to increase occlusal force in patients with DMD. However, these exercises do not fit the criteria suggested for exercise programs for patients with neuromuscular disease, since these have to be low-intensity aerobic

exercises at a submaximal level (Jansen et al., 2013), and also be able to be performed by the patient themselves and fit into the daily life routine. Van Bruggen et al. (2015) tried using chewing gum as low-intensity aerobic masticatory training and found promising results with an improvement in masticatory performance. While these exercises may provide some benefit, it is still to be shown if they will be able to prevent aggravation of the developing malocclusion.

Other neuromuscular diseases

Facio-scapulo-humeral muscular dystrophy

Facio-scapulo-humeral muscular dystrophy (OMIM #158900) is a progressive skeletal muscle disorder involving the muscles of the face (facio-), shoulder girdle (scapulo-), as well as those of the upper arm (humeral) (Schätzl et al., 2021). Along with DM and DMD, facio-scapulo-humeral muscular dystrophy is one of the most common muscular dystrophies (Schätzl et al., 2021). Although most patients present with symptoms in the second decade of life, symptoms can develop between infancy and late adulthood (Richards et al., 2012; Schätzl et al., 2021).

Regarding the orofacial muscles in this population, the maximum bite force is small, with the masseter and pterygoid muscles exhibiting asymmetrical atrophy and fatty infiltration (Liu et al., 2016), and tongue atrophy has also been reported (Yamanaka et al., 2001). Facial weakness has also been shown when performing various facial tasks (Loonen et al., 2021; Konstantonis et al., 2022). The craniofacial and dentoalveolar characteristics show a high palatal vault, a narrow arch, a steep mandibular plane, and varying degrees of malocclusion (Liu et al., 2016).

There have been a few case reports describing orthodontic treatment of patients with facio-scapulo-humeral muscular dystrophy, all of which have been combined treatments with orthognathic surgery, perhaps introducing publication bias toward more severe forms of the disease. An early report described two cases with open bite and Class III malocclusion treated with orthodontics and bimaxillary orthognathic surgery (Goldberg et al., 1989), but without much detail or documentation of the cases. Another case treated with orthodontics and bimaxillary orthognathic surgery has also been presented on an adult patient with facio-scapulo-humeral muscular dystrophy and Class III malocclusion (Marchetti et al., 1997), with apparent stability at the two-year follow-up, although documentation is incomplete. Two more recent cases present open bite malocclusions, one in which the open bite is associated with a Class III malocclusion and treated with a mandibular osteotomy but without long-term results (Kriwalsky et al., 2008), and the other treated with bimaxillary osteotomy, with promising stability shown three years after the osteotomies (Kawasaki et al., 2016).

Nemaline myopathy

Nemaline myopathy (OMIM #161800) is a congenital myopathy with a varying age at onset and severity, with typical muscle weakness involving proximal muscles as well as facial, bulbar, and respiratory muscles (Gaspar et al., 2019b).

Children with nemaline myopathy have been shown to present facial weakness with a long-face deformity, lip incompetence, and an open-mouth posture (Antoniades et al., 1991). Skeletally, a high-angle skeletal pattern and an obtuse gonial angle are seen, with anterior open bite being prominent (Antoniades et al., 1991), and a narrow maxillary dental arch and Class II division 1 malocclusion sometimes also being observed (Anderson et al., 2005). Severe cases of nemaline myopathy can show severe craniofacial phenotypical manifestations. This can include minimal facial and oral movement, with the patient's mouth remaining open without the ability to close it, and severely excessive vertical facial dimensions with a consequent severe anterior open bite (Xue et al., 2017). Computed tomography shows a fatty infiltrate with atrophy of the facial and oral floor musculature as well as the tongue (Xue et al., 2017). Figure 13.12 shows a young boy with nemaline myopathy demonstrating the characteristic extreme hyperdivergent skeletal pattern.

Management of the craniofacial manifestations of nemaline myopathy has been very seldomly evaluated, with only a few case reports available in the literature. An early case report presented a patient with nemaline myopathy and severe anterior open bite treated with bimaxillary osteotomies and orthodontics with a satisfactory result obtained (Steinhauser and Lines, 1975). Another report described an adolescent treated with maxillary expansion and bimaxillary orthognathic surgery, with apparent

stability 18 months postoperatively (Anderson et al., 2005), although this is not documented. A further report presents a very severe case of nemaline myopathy in an adolescent female patient with the inability to close her mouth, very narrow dental arches, and an extreme hyperdivergent skeletal pattern associated with a very marked anterior open bite (Quereshy et al., 2020). The treatment for this case was orthodontic treatment combined with bimaxillary osteotomy that was done in three surgical stages, first with surgically assisted rapid maxillary expansion, then a segmental Le Fort I maxillary osteotomy, and finally a bimaxillary osteotomy. Although the final treatment result was favorable, it is not known whether the treatment results were ultimately stable.

(a) (b)

Figure 13.12 (a, b) A young boy with nemaline myopathy showing the characteristic extreme hyperdivergent skeletal pattern.

Becker muscular dystrophy

Becker muscular dystrophy (OMIM #300376) is an inherited muscular dystrophy characterized by progressive muscular weakness, mainly of the proximal muscles. It is somewhat similar to DMD in regard to the distribution of muscle wasting and weakness, but has a milder course, with age of onset being at around 12 years (Emery, 2002).

With regard to the orofacial and craniofacial phenotypes of patients with Becker muscular dystrophy, there is little in the literature to systematically describe these. However, there are a few case reports describing orthodontic treatment in these patients. One such report presents a case with anterior open bite and interocclusal contacts only on the second permanent molars, large dental arch widths perhaps associated with a voluminous tongue, and spaced dental arches with proclined incisors (Suda et al., 2004). There was also a large gonial angle. The patient was successfully treated with orthodontics alone using multiloop edgewise archwires and intermaxillary elastics to close the anterior open bite, although the treatment took more than three and a half years (Suda et al., 2004). Just three months after debonding, however, there was already some relapse of the open bite, and five months after treatment marked relapse was noted, highlighting that stability is difficult to maintain in these patients. A further case with Becker muscular dystrophy reports a milder malocclusion with a unilateral lateral open bite that was successfully treated, within three years, with fixed orthodontic appliances and intermaxillary elastics (Aristizabal and Smit, 2014). Five years post treatment the results remained relatively stable, but with some vertical relapse on the side with the pretreatment lateral open bite.

Spinal muscular atrophy

Spinal muscular atrophy (OMIM #253300) is a group of neuromuscular disorders characterized by the degeneration of motor neurons of the spinal cord, resulting in progressive muscular weakness followed by muscle atrophy, most often diagnosed in infancy or early childhood (Wirth, 2000; Lunn and Wang, 2008).

The masticatory muscles seem to be affected by spinal muscular atrophy, with bite force being significantly reduced in this population (Granger et al., 1999). Moreover, masticatory muscles are fatigued more quickly than in healthy children, and mandibular range of motion is also reduced. Some work has been done on attempting to characterize the craniofacial morphology and occlusal characteristics of individuals with spinal muscular atrophy. Children with spinal muscular atrophy tend to show excessive vertical craniofacial development, particularly of the lower face, with a large anterior face height but only moderate anteroposterior discrepancies (Houston et al., 1994b; Pucciarelli et al., 2020). The prevalence of malocclusions in this population is also with common characteristics including a Class II malocclusion with an increased overjet, rotated and crowded teeth, anterior open bite, and flaring of maxillary incisors (Houston et al., 1994a, 1994b). No reports have been identified in the literature with regard to orthodontic or orthognathic treatment of individuals with spinal muscular atrophy.

Other neuromuscular diseases

Other neuromuscular diseases affecting the orofacial or masticatory muscles may also show adverse effects on craniofacial growth and the development of malocclusions. There have been occasional case reports describing orthodontic and orthognathic treatments of individuals with more rare neuromuscular disorders. One such report describes a severe case of congenital fiber-type disproportion (OMIM #255310), a rare congenital myopathy, presenting with severe anterior open bite associated with excessive vertical craniofacial growth and resulting lip incompetence (Lehman et al., 2012). The patient was treated with orthodontics and bimaxillary orthognathic surgery, with a good stable result five years post treatment. Another report described the case of a patient with merosin-deficient congenital muscular dystrophy (OMIM #607855), presenting with a severe anterior open bite, Class III malocclusion, and macroglossia (Jones and Waite, 2012). The patient was treated orthodontically with a combined glossectomy followed by bimaxillary orthognathic surgery, resulting in a favorable outcome, albeit no long-term follow-up was documented. Figure 13.13 shows a young patient with merosin-deficient congenital muscular dystrophy with a similarly severe malocclusion and a large anterior open bite. A final report discussed a case of minicore myopathy (OMIM #255320), an inherited neuromuscular disorder. The patient described was an adolescent boy with anterior open bite, bilateral posterior crossbite, and crowding. He was treated with rapid maxillary expansion followed by premolar extractions and fixed orthodontic appliances (Kuroda et al., 2012). The treatment took almost five years to complete, but unfortunately there were signs of relapse of the anterior open bite at the one-year follow-up appointment.

It is important to note that not all neuromuscular diseases affect the masticatory or orofacial muscles to the same extent. Variation can be due to the specific disease as well as the age of onset or the severity of the disease. Central core myopathy (OMIM #255320), for example, is a relatively mild congenital myopathy, and may show more mild craniofacial aberrations and malocclusion patterns. Figure 13.14 shows a young boy with central core myopathy who did not present with severe malocclusion, but did show significant gingival enlargement due to cyclosporin use. Finally, one last matter worth mentioning is that not all individuals with neuromuscular diseases are diagnosed with a previously-described and known condition. Figure 13.15 shows an adolescent patient with an unknown neuromuscular disorder showing an extreme openbite with mandibular prognathia.

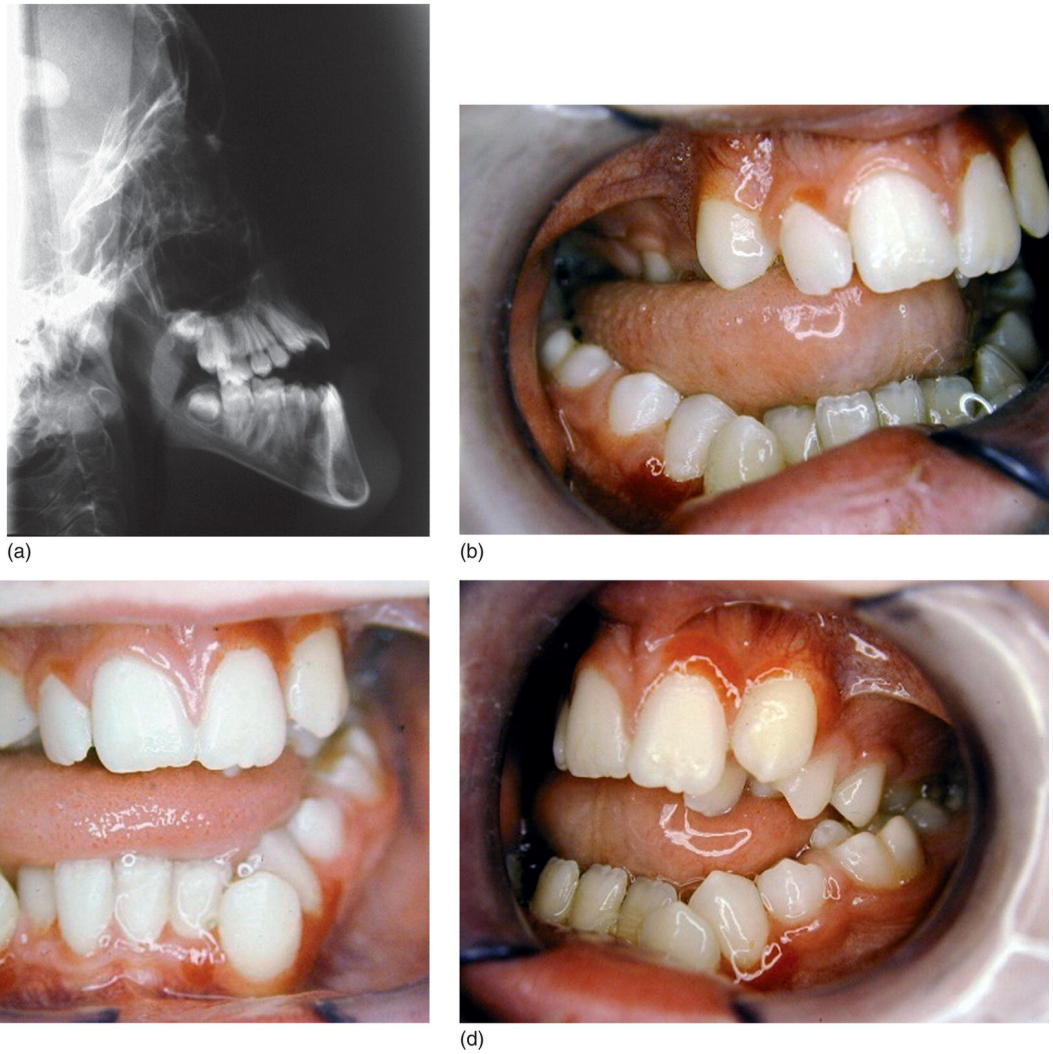


Figure 13.13 (a) Lateral cephalogram and (b–d) intraoral photographs of a young patient with merosin-deficient congenital muscular dystrophy with an extreme hyperdivergent skeletal pattern, a posterior crossbite, as well as a severe anterior and lateral open bite.

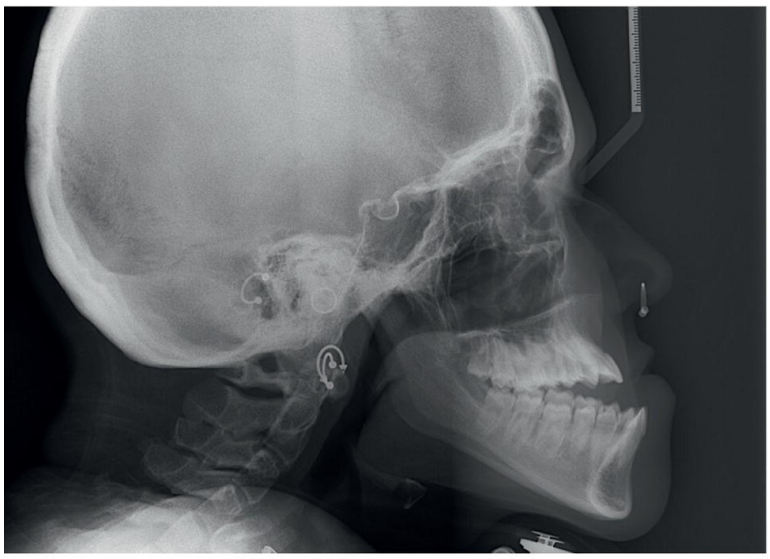
(a)

(b)

Figure 13.14 (a) Lateral cephalogram of a young boy with central core myopathy who did not present with severe malocclusion, but did show significant gingival enlargement (b) due to cyclosporin use.

Conclusions

A closer look at two less rare myopathies, namely DM and DMD, indicates that the reduced muscle function of the masticatory muscles may influence the dentofacial growth and development of these patients. Nevertheless, the induced dentofacial growth aberrations are caused by different etiological factors (Kiliaridis and Katsaros, 1998). A high prevalence of malocclusions is present among patients affected by both of these diseases, but patients with DM seem to develop their dentofacial aberration early in childhood, while patients with DMD develop serious dentofacial malocclusions during the pubertal and postpubertal periods.



(a)

(b)

Figure 13.15 (a) Lateral cephalometric radiograph and (b) intraoral photograph showing a severe open bite and mandibular prognathia with the presence of a voluminous tongue, in a patient with an unknown neuromuscular disease.

The development of malocclusions in patients with DM is strongly related to vertical aberration of craniofacial growth due to involvement of the masticatory muscles in association with the possibly less affected suprahyoid musculature. This may lead to the lowering of the mandible and the tongue, which is then not in a position to counterbalance the forces developed transversally on the upper arch by the stretched facial musculature. The new situation may affect the teeth transversely, decreasing the width of the palate and causing posterior crossbite. Lowering the mandible, in relation to decreased bite forces, may permit an overeruption of the posterior teeth, with the development of anterior open bite and a deep palatal vault.

The development of malocclusions in patients with DMD also seems to be strongly related to the disease's involvement of the orofacial muscles. However, the posterior crossbite does not develop owing to the narrow maxillary arch, as in patients with DM. On the contrary, the posterior crossbite in those with DMD is due to the transversal expansion of the mandibular arch, because of the decreased tonus of the masseter muscle near the molars, in combination with the enlarged hypotonic tongue and the predominance of the less affected orbicularis oris muscle.

Any interceptive measures proposed to impede the development of these dentofacial aberrations must therefore be disease specific and cannot share a common protocol, but should be adapted to the profile and demands of the different types of neuromuscular disease. It may be the case that any progress in the medical field that improves the condition of patients with neuromuscular disorders may be useful in decreasing the severity of their dentofacial anomalies. In the meantime, however, efforts should be made to prevent or improve the deterioration occurring with time regarding craniofacial growth and the development of malocclusions. In patients with DMD, the use of rigid lingual arches, as shown in this chapter, may help in this respect, as may therapeutic exercises of masticatory function such as with chewing gum. Improvement of patients' masticatory function is important in helping them gain better chewing ability and increasing their quality of life.

When proposing orthodontic treatment with or without orthognathic surgery to treat the malocclusions and dentofacial anomalies caused by neuromuscular disorders, especially where excessive vertical growth has led to the development of a severe anterior open bite, one must be very vigilant when it comes to long-term stability, as such treatments in these patients are inherently prone to be unstable due to the nature of the diseases in question. Informed consent is therefore primordial. Treatment planning in these cases needs to consider the severity and progression of the neuromuscular disease in consultation with the neurologist and other specialists involved in the care of these patients.

References

Anderson, P.J., Barker, J.H., and David, D.J. (2005). Management of facial dysmorphogenesis in nemaline myopathy: A case report. *World Journal of Orthodontics* 6(2): 156–160.

Antonarakis, G.S., Herzog, G., and Kiliaridis, S. (2019). Vertical relapse after orthodontic and orthognathic surgical treatment in a patient with myotonic dystrophy. *European Journal of Paediatric Dentistry* 20(1): 53–58.

Antonarakis, G.S., Morel, C., and Kiliaridis, S. (2020). Management of the dentoalveolar effects of tongue hypertrophy in patients with Duchenne muscular dystrophy: A pilot study. *Neuromuscular Disorders* 30(2): 105–110.

Antoniades, K., Taskos, N., Mavromatis, J. et al. (1991). Familial nemaline myopathy: Case reports. *Oral Surgery, Oral Medicine, and Oral Pathology* 72(1): 51–54.

Aristizabal, J.F., and Smit, R.M. (2014). Orthodontic treatment in a patient with unilateral open-bite and Becker muscular dystrophy. A 5-year follow-up. *Dental Press Journal of Orthodontics* 19(6): 37–45.

Askanas, V., and King Engel, W. (2015). Update on neuromuscular diseases: Pathology and molecular pathogenesis. *Biochimica and Biophysica Acta* 1852(4): 561–562.

Balasubramaniam, R., Sollecito, T.P., and Stoopler, E.T. (2008). Oral health considerations in muscular dystrophies. *Special Care in Dentistry* 28(6): 243–253.

Bezak, B.J., Arce, K.A., Jacob, A. et al. (2016). Orthognathic surgery in patients with congenital myopathies and congenital muscular dystrophies: Case series and review of the literature. *Journal of Oral & Maxillofacial Surgery* 74(3): 601–609.

Bhatt, J.M. (2016). The epidemiology of neuromuscular diseases. *Neurology Clinics* 34(4): 999–1021.

Bird, T.D. (1993). Myotonic dystrophy type 1. In: *GeneReviews*. Seattle, WA: University of Washington. https://www.ncbi.nlm.nih.gov/books/NBK1165.

Botteron, S., Verdebout, C.M., Jeannet, P.Y. et al. (2009). Orofacial dysfunction in Duchenne muscular dystrophy. *Archives of Oral Biology* 54(1): 26–31.

Broomfield, J., Hill, M., Guglieri, M. et al. (2021). Life expectancy in Duchenne muscular dystrophy: Reproduced individual patient data meta-analysis. *Neurology* 97(23): e2304–e2314.

Bushby, K., Finkel, R., Birnkrant, D.J. et al. (2010). Diagnosis and management of Duchenne muscular dystrophy, part 2: Implementation of multidisciplinary care. *Lancet Neurology* 9(2): 177–189.

Cacucci, L., Ricci, B., Moretti, M. et al. (2017). Surgical orthodontic treatment of a patient affected by type 1 myotonic dystrophy (Steinert syndrome). *Case Reports in Dentistry* 2017: 7957961.

Deconinck, N., and Dan, B. (2007). Pathophysiology of Duchenne muscular dystrophy: Current hypotheses. *Pediatric Neurology* 36(1): 1–7.

Eckardt, L., and Harzer, W. (1996). Facial structure and functional findings in patients with progressive muscular dystrophy (Duchenne). *American Journal of Orthodontics and Dentofacial Orthopedics* 110(2): 185–190.

Egli, F., Botteron, S., Morel, C. et al. (2018). Growing patients with Duchenne muscular dystrophy: Longitudinal changes in their dentofacial morphology and orofacial functional capacities. *European Journal of Orthodontics* 40(2): 140–148.

Emery, A.E. (2002). The muscular dystrophies. *Lancet* 359(9307): 687–695.

Ertürk, N., and Doğan, S. (1991). The effect of neuromuscular diseases on the development of dental and occlusal characteristics. *Quintessence International* 22(4): 317–321.

Fontinha, C., Engvall, M., Sjögreen, L. et al. (2018). Craniofacial morphology and growth in young patients with congenital or childhood onset myotonic dystrophy. *European Journal of Orthodontics* 40(5): 544–548.

Fontinha, C., Engvall, M., Sjögreen, L. et al. (2021). Occlusal traits and longitudinal dental changes in children and adolescents with congenital or childhood onset myotonic dystrophy. *European Journal of Orthodontics* 43(5): 527–533.

Gaspar, B.L., Vasishta, R.K., and Radotra, B.D. (2019a). *Classification of Skeletal Muscle Diseases*. Singapore: Springer.

Gaspar, B.L., Vasishta, R.K., and Radotra, B.D. (2019b). *Congenital Myopathies and Related Diseases*. Singapore: Springer.

Georgiakaki, I., and Kiliaridis, S. (1998). Intensive chewing and chewing training on Masseter muscle thickness. *Journal of Dental Research* 77: 1018.

Goldberg, M.H., McNeish, L., and Clarizzio, L. (1989). Correction of facial-skeletal deformities in two patients with facio-scapulo-humeral muscular dystrophy. *Journal of Oral & Maxillofacial Surgery* 47(9): 996–999.

Granger, M.W., Buschang, P.H., Throckmorton, G.S. et al. (1999). Masticatory muscle function in patients with spinal muscular atrophy. *American Journal of Orthodontics and Dentofacial Orthopedics* 115(6): 697–702.

Guimaraes, A.S., Carlsson, G.E., and Marie, S.K. (2007). Bite force and handgrip force in patients with molecular diagnosis of myotonic dystrophy. *Journal of Oral Rehabilitation* 34(3): 195–200.

He, T., Stavropoulos, D., Hagberg, C. et al. (2013). Effects of masticatory muscle training on maximum bite force and muscular endurance. *Acta Odontologica Scandinavica* 71(3–4): 863–869.

Houston, K.D., Buschang, P.H., Duffy, D. et al. (1994a). Occlusal characteristics of children with spinal muscular atrophy. *Pediatric Dentistry* 16(1): 59–61.

Houston, K., Buschang, P.H., Iannaccone, S.T. et al. (1994b). Craniofacial morphology of spinal muscular atrophy. *Pediatric Research* 36(2): 265–269.

Ingervall, B., and Bitsanis, E. (1987). A pilot study of the effect of masticatory muscle training on facial growth in long-face children. *European Journal of Orthodontics* 9(1): 15–23.

Jansen, M., van Alfen, N., Geurts, A.C. et al. (2013). Assisted bicycle training delays functional deterioration in boys with Duchenne muscular dystrophy: The randomized controlled trial “no use is disuse.” *Neurorehabilitation and Neural Repair* 27(9): 816–827.

Jones, L.C., and Waite, P.D. (2012). Orthognathic surgery and partial glossectomy in a patient with merosin-deficient congenital muscular dystrophy. *Journal of Oral & Maxillofacial Surgery* 70(2): e141–e146.

Kaufman, J., Friedman, J.M., Sadowsky, D. et al. (1983). Myotonic dystrophy: Surgical and anesthetic considerations during orthognathic surgery. *Journal of Oral & Maxillofacial Surgery* 41(10): 667–671.

Kawasaki, T., Ohba, S., Fujimura, Y. et al. (2016). Bimaxillary osteotomy for jaw deformity with facioscapulohumeral muscular dystrophy. *Journal of Craniofacial Surgery* 27(3): 776–778.

Kawazoe, Y., Kobayashi, M., Tasaka, T. et al. (1982). Effects of therapeutic exercise on masticatory function in patients with progressive muscular dystrophy. *Journal of Neurology and Neurosurgical Psychiatry* 45(4): 343–347.

Kieny, P., Chollet, S., Delalande, P. et al. (2013). Evolution of life expectancy of patients with Duchenne muscular dystrophy at AFM Yolaine de Kepper centre between 1981 and 2011. *Annals of Physical and Rehabilitation Medicine* 56(6): 443–454.

Kiliaridis, S. (1995). Masticatory muscle influence on craniofacial growth. *Acta Odontologica Scandinavica* 53(3): 196–202.

Kiliaridis, S., Engvall, M., and Tzakis, M.G. (1995a). Ultrasound imaging of the masseter muscle in myotonic dystrophy patients. *Journal of Oral Rehabilitation* 22(8): 619–625.

Kiliaridis, S., Jonasson, G., and Huanca Ghislanzoni, L.T. (2019). Functional factors associated with continuous eruption of maxillary incisors in adulthood: A 10-year prospective cohort study. *International Journal of Oral Implantology* 12(3): 329–335.

Kiliaridis, S., and Katsaros, C. (1998). The effects of myotonic dystrophy and Duchenne muscular dystrophy on the orofacial muscles and dentofacial morphology. *Acta Odontologica Scandinavica* 56(6): 369–374.

Kiliaridis, S., Lyka, I., Friede, H. et al. (2000). Vertical position, rotation, and tipping of molars without antagonists. *International Journal of Prosthodontics* 13(6): 480–486.

Kiliaridis, S., Mejersjö, C., and Thilander, B. (1989). Muscle function and craniofacial morphology: A clinical study in patients with myotonic dystrophy. *European Journal of Orthodontics* 11(2): 131–138.

Kiliaridis, S., Tzakis, M.G., and Carlsson, G.E. (1995b). Effects of fatigue and chewing training on maximal bite force and endurance. *American Journal of Orthodontics and Dentofacial Orthopedics* 107(4): 372–378.

Konstantonis, D., Kekou, K., Papaefthymiou, P. et al. (2022). Orofacial muscle weakening in facioscapulohumeral muscular dystrophy (FSHD) patients. *Children* 9(1): 96.

Kriwalsky, M.S., Deschauer, M., Eckert, A.W. et al. (2008). Orthognathic surgery in a case of infantile facioscapulohumeral muscular dystrophy with macroglossia. *Oral & Maxillofacial Surgery* 12(4): 195–198.

Kuroda, T., Ohyama, K., Motohashi, N. et al. (2012). *Atlas of Orthodontic Treatment for Patients with Birth Defects*. Ann Arbor, MI: Needham Press.

Lehman, H., Harari, D., Tarazi, E. et al. (2012). Orthognathic surgery in primary myopathies: Severe case of congenital fiber type disproportion with long-term follow-up and review of the literature. *Journal of Oral & Maxillofacial Surgery* 70(7): 1636–1642.

Liu, Y.H., Ma, Y.X., Hu, J. et al. (2016). [Features of facioscapulohumeral muscular dystrophy in oral and maxillofacial region and MRI analysis of facial muscles]. *Zhonghua Kou Qiang Yi Xue Za Zhi* 51(12): 739–745.

Loonen, T.G.J., Horlings, C.G.C., Vincenten, S.C.C. et al. (2021). Characterizing the face in facioscapulohumeral muscular dystrophy. *Journal of Neurology* 268(4): 1342–1350.

Lunn, M.R., and Wang, C.H. (2008). Spinal muscular atrophy. *Lancet* 371(9630): 2120–2133.

Mah, J.K., Korngut, L., Fiest, K.M. et al. (2016). A systematic review and meta-analysis on the epidemiology of the muscular dystrophies. *Canadian Journal of Neurological Science* 43(1): 163–177.

Manzon, S., and Philbert, R. (2007). Orthognathic surgery in a patient with myotonic dystrophy: Review of literature and report of a case. *Journal of Oral & Maxillofacial Surgery* 65(12): 2575–2579.

Marchetti, C., Bianchi, A., Merlini, L. et al. (1997). Rigid internal fixation of the jaws in an adult patient with facio-scapulo-humeral muscular dystrophy: Report of a case. *Journal of Craniomaxillofacial Surgery*, 25(5): 275–278.

Marik, P.K., and Hoag, J.A. (2012). Self-concept in youth with congenital facial differences: Development and recommendations for medical providers. *Pediatric Dermatology* 29(5): 549–554.

Mercier, J., Bennani, F., Ferri, J. et al. (1995). [Maxillofacial manifestations of Steinert's myotonic dystrophy. Clinical and therapeutic aspects]. *Revue de stomatologie, de chirurgie maxillo-faciale et de chirurgie orale* 96(2): 74–82.

Mielnik-Błaszczak, M., and Małgorzata, B. (2007). Duchenne muscular dystrophy—a dental healthcare program. *Special Care in Dentistry* 27(1): 23–25.

Miller, J.R. (2013). Orthodontic treatment of a patient with Duchenne muscular dystrophy and macroglossia: How informed consent was critical to success. *American Journal of Orthodontics and Dentofacial Orthopedics* 144(6): 890–898.

Morel-Verdebout, C., Botteron, S., and Kiliaridis, S. (2007). Dentofacial characteristics of growing patients with Duchenne muscular dystrophy: A morphological study. *European Journal of Orthodontics* 29(5): 500–507.

Morinushi, T., and Mastumoto, S. (1986). Oral findings and a proposal for a dental health care program for patients with Duchenne type muscular dystrophy. *Special Care in Dentistry* 6(3): 117–119.

Müller, H., and Punt-van Manen, J.A. (1982). Maxillo-facial deformities in patients with dystrophia myotonica and the anaesthetic implications. *Journal of Maxillofacial Surgery* 10(4): 224–228.

Nozaki, S., Kawai, M., Shimoyama, R. et al. (2010). Range of motion exercise of temporo-mandibular joint with hot pack increases occlusal force in patients with Duchenne muscular dystrophy. *Acta Myologica* 29(3): 392–397.

Odman, C., and Kiliaridis, S. (1996). Masticatory muscle activity in myotonic dystrophy patients. *Journal of Oral Rehabilitation* 23(1): 5–10.

Phillips, C., and Beal, K.N. (2009). Self-concept and the perception of facial appearance in children and adolescents seeking orthodontic treatment. *Angle Orthodontist* 79(1): 12–16.

Pucciarelli, V., Gibelli, D., Mastella, C. et al. (2020). 3D facial morphology in children affected by spinal muscular atrophy type 2 (SMAII). *European Journal of Orthodontics* 42(5): 500–508.

Quereshy, F., Quereshy, A., Levintov, N. et al. (2020). Orthognathic surgical rehabilitation in a patient with nemaline rod myopathy: A case report. *Journal of Surgery Current Trends & Innovation* S2: 3.

Richards, M., Coppée, F., Thomas, N. et al. (2012). Facioscapulohumeral muscular dystrophy (FSHD): An enigma unravelled? *Human Genetics* 131(3): 325–340.

Schätzl, T., Kaiser, L., and Deigner, H.P. (2021). Facioscapulohumeral muscular dystrophy: Genetics, gene activation and downstream signalling with regard to recent therapeutic approaches: An update. *Orphanet Journal of Rare Diseases* 16(1): 129.

Sjögreen, L., Engvall, M., Ekström, A.B. et al. (2007). Orofacial dysfunction in children and adolescents with myotonic dystrophy. *Developmental Medicine & Child Neurology* 49(1): 18–22.

Solano-Hernandez, B., Antonarakis, G.S., Scolozzi, P. et al. (2013). Combined orthodontic and orthognathic surgical treatment for the correction of skeletal anterior open-bite malocclusion: A

systematic review on vertical stability. *Journal of Oral & Maxillofacial Surgery* 71(1): 98–109.

Soltanzadeh, P. (2022). *Myotonic dystrophies: A genetic overview*. *Genes* 13(2): 367.

Staley, R.N., Bishara, S.E., Hanson, J.W. et al. (1992). Craniofacial development in myotonic dystrophy. *Cleft Palate-Craniofacial Journal* 29(5): 456–462.

Steinhauser, E.W., and Lines, P.A. (1975). Correction of severe open-bite associated with muscular disease. Report of a case. *Oral Surgery, Oral Medicine, and Oral Pathology* 39(4): 509–521.

Suda, N., Matsuda, A., Yoda, S. et al. (2004). Orthodontic treatment of a case of Becker muscular dystrophy. *Orthodontics & Craniofacial Research* 7(1): 55–62.

Symons, A.L., Townsend, G.C., and Hughes, T.E. (2002). Dental characteristics of patients with Duchenne muscular dystrophy. *ASDC Journal of Dentistry for Children* 69(3): 277–283.

Thind, B.S., and Turbill, E.A. (2015). Orthodontic camouflage treatment of Class II Division I malocclusion in a patient with myotonic dystrophy. *International Journal of Orthodontics* 26(4): 55–58.

Turner, C., and Hilton-Jones, D. (2014). Myotonic dystrophy: Diagnosis, management and new therapies. *Current Opinion in Neurology* 27(5): 599–606.

van Bruggen, H.W., van den Engel-Hoek, L., Steenks, M.H. et al. (2015). Fighting against disuse of the masticatory system in Duchenne muscular dystrophy: A pilot study using chewing gum. *Journal of Child Neurology* 30(12): 1625–1632.

van den Engel-Hoek, L., de Groot, I.J., Sie, L.T. et al. (2016). Dystrophic changes in masticatory muscles related chewing problems and malocclusions in Duchenne muscular dystrophy. *Neuromuscular Disorders* 26(6): 354–360.

Verhaart, I.E.C., and Aartsma-Rus, A. (2019). Therapeutic developments for Duchenne muscular dystrophy. *Nature Reviews Neurology* 15(7): 373–386.

Wirth, B. (2000). An update of the mutation spectrum of the survival motor neuron gene (SMN1) in autosomal recessive spinal muscular atrophy (SMA). *Human Mutation* 15(3): 228–237.

Xue, Y., Magoulas, P.L., Wirthlin, J.O. et al. (2017). Craniofacial manifestations in severe nemaline myopathy. *Journal of Craniofacial Surgery* 28(3): e258–e260.

Yamanaka, G., Goto, K., Matsumura, T. et al. (2001). Tongue atrophy in facioscapulohumeral muscular dystrophy. *Neurology* 57(4): 733–735.

Yiu, E.M., and Kornberg, A.J. (2015). Duchenne muscular dystrophy. *Journal of Paediatrics and Child Health* 51(8): 759–764.

14
Orthodontics for Children with Disabilities

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Summary

Persons with disabilities are children or adults who are prevented by a physical or mental condition from full participation in the normal range of activities of their age group. They usually exhibit high orthodontic treatment need, because of an increased prevalence and severity of malocclusion. Although parents may be highly motivated to improve a child's quality of life by enhancing appearance and oral function, these children are the least likely to receive orthodontic treatment. This chapter discusses orthodontic treatment for patients with developmental disability involving behavioral problems. It is based on the authors' earlier published studies and clinical experience in the treatment of this compromised minority group within the community. The chapter discusses the major obstacles that may preclude the delivery of orthodontic treatment or are encountered during treatment, together with the different management modalities that may be employed to overcome the behavioral limitations. Guidelines are provided to enable the orthodontist to gain therapeutic access to these patients.

"Disabilities" is an umbrella term under which a staggering array of diagnoses may be included, from mild learning disabilities to

profound intellectual disability; from food allergies to terminal illness; from developmental delays that are transitory to those that are intractable; and from occasional panic attacks to serious psychiatric problems. The designation is useful for garnering needed professional help and services, setting appropriate goals, and gaining understanding for a child and his or her distressed family. This chapter will focus on children with developmental disability involving behavioral problems.

Therapeutic access

Children with behavioral issues do not respond to traditional discipline, nor do they necessarily wish to be subjected to the various procedures they may need to undergo. Their intellectual level may also be inadequate for them to understand the need for compliance in the intricacies of a standard biomechanical apparatus. They require specialized and, often, simplified strategies that are tailored to their specific abilities and disabilities. If these important steps are not considered by the operator, therapeutic access may be impossible to obtain. The clinician needs to be understanding, flexible, and creative.

There are several specific areas in which the child with disabilities will unintentionally obstruct the delivery of treatment (Becker and Shapira, 1996) and this is because he or she typically has shortcomings not usually seen in children without disabilities, such as (Shapira et al., 1999):

- Increased apprehension, reduced understanding, limited tolerance, and short attention span.
- Exaggerated gag reflex (which seems to be a consequence of fear).
- Inability to remain still for any appreciable time, uncontrolled body movements.
- Reduced level of cooperation.
- Drooling.

Under these conditions, simple tasks such as taking radiographs, making dental impressions, and bonding orthodontic brackets become tasks of major proportions. To address these normally modest and routine procedures, behavior modification techniques may need to be employed, with or without specific pharmacological aids, including conscious and deep sedation or general anesthesia.

Over the past 20 years or so, both the absolute number and proportion of persons with disabilities in society have increased (Waldman et al., 2000), despite prenatal diagnostic techniques and the improvement in prenatal identification of congenital anomalies. The main reasons are first that sophisticated medical care, both perinatal and adult, has increased the newborn's survival rate and overall life expectancy. Second, given the more enlightened attitude of society today, as well as changing social policies and legislation, many more children with disabilities are seen as an integral part of their family, within adoptive families, or in sheltered housing, and are thus far more visible in general, while 40–50 years ago they were largely housed in institutions. This gradual but palpable process of "mainstreaming" has brought about greater awareness and appreciation on the part of the general public.

With these children's higher public profile, the present-day affluent society of the Western world has created a general improvement in their quality of life, which expresses itself in an increased demand for esthetics and normal function. The aim is acceptance into society, including the opportunity for employment toward self-sufficiency. As the direct result, the concern for facial appearance has become an item for discussion among their parents and this has generated a demand for orthodontic treatment (Becker and Shapira, 1996).

In general, the main goals of orthodontics are to improve the alignment and occlusion of the teeth and thus to contribute to one of the more important factors involved in improvement of the facial appearance (Shaw et al., 1980). However, its efficacy is limited and it cannot provide a satisfactory answer for every situation. Individual benefits that are principally associated with patients' own concept of themselves might have been gained by those patients and these are often strongly influenced by the people around them (Sticker, 1970).

Studies of the effects that dental appearance has on individuals and their surroundings have found it to be extremely important in overall facial esthetics (Lew, 1993). In adverse conditions, dental appearance is a principal focus for teasing and bullying among school children (Shaw et al., 1980), has a significant emotional impact on the individual, and is a factor used in social acceptability and personality judgment by others (Shaw, 1981).

In their everyday life, children with disabilities comprise a group of individuals who depend heavily on their families and others for their welfare. From earlier observations (Oreland et al., 1987), we learn that they have malocclusion that is more frequent, more severe, and more skeletally based than in the general population. Several conditions, such as cerebral palsy, Down syndrome, and intellectual disability, exhibit increased prevalence of specific dental features (Cohen and Winer, 1965; Franklin et al., 1996), which can adversely affect function (Proffit et al., 2007). Yet these patients are those least likely to receive orthodontic treatment.

Beneficial but not essential

The pediatric dentist is a medical professional who is ethically bound to treat a patient, in order to eliminate dental disease and to relieve pain, regardless of whether the child is cooperative in the dental chair and/or diligent in his or her routine homecare. At the same time, the medical professional has the responsibility to encourage behavior modification in both these areas. By contrast, orthodontics performed under these adverse conditions is contraindicated, since a successful outcome is doubtful and iatrogenic damage, in the form of caries and gingival inflammation, is likely. Thus, while treatment need is often high and its object beneficial, the relative gain that orthodontics may offer must be set against the damage that it may be complicit in producing. Accordingly, orthodontics must still be considered to be an elective item, to be decided in relation to the prevailing level of oral health and homecare. This is the point where parental involvement will usually be essential.

Motivation and expectation

The motivation for treatment in most of these cases comes from the parents of the child with disabilities, rather than from other medical or dental professionals (Becker et al., 2000). A majority of these children live at home, receiving daily one-on-one or two-on-one attention from highly motivated parents and siblings, who are often prepared to sacrifice much to improve the child's well-being (Becker et al., 2000). Certainly, many of the affected children will be sufficiently aware to believe that treatment is desirable, but there is a deep abyss between their "in principle" agreement and the compliance that will be required when the first clinical steps need to be taken.

The wearing of a simple removable orthodontic appliance, together with maintaining adequate oral hygiene either alone or permitting the parents to do it, may represent the first challenge of accepting responsibility on the part of the child. Children with disabilities are usually positively influenced by praise and compliments from the practitioner, the parent, and those around them when certain functions and stages are completed successfully, and this combines to form an environment that encourages compliance. A marred facial appearance is the principal factor motivating the request for orthodontic treatment among children in general, but for the child with disabilities the request for treatment of the marred appearance will come from the parent. The affected individual is usually completely unaware. Nevertheless, the recognition of poor oral health and function and their improvement must remain parallel aims (Becker et al., 2000).

Pretreatment visits, patient assessment, and future management

For every orthodontic case in routine orthodontic practice, assessment of the patient's future compliance potential is an essential part of the pretreatment examination, which may usually be completed within a short half-hour initial visit. In the context of the child with disabilities, this assessment has particular relevance and it may take as many as three, four, or five additional visits to learn

what may be expected of the child and the parent. Due to medical conditions that feature hypotony and myopathy, morbidity is high among this group, which means that food debris is not efficiently cleared from the mouth and is commonplace. Manual dexterity is much reduced and inadequate for adeptly wielding a toothbrush, with most subjects practicing no oral hygiene whatsoever. Pretreatment visits are therefore essential and are used for four specific purposes:

- To allay the patient's anxiety and raise the confidence level in the dental chair.
- To evaluate the existing level of homecare oral hygiene, to point out to both child and parent where it may be lacking.
- To demonstrate how improvement can and must be achieved always with parental supervision, often with active parental participation, as a precondition to acceptance for treatment.
- To assess the level of actual compliance and whether this can be maintained through treatment.

At the first visit, the child and parent are shown the debris surrounding the teeth, the collections of partially masticated food in a high palatal vault, in the cheek area, and elsewhere, together with the accompanying gingival inflammation, and are taught to recognize this situation. In order for the child to reach a level of oral hygiene consistent with the pursuit of orthodontic treatment, it is inevitable that the parent must be the dominant tooth brusher, with the child "finishing off" the exercise to include them in accepting responsibility that will take them through later life. The act of tooth brushing carried out by a parent on a daily basis is itself a potentially helpful exercise, since it familiarizes the child with the insertion of foreign items into the oral cavity, by another individual and in a nonthreatening environment, which helps to overcome apprehension and gagging (Becker and Shapira, 1996). Perhaps the most reliable sign of a good and potentially compliant patient is seen at the visit after oral hygiene instruction has been given and its importance stressed. The patient and parent arrive with an optimistic disposition, having put into practice what they have learned. However, the acid test is not merely to show the dentist clean teeth,

which may have been brushed solely on the day of the visit. Rather, it should be to check for resolution of the gingival inflammation, which can only occur with efficient elimination of food debris and biofilm with at least twice-daily regularity over a sustained period.

Maintenance of adequate oral hygiene among patients receiving orthodontic treatment with removable appliances is obviously easier than for those with fixed appliances. The patient's teeth and the removable orthodontic appliance may be brushed separately, under more favorable conditions. Those with fixed orthodontic appliances face the additional challenge of plaque removal due to the retentive properties of brackets and other components and, without a parent's help, they are surely doomed to fail. Orthodontic treatment is often performed on teenagers who might lack motivation and, without long-term compliance, will inevitably result in caries and gingival inflammation (Petrauskiene et al., 2019).

Despite extensive preventive measures utilized over the years, white spot lesion development in association with orthodontic treatment remains a serious clinical problem. It is difficult to stem the long-term deterioration of these lesions, even after appliance removal. It was therefore suggested by the American Academy of Pediatric Dentistry (AAPD, 2018) and the European Academy of Paediatric Dentistry (EAPD, 2009) that topical fluorides should be used in children considered to be at increased risk for caries development, such as children undergoing orthodontic treatment. Needless to say, the effect of the topical applied fluorides would be much greater when combined with good oral hygiene and the use of fluoride toothpastes. Fluoride varnishes are very effective, easily applied products that enhance remineralization. The varnishes are used as a preventive measure to reduce demineralization of the enamel around the brackets and promote the remineralization of existing carious lesions. Application in the dental office minimizes the need for individual patient compliance with the home use product (Weintraub, 2006). According to the reference manual of the AAPD (2018), the most commonly used agents for professionally applied fluoride treatment are 5% fluoride varnish (22,600 ppm) and acidulated phosphate fluoride (AFP; 1.23% F, 12,300 ppm). A meta-analysis of 23 clinical trials favors the use of the fluoride varnish (Weyant et al., 2013; Zhou et al., 2019). Advantages of fluoride

varnishes, especially over other topical fluoride regimens, include protection of enamel in the absence of patient compliance and continuous fluoride release over a long period of time. The application of a fluoride varnish was shown to result in a 44.3% decrease in enamel demineralization in patients undergoing orthodontic treatment (Zabokova-Bilbilova et al., 2014). Some studies have recommended an application even every 90 days to promote adequate protection (Vivaldi-Rodrigues et al., 2006).

It should be recognized that most visits for the duration of orthodontic treatment will require the use of behavior management techniques. Sedation and general anesthesia should only be used for essential, lengthy, and involved procedures – perhaps one or two such occurrences during the treatment. For this reason, time invested in pretreatment preparation and critical scrutiny is usually time well spent (Chaushu and Becker, 2000). If the parent–patient "team" is unable to achieve a healthy mouth at home, following a series of visits for prophylaxis, oral hygiene instruction, and caries prevention education, then the orthodontist should refuse to treat at that time and suggest follow-up to review the status at a much later date. The parent should be encouraged with reassuring departing words, such as "the office door is open to you in the future, but you must be prepared and able to attend to the homecare, with demonstrable and consistently satisfactory results." The orthodontist cannot afford to rely on the promise of future compliance from a parent anxious to begin treatment. Orthodontic therapy is almost never an emergency situation and the results of adequate oral hygiene are usually clinically apparent within a few weeks.

Children with disabilities require much more time and understanding for progress to be made in treatment and this requirement may exceed the endurance of many otherwise highly productive providers, since it is difficult to rise to the challenge and yet blend it with the smoothly run efficiency of a regular orthodontic office (Waldman et al., 2000; Becker et al., 2001). Sedation or general anesthesia sessions are sometimes needed and it makes sense to take advantage of the clinical access that these modalities provide to address other dental treatment needs, including endodontic, oral surgical, and restorative procedures (Chaushu and Becker, 2000). An orthodontic facility that can accommodate all

these specialists and provide a trained anesthetist close at hand is not often to be found outside a hospital-type setting. Accordingly, the capability of the purely orthodontic practice to successfully manage more than the simplest of cases of this type, in the integrative context, may be limited.

Orthodontic records

Treatment plans are usually the product of the gathering and collation of information contributed from a clinical examination, photographic and radiographic records, cephalometric analysis, digital models or plaster casts, and other aids to diagnosis. Under normal conditions, these records are simply and routinely acquired, in order to establish a diagnosis and treatment plan, before any treatment is commenced. Patient anxiety is commonly translated into an exaggerated gag reflex, making intraoral radiography and impression taking impossible to achieve and causing many orthodontists to raise their hands in despair. In the present (often anxiety-loaded) environment, these same diagnostic aids may become a major undertaking as alginate-heaped impression trays, the orthodontist's gloved fingers, and instruments are introduced into the mouth. When the orthodontist nevertheless persists forcefully to achieve the all-important goal of collecting these essential records, an objectively successful but badly managed outcome may result in a frightened child for months or years to come. Each of these problems may be overcome very satisfactorily today. Thus, extraoral (panoramic) radiography may usually be employed as a satisfactory alternative to periapical radiographs and the use of an intraoral digital scanner for digital models is an excellent and preferred alternative to alginate impression taking, particularly in the treatment of highly anxious children with disabilities (Christopoulou et al, 2022). The use of such scanners has proven to be as accurate as conventional alginate impressions (Tomita et al., 2018). Furthermore, alginate materials may sometimes have an unpleasant smell/taste, a poor impression must be repeated, and inaccuracy is sometimes seen only after cast pouring.

A standardized lateral or P-A skull radiograph for cephalometric evaluation requires accurate positioning of the head in the cephalostat and may often be impossible to acquire, because this is dependent on the typically painful head posture-restraining influence of the ear rods in the external auditory meatus, for the duration of the exposure.

Overall treatment plan

At the conclusion of this important first visit, the new records are studied and a reasoned working treatment plan established. This should start with the simpler and more easily achieved tasks before moving on to those that are more ambitious, on a stage-by-stage itemized list of individual aims of the patient's treatment. In this manner, the treatment may become a confidence-building series of visits, which should be looked on as an investment for the future dental and wider medical experience of the patient.

Control of adverse behavior during treatment

Orthodontics involves many visits for a variety of different treatment activities and functions, and it must be clear from the outset that, while negative behavior may be overcome with general anesthesia for a one-time emergency procedure, that cannot be justified at every visit for the implementation of routine procedures. Certainly, for the more anxious child with disabilities, for difficult, exacting, and protracted visits, and for those sessions in which more meticulous intraoral fixed appliance biomechanics is needed, pharmacological assistance will be needed, but this needs to be properly planned and kept to a minimum. This means that the use of "tell–show–do" behavior modification techniques, with positive and negative reinforcement, has to become the modus operandi for the major part of any treatment program, leaving a decision to be made regarding the supplementary modalities required for those procedures that are poorly tolerated (Becker and Shapira, 1996).

A conscious and highly anxious patient can be brought to a relaxed state by pharmacological agents through several routes, including inhalation (nitrous oxide and oxygen), transmucosally (midazolam

via nasal drops), orally (chloral hydrate, valium, midazolam), or intravenously (propofol). Through the use of these agents, the patient's compliance may be assured for the duration of the treatment, increasing the range of procedures that may be performed on the unwilling and apprehensive patient, and even permitting the orthodontist to provide treatment formerly considered impossible. Combinations of these drugs, such as midazolam (anxiolytic, sedative, and amnestic) with nitrous oxide (analgesic and relaxing effects), can produce conscious sedation with virtually no side effects and may be used relatively inexpensively for short procedures (Malamed, 1995). General anesthetic carries with it the accompanying need for short-term hospitalization, a specialized operating theatre, and preoperative and postoperative care. Nevertheless, until recently it was considered the only answer for the more routine orthodontic procedures in this challenging subsection of the population (Jackson, 1967; Chadwick and Asher-McDade, 1997).

Several years ago we introduced intravenous deep sedation for the more difficult orthodontic patients as an alternative to general anesthesia, and this has permitted us to increase the uptake of such patients (Chaushu et al., 2002b) without the need for an operating room. The orthodontic clinic is the ideal environment to carry out orthodontic procedures, but it must be properly equipped for sedation, with availability of the services of an anesthetist if sedation is to be performed. The sedation agent used is intravenous propofol, which induces a safe level of sedation very rapidly and is relatively free of side effects. Risk of aspiration and other emergencies is very low and the patient's vital reflexes are maintained for the duration of the sedation. Intubation is not usually necessary and recovery is very fast. This modality permits short- to medium-duration orthodontic procedures to be undertaken, including collaboration with oral surgeons, pediatric dentists, and endodontists, in the comprehensive treatment of the patient. Intravenous sedation has greatly improved our ability to achieve therapeutic access in these patients and has facilitated the smooth pursuit of treatment on an outpatient basis (Chaushu et al., 2002b).

Special considerations in orthodontics under sedation

Certain precautions are necessary when treating the sedated patient and the most important concern relates to aspiration because of partial or total loss of the patient's protective reflexes. It is essential to prevent the leakage of water, saliva, blood, debris, or loose orthodontic brackets into the airway, to avoid laryngospasm or tracheal or bronchial infection. Children with cerebral palsy and muscular dystrophy may have an impaired cough reflex due to their condition and thus are at greater risk. The best way to significantly reduce this palpable danger is to use a rubber dam under these circumstances (Chaushu et al., 2000). When this is impossible, as with impression taking, band fitting, and the cementation of soldered lingual/palatal arches, an oropharyngeal pack is mandatory. Indirect bonding has also been used in these situations and has much to recommend it (Thomas, 1979).

Molar band placement is more difficult when the patient cannot bite on a band-seating instrument or bite stick, and it is difficult to apply manual pressure, particularly in the mandible, when the anesthetist is trying to hold the jaw forward to increase the size of the airway. However, band cementation requires less critical and less stringent conditions of saliva control than bracket bonding and, wherever possible, should be performed in a separate visit, before the sedation session. If the child with disabilities has been taken patiently through the stages outlined, this is usually possible to achieve and, if so, is of considerable advantage.

Bracket bonding must be as accurate and as perfect as possible to reduce the chances of bond failure later on, as a rebond will be much more difficult. Orthodontists should use the method and materials that they are most comfortable with and have proved to be the most reliable. Aluminum oxide sandblasting is recommended, provided that suitable precautions regarding aspiration are in place. Anti-sialagogue drugs should be used if needed.

Adapting orthodontics to the child with disabilities

Modifications to orthodontic treatment and the manner in which it is delivered are needed if success is to be achieved with these patients:

- *Pragmatic treatment aims*. Ideal results are not always achievable because various adverse factors may be present in the particular individual. These include large skeletal discrepancies, high caries incidence, and behavioral limitations, which dictate aiming for more limited goals.
- *Record taking*. We have already mentioned the problems involved in taking impressions and how these may be circumvented. Intraoral radiographs are often just as difficult to take in these cases when the child is fully conscious, and these too may need to be taken under sedation. On the other hand, extraoral films, such as panoramic radiographs and cephalograms, are usually better tolerated. However, holding the head of a frightened child in a cephalostat, or having him/her sit still in a particular posture for several seconds while the x-ray tube circles the head, may not be possible and sedation may not be an asset in this situation. Accordingly, diagnosis may have to be made with fewer diagnostic aids, placing greater emphasis on the clinical examination.
- *Modular treatment*. A problem list should be drawn up and its various components prioritized into modules, beginning with the simpler tasks and progressing to the next, while being prepared to make adaptive alterations that may be needed at each stage.
- *Simplified treatment methods* include the following:
  - Placement of removable appliances is very simple, easily learned, and well tolerated (Becker et al., 2001). Adjustment and activation are made extraorally, which means that the patient's mouth is not disturbed by the operator's hands and by the insertion and manipulation of dental instruments. Oral hygiene is considerably easier than with fixed appliances, as discussed earlier, for both parent and child. It

is recommended to continue the use of removable appliances to achieve as much as possible before moving on to the fixed appliance stage or, possibly, even to be in the position to occasionally eliminate that (usually important) stage. Care should be taken in the design and construction of the removable appliance to include several retention clasps, so that even the more rebellious child with limited dexterity will have difficulty in removing it, until he or she quickly becomes accustomed to its presence.

- Appliances with a long range of action should be preferred, to increase the time between visits. The use of a removable plate with a headgear cured into the acrylic (Figure 14.1) and worn full time has been found to be very acceptable to these patients (Becker and Shapira, 1996; Becker et al., 2001) and the corrective influence of this *en bloc* appliance on a severe Class II relationship is often dramatic (Thurow, 1975). It is simple to use, requires few visits for adjustments, and, above all, is extremely safe since, with no detachable parts, it contrasts very favorably with a headgear whose inner arms slot into molar tubes. With its use, fewer premolar extractions are needed and, therefore, there are fewer space-closing root movements to deal with later.
- When extractions are nevertheless necessary, the Class II relation is more efficiently corrected with this removable integral headgear appliance than with Class II elastics, with which both child and parent are often highly "dexterity challenged." This means that space closure will need to be effected with intraarch mechanics, which are more appropriately performed by the orthodontist, for more reliable control.
- With the Class II corrected to a Class I relationship, the remainder of the treatment is best carried out with a fixed appliance that offers minimum frictional resistance to sliding mechanics, such as self-ligating bracket systems. Breakages may occasionally occur, although experience has shown that this is less of a problem than in most other patients, possibly due to the hypotonic facial and masticatory musculature.

– Mechanics may often be simplified by nonroutine extractions and this should certainly be considered in this subgroup of the population, if not among all individuals.

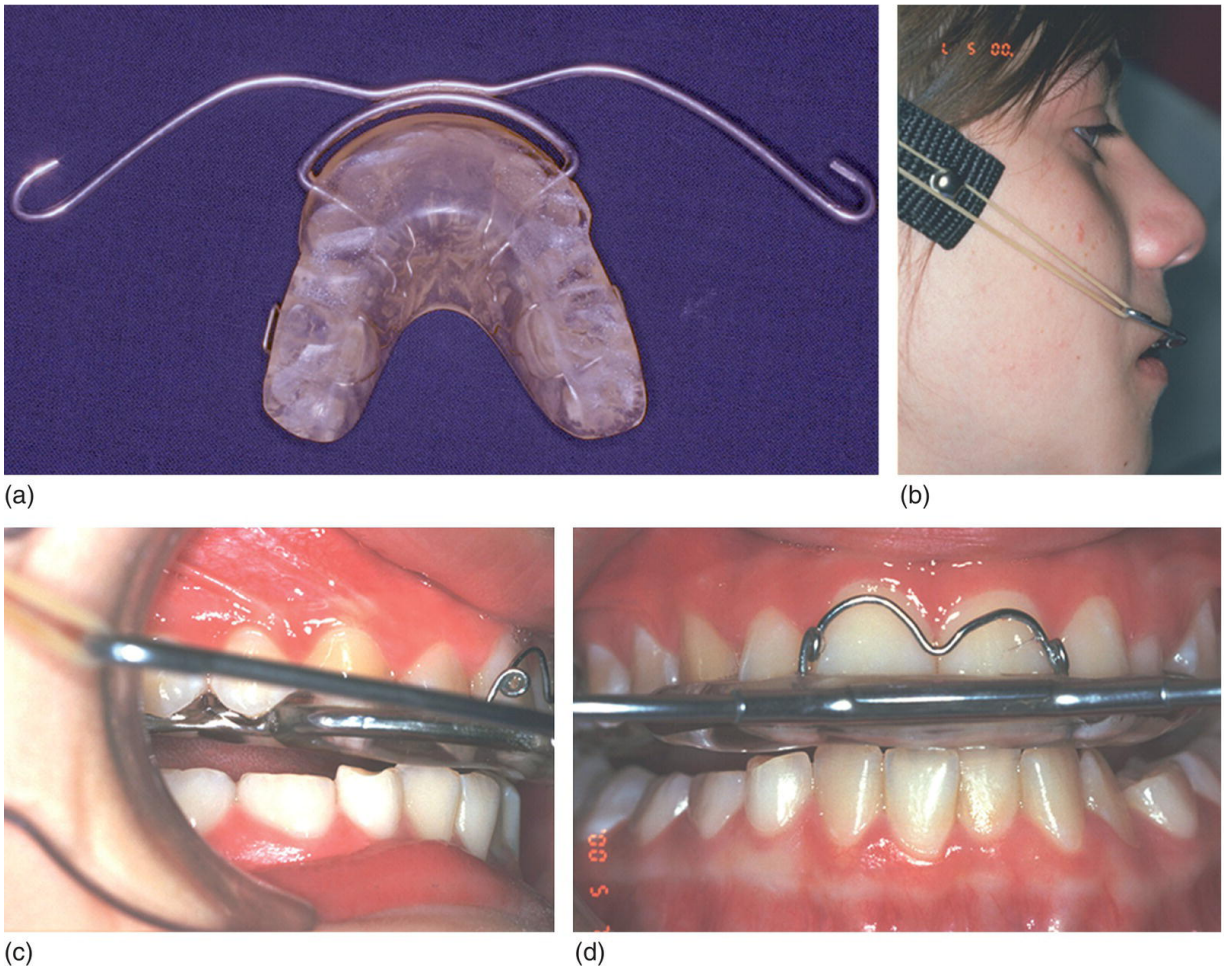


Figure 14.1 (a) A full-coverage acrylic with headgear cured into the acrylic. (b) A high-pull headgear applies vertical and distal force on the entire maxillary dentition, with vertical control anteriorly or posteriorly depending on the length of the extraoral arms. (c, d) An anterior bite plane may be used to permit posterior eruption to reduce the overbite and a Bass torqueing spur may be added for incisor lingual torque.

Clear aligners are an efficient and useful alternative to the traditional fixed appliances. Oral hygiene is easier to maintain since they are removable (Boyd, 2009). The pain during the first few days of treatment is lower (Cardoso et al., 2020) and the number of emergencies is decreased since there are no loose brackets or

popping out wires, and this is especially important for a child who is hyperactive or has spastic cerebral palsy. The appointments are much shorter, and their intervals may be increased to 8–10 weeks, by delivering 4–6 aligners to be replaced every 10–14 days. This can significantly decrease the burden of a monthly appointment for a patient who uses a wheelchair and the parents. The aligners can be easily handled, inserted, removed, and cleaned by the home carers.

However, there are some important drawbacks to overcome. Bonding of the composite attachments requires the patient to sit still and maintain a dry field for several minutes per jaw. In a partially cooperative child this procedure can be divided in several sessions since there is no wire to insert. In a very uncooperative child who cannot sit still at all, bonding can be done under sedation or even general anesthetic. Nevertheless, since the attachments are bonded with an indirect bonding tray, the procedure is safer and the risk of debonding and aspiration is minimal.

Another problem is that generally clear aligners are not worn during meals, since normal masticatory function produces rapid deterioration of the form of the aligner, with consequent reduction or elimination of the programmed forces that have been built into the appliance. Occlusal forces in a healthy patient are quite considerable and the occlusal contact surfaces of aligners will be quickly worn through, leading to appliance fracture and the creation of sharp residual edges. At first glance, therefore, the use of clear aligners is contraindicated for the orthodontic treatment of children with disabilities because of the high risk that the patient will lose one that had been taken out prior to a meal. However, many of the young patients in this subsection of the population have extremely sluggish masticatory function. As pointed out earlier, this group of patients includes a high proportion of individuals with muscular weakness. Many have abnormal soft tissue behavior, including tongue thrusting and an abnormal anterior oral seal, both at rest and during speech and swallowing. Hypotonia and the various myopathies, cerebral palsy, Down syndrome, and intellectual disability represent a large section of those classified as persons with disabilities. Those with these conditions typically exhibit excessive vertical growth of the lower third of the face, narrow arches, and severe open bites. For many, the mandible appears to hang open with flaccid lips and a

sluggish and forward-posturing tongue at rest. Their swallowing pattern diverges from the norm by the tongue inserting between the occlusal surfaces of the posterior teeth and the broad, vertical, interincisal gap. Food is partially and poorly masticated by the posterior teeth occluding on the enlarged and lethargic tongue, rather than on their antagonists in the opposite jaw. The patient is a "messy eater" with food escaping through the interocclusal space between the incisor teeth and between the flaccid and open-postured lips.

Such a patient may be instructed to wear the aligners on a full-time basis, with little danger of occlusal damage or distortion during eating. The appliance is placed in the mouth by the patient or the parent and is held very firmly on the teeth with its intimate all-around fit. The bonded aligner attachments on the teeth significantly increase the retentive properties of the device and its removal from the mouth often requires the patient–parent "team," because the patient alone may be unable to do it. This way, it must be removed twice daily for a careful and thorough oral hygiene session. It seems, too, that it qualifies as a valuable preventive anti-caries vehicle, with the advised use of fluoride varnish and the placement of fluoride gel or foam in the aligner, prior to reinsertion for overnight application.

Relapse and retention

Teeth move throughout life, whether or not orthodontic treatment has been performed. Accordingly, when a beautiful result has been achieved with any patient, it usually needs to be maintained with a suitable retainer for a long period of time. For some treated malocclusions that are not retained effectively, the degree of change/relapse that will occur post retention may be hardly noticeable. For others it may be very significant, due to an untreated or unaccounted for underlying etiological factor. The very high prevalence of abnormal soft tissue behavior and muscular weakness, which are not often amenable to treatment in children with disabilities, represents a major cause of posttreatment relapse, rendering long-term retention a more important factor than for another case within the general child population. "Active" nocturnal retention, with high-pull headgear, twin blocks, and the like, is

sometimes needed against the recurrence of some of the more severe skeletal Class II and open bite cases. Some of these may be surgical cases from the outset, but because of poor health or other reasons, a conservative approach had been advised. Most of the failures that we see are due to noncompliance with the retaining devices and, inevitably, retreatment may be necessary, although not before parent and child accept that more disciplined retention must be assured in the end. As already noted, some medical conditions may generate the adverse changes.

Clear aligners are an excellent alternative to the traditional removable (Hawley) appliances with clasps, when considering the need for retainers of the orthodontic outcome. They may be fabricated either on a new intraoral scan or by using the last stage of the active treatment, after requiring removal of the aligner attachments. Precision cuts and buttons can be planned in the aligners for active retention of a Class II, III, or open bite correction with intermaxillary elastics. An additional advantage is the storage of the final scanned model in the computer, allowing the immediate fabrication of a replacement last aligner in case it is broken or lost, without the need for taking a new impression. Furthermore, since the aligner is fabricated on the last scanning at the end of the active treatment, it can even correct minor tooth relapse.

Posttreatment parental evaluation

There can be no question that those parents who request treatment for their children with disabilities are highly motivated and most appreciative of the efforts made in the delivery of treatment in these difficult circumstances. Although they are not a random sample of parents of children with disabilities, when polled in a survey they expressed considerable satisfaction at the results achieved (Becker et al., 2000). From a subjective view of their child, they pointed to improvement in oral function, swallowing and drooling, speech, and masticatory function, in addition to improvement in facial and dental appearance. Among those children who were sufficiently aware of improvement, the parents reported that their children showed greater self-confidence and pride in their appearance (Becker et al., 2001).

Case descriptions

In the opening lines of this chapter, we asserted that the list of medical and psychological diagnoses that a child with disabilities may have is inordinately long and it is beyond the scope of this chapter to describe orthodontic management in all of them. Accordingly, a case description of three of the more commonly seen conditions among children with disabilities in which orthodontic treatment is likely to be highly beneficial, and in which special attention needs to be given to compliance and management issues, will be presented here.

Cerebral palsy

Cerebral palsy affects 2/1000 live-born children (Longo and Hankins, 2009). It refers to a group of chronic conditions affecting body movements and muscle coordination, caused by brain damage occurring during fetal development or infancy. Cerebral palsy patients can be classified by the type of movement problem into three subgroups:

- Spastic – inability of a muscle to relax.
- Athetoid – inability to control muscle movement.
- Ataxic – impaired balance and coordination.

Alternatively, they may be grouped by the body parts involved, such as hemiplegia (one arm and one leg), diplegia (both legs), and quadriplegia (all the limbs, trunk, and neck). There are several associated neurological features including epilepsy, intellectual disability, learning disabilities, and attention deficit-hyperactivity disorder (Blair and Watson, 2006).

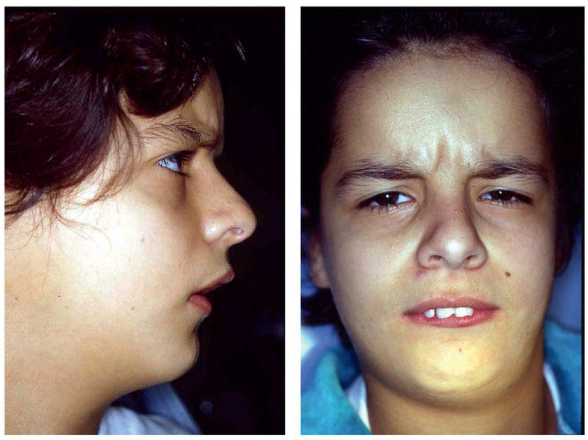
The dental and maxillofacial skeletal features include a Class II jaw relationship, increased lower facial height, backward mandibular rotation, broad mandible, and anterior open bite. The oral characteristics are uncontrolled head and tongue movements, forward tongue posture, hypotonic orofacial musculature, grossly incompetent lips, and drooling (Strodel, 1987; Rodrigues dos Santos et al., 2003). The following dental features are commonly seen: Class

II Division 1 malocclusion, an anterior open bite, a posterior crossbite due to the wide mandibular dental arch, gingival inflammation, and traumatized upper incisors (Franklin et al., 1996; Carmagnani et al., 2007).

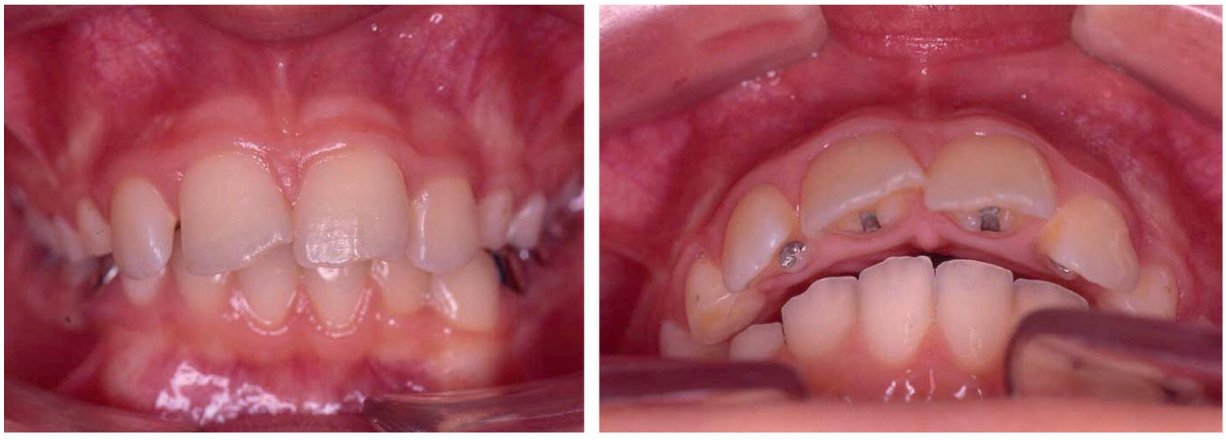
Treatment need is very high (Oreland et al., 1987; Vittek et al., 1994; Figures 14.2a and 14.3a), but these patients present a plethora of justifiable reasons why treatment is likely to be denied. Typically, they exhibit exaggerated apprehension and reduced understanding. This, together with their physical impairment and involuntary movements, undermines their ability to cooperate. In addition, they suffer from drooling (Harris and Purdy, 1987), a highly sensitive gag reflex, and poor oral hygiene (Guare and Ciamponi, 2003), with food accumulation and stagnation that is largely due to poor muscle function.

Recent evidence is not supportive of two-phase orthodontic treatment in the general population of children. Although minor and temporary skeletal change may occur in the younger patient, early treatment may not provide patients with any advantage over those treated at a later age, regarding the long-term outcome in Class II cases (Dolce et al., 2007; Harrison et al., 2007). It is essential to be aware that the day-to-day experience of children with cerebral palsy is peppered with traumatic episodes of loss of balance and falling. Without the ability to protect themselves with their hands, traumatic injury to the maxillary incisors is more frequently seen than in other children. It is for this reason that prevention of trauma and its consequences is mandatory and a short course of early treatment to reduce an increased overjet is, therefore, to be encouraged. This treatment should be initiated as early as possible after eruption of the maxillary incisors and it should also be aimed at improving a skeletal discrepancy, by restraining the forward and downward growth of the maxilla or by encouraging forward growth of the mandible. Completion of phase 1 should see a reduction of the Class II dental relationship to allow better lip cover and thus protect these teeth from what could otherwise occur as incidental trauma. The second justification for a phase 1 treatment is the orthodontic reduction of displaced anterior teeth following trauma, especially in cases of accidental intrusion or bucco-lingual displacement.

Following traumatic intrusion, the long-term survival of the injured tooth is uncertain. In the absence of timely treatment, pulp necrosis, inflammatory root resorption, ankylosis, replacement resorption, and loss of marginal bone support are likely to occur (Andreasen and Andreasen, 1994). It should be clearly understood and appreciated that extraction and prosthodontic replacement in persons with disabilities is not an option to be countenanced lightly. Three options are available for reduction and realignment of intruded teeth (Chaushu et al., 2004):



(a)



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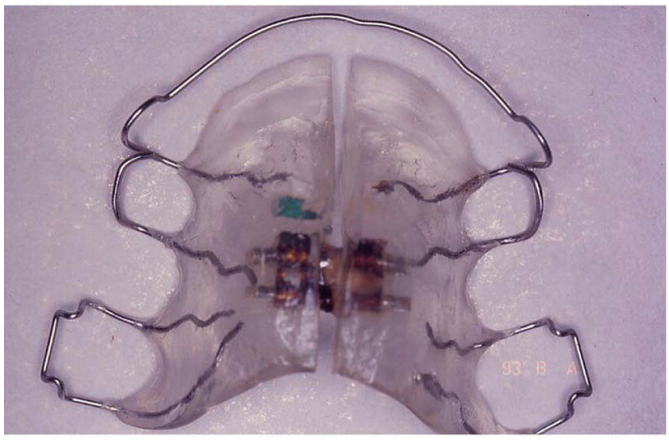
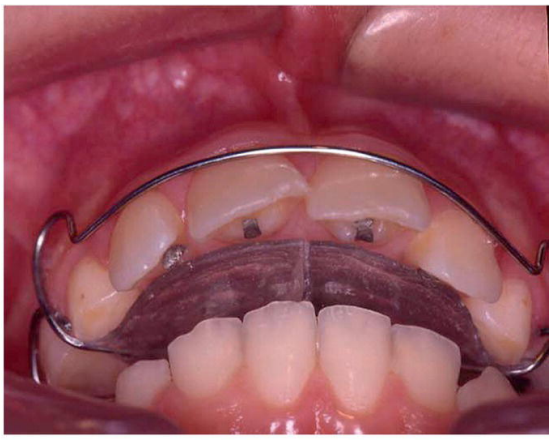

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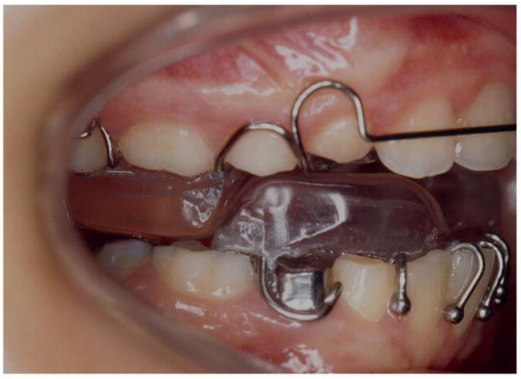

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Figure 14.2 (a) Pretreatment profile and en face views of the patient at rest. (b) Pretreatment intraoral photographs. (c) The "trainer" Hawley-type appliance. (d) Intraoral and profile views of the twin-block appliance to show the protrusive construction bite. (e) The occlusal relations of the teeth at the conclusion of the phase 1 treatment, showing the deliberate "overtreatment" into a Class III relation. (f) The occlusal relations of the teeth at the subsequent eruption of the premolars and canines in both jaws, at the time that phase 2 of the treatment began. (g) The occlusal relations of the teeth at the conclusion of the phase 2 treatment. (h) The extraoral views of the patient at the completion of treatment. (i) A series of profile views of the patient before treatment, at the end of phase 1, and at the completion of the treatment, to show the improvement in her profile.

- Observation alone, in the optimistic expectation of spontaneous re-eruption.
- Immediate surgical repositioning into the presumed previous locations.
- Early orthodontic repositioning, which is largely a valid procedure to be initiated during a period of up to 2–3 months post trauma.

Observation in anticipation of spontaneous re-eruption of a traumatically intruded tooth is highly unreliable, but individual successes have been reported (Shapira et al., 1986). Nevertheless, in more severely intruded teeth, access for essential root canal therapy may only be provided after extensive gingivectomy (Tronstad et al., 1986).

Surgical repositioning has been advocated to immediately relocate moderately or severely intruded teeth and to provide early access for root canal treatment in order to prevent infection pursuant to pulpal necrosis. However, this operation has also been reported as actually increasing the incidence of ankylosis, pulp necrosis, and loss of marginal bone (Chaushu et al., 2004; Andreasen et al., 2006).

Orthodontic repositioning of traumatically displaced teeth has been shown to be superior to the other alternatives in terms of tooth loss

during the follow-up period (Chaushu et al., 2004; Andreasen et al., 2006). Regardless of treatment approach, external inflammatory root resorption and marginal bone loss are frequent complications, and the incidence of root resorption appears to be similar between the three treatment approaches (about 40%). Marginal bone loss was higher in those teeth treated by observation only than in those repositioned either in a one-step surgical approach or over time by orthodontic traction (Chaushu et al., 2004). Thus, it seems that if the tooth remains in its embedded position in the bone, there is the strong likelihood of bone loss, while if the tooth is relocated in its original position and the normal relationship between the tooth and the bone is re-established, marginal bone loss is minimized.

(a)

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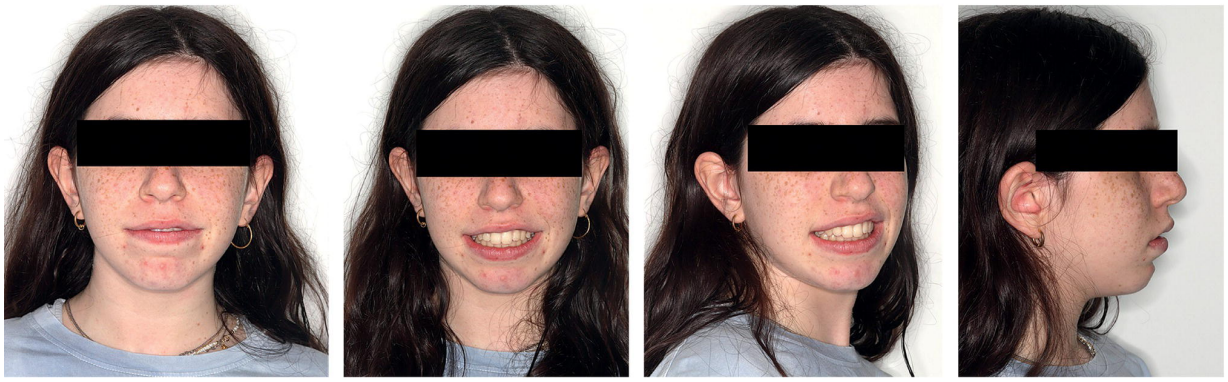

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Figure 14.3 (a, b) Pretreatment extraoral photographs. (c) Pretreatment intraoral views of the teeth in occlusion. (d) Pretreatment lateral cephalogram. (e) Aligner preparation with intraoral scanning: (i) initial scan; (ii) second scan after upper arch treatment (13 aligners); and (iii) final treatment plan to achieve the result after upper arch treatment with 13 aligners. (f) Posttreatment views of the teeth in occlusion. (g) Posttreatment extraoral photographs.

Case 14.1

The patient presented here was a 10-year-old female with ataxic cerebral palsy, showing a convex facial profile due to a marked retrusion of the mandible. There was a reverse relationship between the maxillary incisors and the lower lip and at rest, with the lip lying lingual to and in contact with the lingual side of the maxillary incisor teeth (Figure 14.2a). She had been referred from the Department of Paediatric Dentistry at the Hebrew University–Hadassah School of Dental Medicine in Jerusalem, where her attendance at the clinic had been regular and her homecare prevention treatment had been maintained. Considerable restorative treatment had been undertaken, including of a fractured incisor, and the results were encouraging.

The orthodontic examination revealed an established Class II Division I malocclusion in the mixed dentition stage, with an enlarged overjet and complete overbite, and the mandibular incisal edges in close relationship with the palatal mucosa (Figure 14.2b).

A phase I treatment was planned with the aim of reducing the Class II relation and preventing renewed trauma to the procumbent incisors. The first appliance was a simple removable "trainer" expansion appliance, with an anterior bite plane for anterior overbite reduction (Figure 14.2c). This was followed by a twin-block removable functional appliance to reduce the Class II dental discrepancy and, hopefully, to minimize the skeletal discrepancy (Figure 14.2d).

The child adapted well to the removable appliances and her cooperation with them was excellent, which permitted us to deliberately arrive at an overtreated result at the termination of phase I (Figure 14.2e). The twin block was then worn nightly as a retainer until it no longer fitted, due to the eruption of the canines and premolars (Figure 14.2f).

Phase II began with the extraction of the deeply carious maxillary left first permanent molar, together with the right second premolar. Fixed orthodontic appliances were placed in both jaws, in order to deal with the alignment, leveling, and closure of the extraction spaces, and, with intermaxillary elastic force, to improve the occlusal relations. During this time, the child had become a young adolescent and learned to perform almost all the aspects of homecare that were needed, still occasionally with the assistance of the attentive parent. Toward the end, it was found to be possible even to move on to relevant finishing procedures (Figure 14.2g). The appearance of the teeth at this juncture, together with the adolescent facial maturity that had occurred, served to brighten the patient's self-image (Figure 14.2h). Comparison of her facial profiles before treatment, at the end of phase I, and at treatment completion shows the improvement – a tribute to a good growth pattern and her excellent cooperation with the twin-block appliance (Figure 14.2i).

Case 14.2

The patient was a 13-year-old girl with athetoid cerebral palsy, who showed a convex profile due to protrusion of the upper incisors and incompetent hypotonic lips (Figure 14.3a, b). The orthodontic examination revealed a Class 1 malocclusion in the late mixed dentition stage, with an enlarged overjet and open bite (Figure 14.3c). The pretreatment cephalometric view indicated an increased mandibular plane angle and lower facial height, with proclination of both upper and lower incisors (Figure 14.3d).

The patient was extremely apprehensive of the introduction of foreign items into her mouth, such as trays filled with impression material, and had an exaggerated gag reflex. The parents wanted to provide her treatment in a private clinic, similarly to her siblings, and they had refused sedation or general anesthesia, which would otherwise have been necessary were alginate impressions administered.

The intraoral scanning provided an excellent alternative and was easily accepted. The scanner does not touch the patient's teeth or soft palate and, as such, is to be recommended for patients with a sensitive gag reflex.

Treatment was performed with clear aligners from Align Technology (San Jose, CA, USA). The aligner attachments were bonded chairside by an indirect bonding method, using the tray provided by the company, which enabled exact and reliable bonding in spite of the patient's uncontrolled head movements (Figure 14.3e). The child adapted very well to the clear aligners. However, without parental assistance for removal and reinsertion of the aligners at school, she lost two aligners. Consequently, the parents were instructed to leave the aligners in place for 24 hours a day, including meals, and take them out solely for tooth brushing. The aligners were replaced every two weeks. Initially, lower arch treatment was also planned, but only the upper arch was eventually treated, due to exfoliation of lower deciduous teeth. At the end of the upper arch treatment, a significant improvement was achieved in alignment and overjet and the open bite was closed. A second intraoral scanning was performed without any difficulty, after upper arch treatment with 13 aligners. Favorable eruption of the permanent successors left tooth #15 severely rotated,

but the parents did not consider that this correction justified bonding a partial fixed appliance.

The final intraoral views at the end of the second set of 10 aligners show the significant improvement in the occlusion (Figure 14.3f) and in the facial photos and smile (Figure 14.3g), all of which was achieved during 14 months of active treatment.

Down syndrome

Down syndrome or trisomy 21 is an autosomal genetic disorder caused by an extra chromosome 21, with an incidence of 1/800–1000 live births. The patient has a short stature, intellectual disability, and phenotypic anomalies that are oral, cardiovascular, hematopoietic, musculoskeletal, nervous, and behavioral (Hawli et al., 2009). Individuals with Down syndrome are prone to the development of infectious, malignant, and autoimmune diseases (Desai, 1997). There is also a high incidence of hypothyroidism (Fort et al., 1984; Goday-Arno et al., 2009) and delayed motor function (Vicari, 2006).

Patients with Down syndrome are characterized by many skeletal and dental anomalies, which have been widely reported in the literature. A skeletal Class III pattern is usually present due to an underdeveloped midface. The maxilla is deficient in all three planes of space: it is retruded in the sagittal plane, narrow in the coronal plane, and short in the vertical plane. The palate is V-shaped and high (Limbrock et al., 1991; Desai and Flanagan, 1999). The mandible is usually of normal size (Reuland-Bosma and Dibbets, 1991), but there is overclosure of the mandible, resulting in decreased lower facial height and a relative mandibular prognathism (Figure 14.4a).

The dental anomalies include a Class III dental relationship with anterior and posterior crossbites (Oliveira et al., 2008), as well as anomalies in the number (fewer), size (smaller), and morphology (peg-shaped and other deficiencies of tooth form; Cohen and Winer, 1965; Townsend, 1983; Peretz et al., 1996), and the timing of tooth development (late dentition; Garn et al., 1970), which are constant features of this syndrome. There is increased incidence of

canine/premolar transpositions and of impacted canines (Roger, 1994; Shapira et al., 2000). The tongue is large and is postured forward at rest and during function (Glatz-Noll and Berg, 1991). There is often an open mouth posture and mouth breathing, in part due to the hypotonic musculature (Morris et al., 1982; Merrick et al., 2000), and recurrent chronic upper respiratory infections (Shott, 2006). Salivary output is reduced and this is reflected in dry lips and oral mucosa, with frequent ulceration (Chaushu et al., 2002a, 2002c, 2007). The salivary immune system is impaired – a characteristic that itself is a potential etiological factor of the recurrent upper respiratory infection (Chaushu et al., 2002a, 2002c). Bruxism is a common finding.

Several previous studies have shown that individuals with Down syndrome have an increased prevalence of periodontal disease compared with age-matched control groups and other patients with intellectual disabilities of a similar age distribution (Orner, 1976; Reuland-Bosma and van Dijk, 1986). The prevalence of periodontitis under the age of 30 is close to 100% and is in sharp contrast with the low incidence of caries (Orner, 1976). The progression and severity, as well as the clinical characteristics of the periodontal destruction reported in individuals with Down syndrome, are consistent with the early-onset/aggressive periodontitis disease pattern (Shaw and Saxby, 1986; Cichon et al., 1998).

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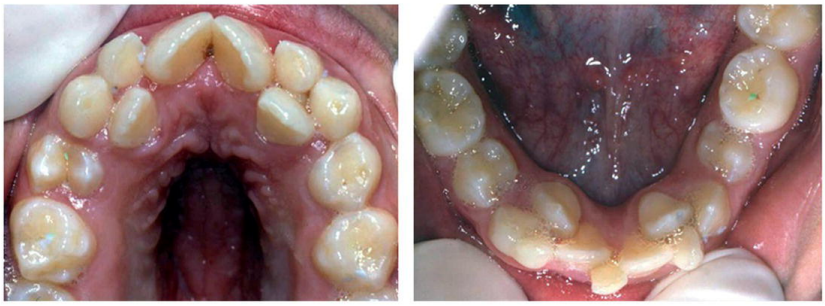

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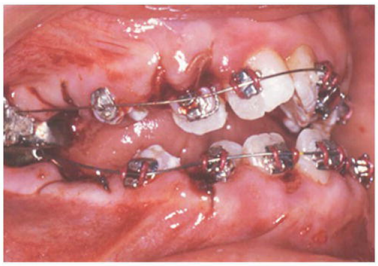

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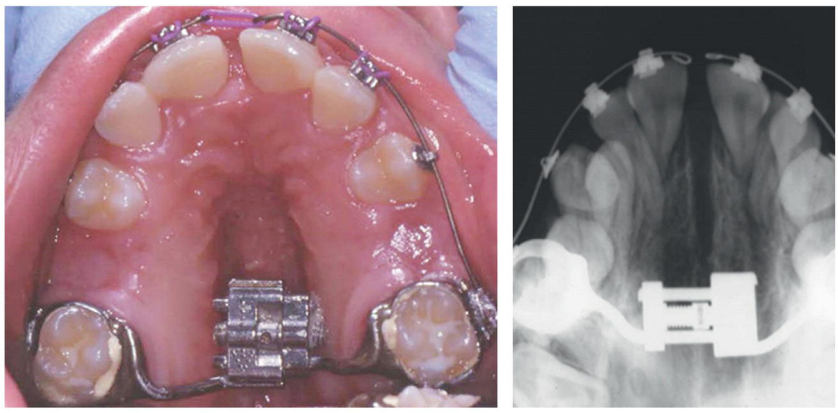

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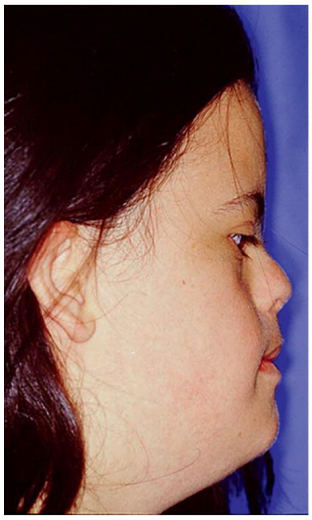

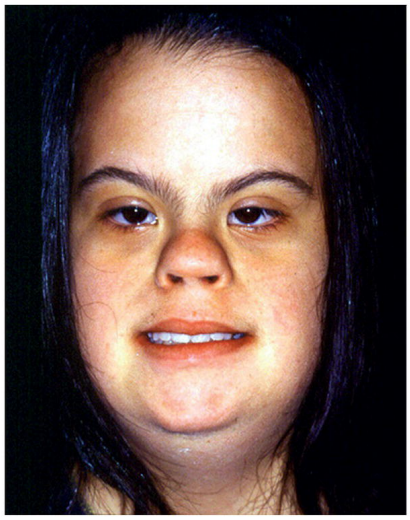

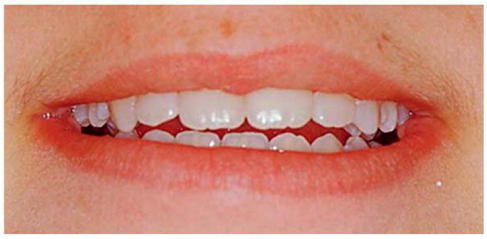

(h)

Figure 14.4 (a) Profile and en face views of the patient at rest. (b) Pretreatment intraoral photographs. (c) Pretreatment panoramic radiograph, in the mixed dentition stage, but with advancing development of the roots of the permanent teeth that is associated with the exfoliation of many more deciduous teeth and more erupted permanent teeth. (d) The intraoral view of the patient at the completion of the surgical phase, under general anesthesia, following extraction of all remaining deciduous teeth, surgical suturing, placement of molar bands with soldered initial screw, bracket bonding of all the accessible teeth, and tie-in of NiTi archwires in both arches. (e) The left-side clinical occlusal view, taken several months following the surgery. The expansion screw is the second screw to be used, following an initial opening, due to the extreme narrowness of the palatal area. The occlusal radiograph shows the expansion achieved with the first screw still in place. Note that for the period of rapid expansion a split archwire was used with an elastomeric ligature holding the mesial hooked ends of the archwire, to prevent excessive expansion force being transferred to the maxillary incisors by the twice-daily screw turning. (f) While good alignment has been achieved with the cooperative patient, the manual dexterity needed for skilled oral hygiene was inadequate. Note the presence of marked gingival inflammation and some white spot lesions. Orthodontic treatment was therefore abandoned in lieu of the extra treatment time that would be necessary to correct the reciprocal torque required on the lateral incisors and the formerly impacted maxillary canines. (g) The posttreatment panoramic view reveals root shortening of the incisor teeth. It also shows the maxillary dental midline continuous with the long axis of the mandibular central incisor. (h) The profile and en face views of the patient show much improvement and an excellent “smile line” of the incisal edges vis-à-vis the curve of the crest of the lower lip.

Because of the high prevalence and severity of skeletal and dental anomalies, patients with Down syndrome present high orthodontic treatment need (Oreland et al., 1987; Desai, 1997). From the skeletal point of view, this commonly requires maxillary expansion and protraction to correct/improve the skeletal Class III jaw relationship and the profile esthetics (Figure 14.4a). A second common complaint demands alignment of their teeth, opening/closing spaces of

congenitally missing teeth, and resolution of impactions and transpositions (Figure 14.4b). However, the clinician encounters many obstacles in pursuing successful orthodontic treatment. The behavior of individuals with Down syndrome often presents problems because of reduced understanding and increased apprehension, a short attention span, and limited tolerance. Although our experience shows that most of these patients can be treated at the chairside using regular behavior management techniques, some need sedation or general anesthesia for more extensive procedures and potentially painful appointments, such as bonding/debonding of brackets or extractions of deciduous teeth (Chaushu and Becker, 2000; Chaushu et al., 2002b). Other impediments are the increased incidence of macroglossia and open mouth posture. These, together with the hypotonic musculature that might impede closing of an anterior open bite, cause relapse of a successfully achieved result. In addition, these patients require close monitoring from the periodontal aspect because of the highly increased risk for periodontal disease. Early-onset periodontitis is an aggressive disease that should be diagnosed and treated with due attention and speed. Sometimes the orthodontic appliances have to be removed and treatment halted during the period of periodontal treatment, only to be restarted after improvement in the periodontal status has been achieved.

Dividing the orthodontic treatment into two phases is indicated in cases of significant skeletal discrepancy. In these cases, phase I treatment is performed at the age of 8–10 years and its main aim is to treat the posterior and anterior crossbite by maxillary expansion and protraction. The best way to achieve this goal is to use a banded or bonded rapid palatal expansion appliance with hooks for simultaneous maxillary protraction with a face mask. We usually recommend the use of a custom-made face mask, which can be constructed from a three-dimensional image of the face, or on a poured model taken from a plaster/alginate impression of the face. This kind of face mask fits the patient's face, can be made with clear acrylic chin and forehead pads, and is less obvious to other people. This is much more readily accepted by the patient, in comparison to the adjustable, "one-size-fits-all" appliances seen in an orthodontic catalogue. The patient in Case 14.3 had only a minor skeletal Class

III relation and was not considered a candidate for orthopedic protraction of the maxilla; treatment was therefore delayed until the late mixed dentition period and a phase 2 treatment plan.

Phase 2 treatment is usually initiated at the age of 12–15 years, depending on the delay in dental age. It is aimed at aligning the teeth, closing or opening spaces of congenitally missing teeth, and treating impactions and tooth transpositions (Figure 14.4b, c). This treatment was performed with fixed appliances, which can usually be placed at the chairside. However, in children with disabilities and in cases where multiple procedures are needed, a sedation session may be planned to accommodate all of these at a single session.

In cases of severe jaw discrepancies in patients after cessation of growth, orthognathic surgery may be planned for maxillary expansion and a down-sliding advancement (Janson et al., 2009).

Case 14.3

The patient was a 13-year-old child with a fairly high grade of intellectual ability, although her facial features, lip posture, large tongue, and sluggish oral musculature belied this. Her facial appearance possessed many of the characteristic features of Down syndrome (Figure 14.4a). The intraoral picture revealed a narrow maxilla with bilateral posterior crossbite and a normally sized mandible. A large number of deciduous teeth were overretained, with their permanent successors largely erupting alongside (Figure 14.4b). A single mandibular permanent incisor was congenitally absent and both maxillary permanent canines were labially impacted, high above the lateral incisor roots. Despite the presence of so many deciduous teeth, the dental age of the patient, as deduced from the stages of root development of the permanent teeth, was calculated to be approximately two years less than her chronological age (Figure 14.4c).

The treatment plan that was devised called for the extraction of all the remaining deciduous teeth and rapid maxillary expansion, while aligning and leveling the dentition in both jaws, including eruption of the impacted canines and closing off the place for the missing mandibular incisor.

Tightly fitting maxillary molar bands were placed on the first orthodontic visit, following alginate impression taking. These were replaced in a “pick-up” impression of the maxillary dentition and a model was cast. The technician then prepared a two-arm rapid expansion appliance. The second visit was performed under general anesthesia in the hospital operating theatre with endotracheal intubation. At this visit, close cooperation between surgeon and orthodontist in the operating theatre permitted the extraction of all the deciduous teeth and appropriate suturing, followed by placement of the rapid expansion appliance. Mandibular molar bands were then cemented and orthodontic brackets were placed on all erupted teeth. Eyelet attachments were also bonded to those that were only partially erupted and a light nickel–titanium wire was placed in each jaw, before the patient was wheeled into the recovery room (Figure 14.4d).

The next visit to the orthodontist occurred four weeks later, when the parent was shown how to activate the screw on the rapid expansion appliance (Figure 14.4e). The rest of the treatment was performed in the orthodontic office (Figure 14.4f) in the usual manner. At the completion of treatment, appliances were removed and removable Hawley retainer appliances were placed and maintained at night only for several years of supervision of retention. The posttreatment panoramic view shows all teeth in place, with some maxillary incisor root apex resorption and the mandibular skeletal midline passing through the long axis of the sole middle incisor (Figure 14.4g). The reader’s attention is drawn to the improved facial appearance, the degree of maxillary incisor exposure under the upper lip, and the smile line of the maxillary incisal edges vis-à-vis the lower lip (Figure 14.4h).

Conclusion

Children with disabilities suffer from more extreme and more disfiguring malocclusions than other patients; anxiety and apprehension levels are far greater than among their peers without disabilities. They have a much reduced level of understanding, a low threshold of tolerance, and consequently experience difficulties with compliance. It follows therefore that in order for the orthodontist to

achieve therapeutic access, a structured approach to treatment is required. This includes the need for considerably more chairside time, exploitation of the full range of behavior management modalities, and itemization of the treatment into individual self-contained tasks in a modular approach. Above all, there is the essential requirement for a caring, patient, and persevering attitude on the part of the treatment delivery team, which includes the orthodontist, the chairside assistant, and the parent, together with the occasional services of several other specialists, chief among them being the pediatric dentist and the anesthetist.

References

American Academy of Pediatric Dentistry (2018). Fluoride therapy. In: *The Reference Manual of Pediatric Dentistry*. Chicago, IL: American Academy of Pediatric Dentistry, pp. 250–253.

Andreasen, J., and Andreasen, F.M. (1994). *Textbook and Color Atlas of Traumatic Injuries to the Teeth*. Copenhagen: Munksgaard.

Andreasen, J.O., Bakland, L.K., and Andreasen, F.M. (2006). Traumatic intrusion of permanent teeth. Part 3. A clinical study of the effect of treatment variables such as treatment delay, method of repositioning, type of splint, length of splinting and antibiotics on 140 teeth. *Dental Traumatology* 22: 99–111.

Becker, A., and Shapira, J. (1996). Orthodontics for the handicapped child. *European Journal of Orthodontics* 18: 55–67.

Becker, A., Shapira, J., and Chaushu, S. (2000). Orthodontic treatment for disabled children: Motivation, expectation, and satisfaction. *European Journal of Orthodontics* 22: 151–158.

Becker, A., Shapira, J., and Chaushu, S. (2001). Orthodontic treatment for disabled children – a survey of patient and appliance management. *Journal of Orthodontics* 28: 39–44.

Blair, E., and Watson, L. (2006). Epidemiology of cerebral palsy. *Seminars in Fetal Neonatology and Medicine* 11: 117–125.

Boyd, R.L. (2009). Periodontal and restorative considerations with clear aligner treatment to establish a more favorable restorative environment. *Compendium of Continuing Education in Dentistry* 30: 280–288.

Cardoso, P.C., Espinosa, D.G., Mecenas, P. et al. (2020). Pain level between clear aligners and fixed appliances: A systematic review. *Progress in Orthodontics* 21: 3.

Carmagnani, F.G., Goncalves, G.K., Correa, M.S. et al. (2007). Occlusal characteristics in cerebral palsy patients. *Journal of Dentistry for Children* 74: 41–45.

Chadwick, S.M., and Asher-McDade, C. (1997). The orthodontic management of patients with profound learning disability. *British Journal of Orthodontics* 24: 117–125.

Chaushu, S., and Becker, A. (2000). Behaviour management needs for the orthodontic treatment of children with disabilities. *European Journal of Orthodontics* 22: 143–149.

Chaushu, S., Becker, A., Chaushu, G. et al. (2002a). Stimulated parotid salivary flow rate in patients with Down syndrome. *Special Care in Dentistry* 22: 41–44.

Chaushu, S., Chaushu, G., Zigmond, M. et al. (2007). Age-dependent deficiency in saliva and salivary antibodies secretion in Down's syndrome. *Archives of Oral Biology* 52: 1088–1096.

Chaushu, S., Gozal, D., and Becker, A. (2002b). Intravenous sedation: An adjunct to enable orthodontic treatment for children with disabilities. *European Journal of Orthodontics* 24: 81–99.

Chaushu, S., Shapira, J., Heling, I. et al. (2004). Emergency orthodontic treatment after the traumatic intrusive luxation of maxillary incisors. *American Journal of Orthodontics and Dentofacial Orthopedics* 126: 162–172.

Chaushu, S., Yefenof, E., Becker, A. et al. (2002c). A link between parotid salivary Ig level and recurrent respiratory infections in young Down's syndrome patients. *Oral Microbiology and Immunology* 17: 172–176.

Chaushu, S., Zeltser, R., and Becker, A. (2000). Safe orthodontic bonding for children with disabilities during general anaesthesia. *European Journal of Orthodontics* 22: 225–228.

Christopoulou, I., Kaklamanos, E.G., Makrygiannakis, M.A. et al. (2022). Patient-reported experiences and preferences with intraoral scanners: A systematic review. *European Journal of Orthodontics* 44(1): 56–65.

Cichon, P., Crawford, L., and Grimm, W.D. (1998). Early-onset periodontitis associated with Down's syndrome—clinical interventional study. *Annals of Periodontology* 3: 370–380.

Cohen, M.M., and Winer, R.A. (1965). Dental and facial characteristics in Down's syndrome (mongolism). *Journal of Dental Research* 44(Suppl): 197–208.

Desai, S.S. (1997). Down syndrome: A review of the literature. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics* 84: 279–285.

Desai, S.S., and Flanagan, T.J. (1999). Orthodontic considerations in individuals with Down syndrome: A case report. *Angle Orthodontist* 69: 85–88.

Dolce, C., McGorray, S.P., Brazeau, L. et al. (2007). Timing of Class II treatment: Skeletal changes comparing 1-phase and 2-phase treatment. *American Journal of Orthodontics and Dentofacial Orthopedics* 132: 481–489.

European Academy of Paediatric Dentistry (2009). Guidelines on the use of fluoride in children: An EAPD policy document. *European Archives of Paediatric Dentistry* 10: 129–135.

Fort, P., Lifshitz, F., Bellisario, R. et al. (1984). Abnormalities of thyroid function in infants with Down syndrome. *Journal of Pediatrics* 104: 545–549.

Franklin, D.L., Luther, F., and Curzon, M.E. (1996). The prevalence of malocclusion in children with cerebral palsy. *European Journal of Orthodontics* 18: 637–643.

Garn, S.M., Stimson, C.W., and Lewis, A.B. (1970). Magnitude of dental delay in trisomy G. *Journal of Dental Research* 49: 640.

Glatz-Noll, E., and Berg, R. (1991). Oral dysfunction in children with Down's syndrome: An evaluation of treatment effects by means of video registration. *European Journal of Orthodontics* 13: 446–451.

Goday-Arno, A., Cerda-Esteva, M., Flores-Le-Roux, J.A. et al. (2009). Hyperthyroidism in a population with Down syndrome (DS). *Clinical Endocrinology* 71: 110–114.

Guare, R. de O., and Ciamponi, A.L. (2003). Dental caries prevalence in the primary dentition of cerebral-palsied children. *Journal of Clinical Pediatric Dentistry* 27: 287–292.

Harris, S.R., and Purdy, A.H. (1987). Drooling and its management in cerebral palsy. *Developmental Medicine and Child Neurology* 29: 807–811.

Harrison, J.E., O'Brien, K.D., and Worthington, H.V. (2007). Orthodontic treatment for prominent upper front teeth in children. *Cochrane Database of Systematic Reviews* 3: CD003452. doi: 10.1002/14651858.CD003452.pub2.

Hawli, Y., Nasrallah, M., and El-Hajj Fuleihan, G. (2009). Endocrine and musculoskeletal abnormalities in patients with Down syndrome. *Nature Reviews Endocrinology* 5: 327–334.

Jackson, E.F. (1967). Orthodontics and the retarded child. *American Journal of Orthodontics* 53: 596–605.

Janson, M., Janson, G., Sant'Ana, E. et al. (2009). Orthognathic treatment for a patient with Class III malocclusion and surgically restricted mandible. *American Journal of Orthodontics and Dentofacial Orthopedics* 136: 290–298.

Lew, K.K. (1993). Attitudes and perceptions of adults towards orthodontic treatment in an Asian community. *Community Dentistry and Oral Epidemiology* 21: 31–35.

Limbrock, G.J., Fischer-Brandies, H., and Avalle, C. (1991). Castillo-Morales' orofacial therapy: Treatment of 67 children with Down syndrome. *Developmental Medicine and Child Neurology* 33: 296–303.

Longo, M., and Hankins, G.D. (2009). Defining cerebral palsy: Pathogenesis, pathophysiology and new intervention. *Minerva Ginecologica* 61: 421–429.

Malamed, S. (1995). *Sedation: A Guide to Patient Management*. St. Louis, MO: Mosby.

Merrick, J., Ezra, E., Josef, B. et al. (2000). Musculoskeletal problems in Down Syndrome European Paediatric Orthopaedic Society Survey: The Israeli sample. *Journal of Pediatric Orthopedics Part B* 9: 185–192.

Morris, A.F., Vaughan, S.E., and Vaccaro, P. (1982). Measurements of neuromuscular tone and strength in Down's syndrome children. *Journal of Mental Deficiency Research* 26: 41–46.

Oliveira, A.C., Paiva, S.M., Campos, M.R. et al. (2008). Factors associated with malocclusions in children and adolescents with Down syndrome. *American Journal of Orthodontics and Dentofacial Orthopedics* 133: 489.e1–8.

Oreland, A., Heijbel, J., and Jagell, S. (1987). Malocclusions in physically and/or mentally handicapped children. *Swedish Dental Journal* 11: 103–119.

Orner, G. (1976). Periodontal disease among children with Down's syndrome and their siblings. *Journal of Dental Research* 55: 778–782.

Peretz, B., Shapira, J., Farbstein, H. et al. (1996). Modification of tooth size and shape in Down's syndrome. *Journal of Anatomy* 188(Pt 1): 167–172.

Petrauskiene, S., Wanczewska, N., Slabsinskiene, E. et al. (2019). Self-reported changes in oral hygiene habits among adolescents receiving orthodontic treatment. *Dentistry Journal* 7: 96.

Proffit, W., Fields, H.W., and Sarver, D.M. (2007). *Contemporary Orthodontics*. St. Louis, MO: Elsevier.

Reuland-Bosma, W., and Dibbets, J.M. (1991). Mandibular and dental development subsequent to thyroid therapy in a boy with Down syndrome: Report of case. *ASDC Journal of Dentistry for Children* 58: 64–68.

Reuland-Bosma, W., and van Dijk, J. (1986). Periodontal disease in Down's syndrome: A review. *Journal of Clinical Periodontology* 13: 64–73.

Rodrigues dos Santos, M.T., Masiero, D., Novo, N.F. et al. (2003). Oral conditions in children with cerebral palsy. *Journal of Dentistry for Children* 70: 40–46.

Roger, K. (1994). Facial dysmorphism and syndrome diagnosis. In: K. Roger (ed.), *Pediatric Orofacial Medicine and Pathology*. London: Chapman and Hall Medical, pp. 42–74.

Shapira, J., Becker, A., and Moskovitz, M. (1999). The management of drooling problems in children with neurological dysfunction: A review and case report. *Special Care in Dentistry* 19: 181–185.

Shapira, J., Chaushu, S., and Becker, A. (2000). Prevalence of tooth transposition, third molar agenesis, and maxillary canine impaction in individuals with Down syndrome. *Angle Orthodontist* 70: 290–296.

Shapira, J., Regev, L., and Liebfeld, H. (1986). Re-eruption of completely intruded immature permanent incisors. *Endodontics and Dental Traumatology* 2: 113–116.

Shaw, L., and Saxby, M.S. (1986). Periodontal destruction in Down's syndrome and in juvenile periodontitis. How close a similarity? *Journal of Periodontology* 57: 709–715.

Shaw, W.C. (1981). The influence of children's dentofacial appearance on their social attractiveness as judged by peers and lay adults. *American Journal of Orthodontics* 79: 399–415.

Shaw, W.C., Addy, M., and Ray, C. (1980). Dental and social effects of malocclusion and effectiveness of orthodontic treatment: A review. *Community Dentistry and Oral Epidemiology* 8: 36–45.

Shott, S.R. (2006). Down syndrome: Common otolaryngologic manifestations. *American Journal of Medical Genetics Part C Seminars in Medical Genetics* 142C: 131–140.

Sticker, G. (1970). Psychological issues pertaining to malocclusion. *American Journal of Orthodontics* 58: 276–283.

Strodel, B.J. (1987). The effects of spastic cerebral palsy on occlusion. *ASDC Journal of Dentistry for Children* 54: 255–260.

Thomas, R.G. (1979). Indirect bonding: Simplicity in action. *Journal of Clinical Orthodontics* 13: 93–106.

Thurow, R.C. (1975). Craniomaxillary orthopedic correction with en masse dental control. *American Journal of Orthodontics* 68: 601–624.

Tomita, Y., Uechi, J., Konno, M. et al. (2018). Accuracy of digital models generated by conventional impression/plaster-model methods and intraoral scanning. *Dental Materials Journal* 37: 628–633.

Townsend, G.C. (1983). Tooth size in children and young adults with trisomy 21 (Down) syndrome. *Archives of Oral Biology* 28: 159–166.

Tronstad, L., Trope, M., Bank, M. et al. (1986). Surgical access for endodontic treatment of intruded teeth. *Endodontics and Dental Traumatology* 2: 75–78.

Vicari, S. (2006). Motor development and neuropsychological patterns in persons with Down syndrome. *Behaviour Genetics* 36: 355–364.

Vittek, J., Winik, S., Winik, A. et al. (1994). Analysis of orthodontic anomalies in mentally retarded developmentally disabled (MRDD) persons. *Special Care in Dentistry* 14: 198–202.

Vivaldi-Rodrigues, G., Demito, C.F., Bowman, S.J. et al. (2006). The effectiveness of a fluoride varnish in preventing the development of white spot lesions. *World Journal of Orthodontics* 7: 138–144.

Waldman, H.B., Perlman, S.P., and Swerdloff, M. (2000). Orthodontics and the population with special needs. *American Journal of Orthodontics and Dentofacial Orthopedics* 118: 14–17.

Weintraub, J.A., Ramos-Gomez, F., Jue, B. et al. (2006). Fluoride varnish efficacy to prevent early childhood caries. *Journal of Dental Research* 85: 172–176.

Weyant, R.J., Tracy, S.L., Anselmo, T.T. et al. (2013). Topical fluoride for caries prevention: Executive summary of the updated clinical recommendations and supporting systematic review. *Journal of the American Dental Association* 144: 1279–1291.

Zabokova-Bilbilova, E., Popovska, L., Kapusevska, B. et al. (2014). White spot lesions: Prevention and management during the orthodontic treatment. *Prilozi (Makedonska Akademija na Naukite i Umetnostite. Oddelenie za Medicinski Nauki)* 35: 161–168.

Zhou, N., Wong, H.M., Wen, Y.F. et al. (2019). Efficacy of caries and gingivitis prevention strategies among children and adolescents with intellectual disabilities: A systematic review and meta-analysis. *Journal of Intellectual Disability Research* 63: 507–518.

15
Orthodontic Care in the Adult Medically Compromised Patient

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Summary

Improvements in industrialization, economic conditions, and technology, along with rapid advancement in medical health facilities, have positively affected human longevity. This has led to a rise in the population of adult patients with medically compromised conditions requiring orthodontic treatment with a desire to improve their stomatognathic functions. Treating such patients requires broad knowledge and understanding of various systemic conditions and their pathophysiology. The orthodontic treatment requires customization of orthodontic mechanics so that there are no adverse effects on the existing health condition. Adult orthodontics in medically compromised patients is full of challenges and requires comprehensive and goal-oriented treatment plans. Orthodontists are often required to get in touch with the treating physician for better insight into the patient's systemic conditions, which will help them customize the treatment plan for its effective and efficient execution. Teamwork is the key to success in such a scenario, where collective efforts from medical and dental colleagues are very much desired to achieve satisfactory oral health outcomes, as achieving the best possible health for the patient is the ultimate aim for healthcare professionals.

The United Nations' "Global population growth and sustainable development report" in 2021 suggested that since the middle of the twentieth century the world's population has more than tripled, increasing from around 2.5 billion in 1950 to almost 7.9 billion by 2021 (United Nations Department of Economic and Social Affairs, 2021). Part of this stems from increased life expectancy in societies around the world. At the biological level, aging results from the impact of the accumulation of a wide variety of molecular and cellular changes over time. This might lead to a gradual decrease in an aging individual's physical and mental capacity, resulting in an increased risk of disease (Tosato et al., 2007; Franceschi et al., 2018). These changes are neither linear nor consistent and are only loosely associated with a person's chronological age. The diversity seen in the mid-age group is not random.

There has been increasing recognition that the health status, type and level of activity, productivity, and other socioeconomic characteristics of adult persons have changed significantly in many parts of the world over the past years. The adult population is also characterized by the emergence of several complex health conditions such as cardiac issues, endocrinal anomalies, infectious disorders, pulmonary disorders, skeletal disorders, mood disorders, and so on (Tosato et al., 2007; Franceschi et al., 2018). The demand for oral healthcare has also increased over the past few decades among adult patients worldwide (Petersen et al., 2005). Many of these patients need orthodontic care and belong to various ethnic backgrounds and socioeconomic strata (Abu Alhaija et al., 2010). With an increase in the flow of the adult population to orthodontic treatment, it is obvious that an orthodontist will see patients with various systemic disorders (Patel et al., 2009; Batista et al., 2018). The recent advancement in medical and oral healthcare sciences has enabled the complex needs of such patients (medical and dental care) to be met with greater satisfaction. However, this requires orthodontists to have a sound understanding of systemic diseases and their pathophysiology, and in case of doubt they should seek opinions from other medical and dental professionals (Patel et al., 2009).

An orthodontist, who is, in turn, part of the oral healthcare professional community, should focus on the patient's overall well-being before treating dentofacial abnormalities. Often patients are

unaware of their systemic problems when they report to the orthodontist with dentofacial problems. Also, orthodontists often focus on the "regional diagnosis," which is more of a local approach and deals with dentofacial issues, rather than looking for a broader or general approach (Kharbanda and Wadhawan, 2012). Regional diagnosis misses the bigger picture of the patient in the form of pathological, medical, mental, or psychological conditions affecting overall well-being. Thus, a comprehensive or holistic approach to diagnosis is essential for the optimal outcome of comprehensive orthodontic care. This will lead to the best possible oral healthcare delivery to medically compromised adult patients, which is also the primary goal of an orthodontist. The protocol for managing patients with various systemic disorders is broadly outlined in Figure 15.1 (van Venrooy and Proffit, 1985) and considered in more depth in this chapter.

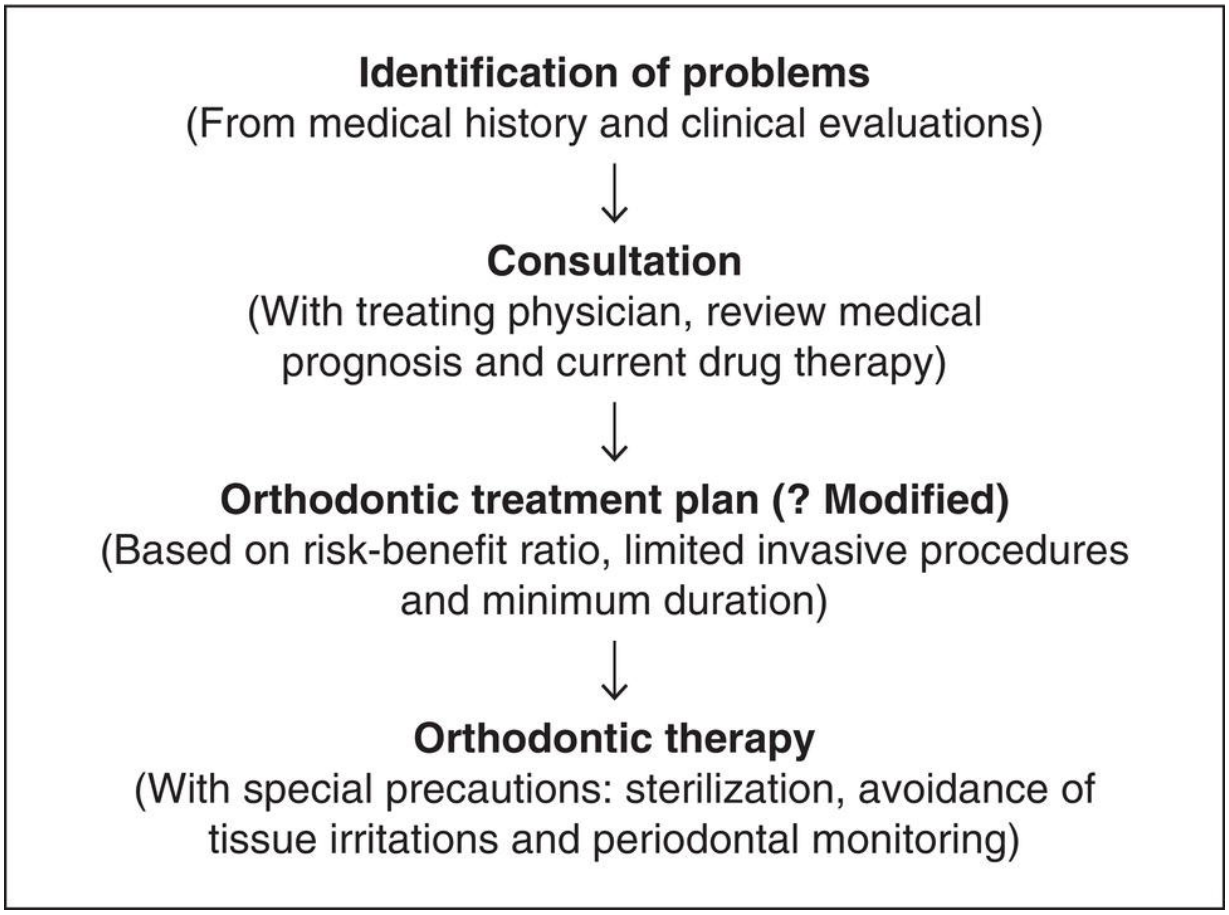

Figure 15.1 Orthodontic treatment protocol for patients with systemic diseases.

Cardiovascular disorders

Infective endocarditis

Infective endocarditis (IE) is a relatively rare disorder with an estimated incidence of 3–10 cases per 100,000 population per year (Khan et al., 2016). The incidence of IE is higher in elderly people, who often are affected by many comorbidities. Such individuals have various clear and observable cardiac changes in the heart's septum, valves, and walls. Up to one-third of patients acquire IE in a healthcare-associated environment, including oral healthcare (Vallejo, 2016). Unexpected fever, common cold symptoms, weight loss, rigor, fatigue, myalgia, joint pain, and back pain are the usual signs and symptoms of IE. Various oral healthcare procedures pose a risk for IE in the individual with structural pathological changes in the heart. Thus, antibiotic prophylaxis is always considered before certain orthodontic or dental procedures that involve the manipulation of gingival tissues (oral prophylaxis), the periapical region of the teeth, or any sort of perforation of the oral mucosa (tooth extraction, banding, interproximal reduction). In individuals with the following cardiac conditions, antibiotic prophylaxis is routinely recommended:

- Prosthetic cardiac valves.
- Hypertrophic cardiomyopathies.
- Prosthetic material used for valve repair.
- Previous episode(s) of IE.
- Unrepaired cyanotic congenital heart defect (CHD), surgically repaired CHD, or palliated structural conditions.
- Intravenous drug misuse/abuse.

A recommended antibiotic prophylactic regimen for dental or orthodontic procedures (Wilson et al., 2021) is described in Table 15.1.

Table 15.1 A single dose of an antibiotic can be administered 30–60 minutes before the dental procedure.

Situation	Medication*	Adult	Children
Oral	Amoxicillin	2 g	50 mg/kg
Unable to take oral medication	Ampicillin OR cefazoline or ceftriaxone	2 g IM/IV 1 g IM/IV	50 mg/kg IM/IV 50 mg/kg IM/IV
Allergic to penicillins or ampicillin – oral regimen	Cephalexin** OR azithromycin or clarithromycin OR doxycycline	2 g 500 mg 100 mg	50 mg/kg 15 mg/kg <45 kg 2.2 mg/kg >45 kg 100 mg
Allergic to penicillin or ampicillin and unable to take oral medication	Cefazoline or ceftriaxone***	1 g IM/IV	50 mg/ kg IM/IV

* Clindamycin is not recommended for antibiotic prophylaxis for any dental procedure.

** Or other first- or second-generation oral cephalosporins in equivalent adult or pediatric dosage.

*** Cephalosporins should not be used in an individual with a history of anaphylaxis, angioedema, or urticaria with penicillin or ampicillin.

IM, intramuscular; IV, intravenous.

Orthodontic implications

- Consultation is necessary with the treating cardiologist/physician before any orthodontic and dental intervention. This will minimize any risk in the future that arises

due to orthodontic or dental care, and such a protocol develops a better understanding of the patient's present and future medical requirements.

- A dental procedure such as routine injection through noninfected tissues, recording dental radiographs, placement of removable orthodontic appliances, adjustment of orthodontic appliances (fixed/removable), and placement of orthodontic brackets does not warrant antibiotic prophylaxis.
- Bonding is preferred over banding. Excessive adhesives around the brackets should be removed.
- For the ligation of archwires, elastomeric ties are preferred over stainless steel ligature ties to prevent any injury to the oral soft tissues.
- All orthodontic appliances or accessories like edges of bands, hooks, and molar tubes should be smoothened and polished to minimize any irritation or injuries.
- Fixed acrylic orthodontic appliances such as rapid maxillary expansion appliances and the Nance button should be avoided, as they tend to increase oral microbial colonization in and around these appliances.
- Patients are encouraged to maintain the highest level of oral hygiene. It is good practice to use 0.2% chlorhexidine mouthwash during orthodontic treatment to reduce the oral microbial load (Jena et al., 2004).
- For more invasive procedures like orthognathic surgery, the patient should be counseled about the risks and benefits of antibiotic prophylaxis and the sign and symptoms of IE.

Thrombocytopenia

Thrombocytopenia is a medical condition related to reduction in the circulating blood platelet count as a result of bone marrow disruption (Lee and Lee, 2016). The bone marrow suppression could be secondary to the malignancy of the bone marrow or an autoimmune condition (Lee and Lee, 2016). Gingival bleeding could be the first or, in many cases, the only clinical sign with which the

patient presents (Sugiura et al., 2018; Sharan et al., 2022). Patients with a confirmed diagnosis of thrombocytopenia most often are on chemotherapy or radiotherapy, which might affect their somatic growth, thus affecting stomatognathic growth too. The altered stomatognathic growth can manifest as mandibular retrognathism, a decrease in the vertical facial dimension, microdontia, a V-shaped pattern of roots, anomalies in root development, and a decrease in the height of alveolar processes of maxillary and the mandibular bone. All these changes have great impacts on the successful outcome of orthodontic care in patients with thrombocytopenia (Patel et al., 2009; Mituś et al., 2015).

Orthodontic implications

- Consultation with the treating oncologist/physician before commencement of orthodontic care is important to know the details of the patient as well as the associated risk factors that can arise during treatment.
- If the patient has been diagnosed with a malignant disorder of bone marrow such as leukemia before the commencement of orthodontic care, the treatment should be delayed until comprehensive chemo- or radiotherapy is over and at least two years have elapsed after bone marrow transplantation.
- These patients have reduced resistance to infection, and at the same time there is a decrease in saliva formation. Such a scenario increases the risk of dental caries (Jena et al., 2004).
- If the medical issue is diagnosed during orthodontic treatment, it is advisable to get in touch with the treating medical oncologist/physician and discuss in detail the need for future orthodontic treatment and progress of treatment. Most cases require removing all existing orthodontic appliances to prevent any soft tissue irritation or injury (Sheller and Williams, 1996). Comprehensive orthodontic treatment can only be commenced when all treatment is over and the patient has had a minimum two years of event-free survival. Before commencement of orthodontic treatment, orthodontists should consult the treating physician and get clearance about patient fitness.

- Orthodontic treatment and mechanics should be kept simple, and the applied force should be gentle and mild to prevent any side effects during comprehensive treatment. Orthodontic appliances should be nonirritating and patients should be advised to use relieving wax. Patients are advised to meticulously keep the highest possible level of oral hygiene to prevent gingivitis and other related issues.
- In growing patients, growth modulation might have a questionable prognosis, as this medical condition might affect stomatognathic growth.
- Imaging of tooth and craniofacial structures is a regular norm in such patients as they have an increased incidence of root resorption, which might affect the orthodontic treatment (Sheller and Williams, 1996; Dahllöf and Huggare, 2004).
- Stainless steel brackets should be avoided as the cytotoxicity is more due to the release of corrosion products (free radicals).

Endocrine disorders

Diabetes mellitus

Diabetes mellitus (DM) is a medical condition that is characterized by a group of metabolic diseases with hyperglycemia resulting from defects in insulin secretion, insulin action, or both (American Diabetes Association, 2018). Periodontal issues are most commonly seen in an individual with uncontrolled DM, which might compromise the tooth-supporting tissues such as the periodontal ligament, gingiva, mucosa, and alveolar bone. In such a scenario, the normal or enhanced loading of the tooth and supporting structures might pose a risk. The current classification of DM is highlighted in Table 15.2 (Baymest, 2015).

Table 15.2 Current classification of diabetes mellitus (DM).

Adapted from Baymest (2015).

Type 1 DM	Insulin-dependent DM Most common among children and young adults Strict insulin management is a must or severe ketoacidosis might result
Type 2 DM	Non-insulin-dependent DM Usually seen in individuals >40 years Caused by insulin resistance and inadequate insulin secretion
Type 3 DM	Due to pancreatic beta-cell destruction (chronic pancreatitis or pancreatic surgery) Due to decreased insulin production and simultaneous development of insulin resistance
Gestational diabetes	Usually seen during pregnancy Typically resolves postpartum

Orthodontic Implications

- Well-controlled DM is not a contraindication to orthodontic treatment. The orthodontist should be in touch with the patient's treating physician/endocrinologist, and regular blood glucose levels should be monitored.
- Early-morning orthodontic appointments are preferred. The patient should have a regular meal and take usual medications before the visit to the orthodontist (Patel et al., 2009).
- Orthodontists and the supporting team should be trained and in a state of readiness to deal with emergencies, such as hypoglycemia (Patel et al., 2009).
- Orthodontic force should be kept light and continuous (Patel et al., 2009).
- Faster orthodontic tooth movement may be due to the upregulation of osteoclast migration and activity and the downregulation of osteoblast differentiation (Braga et al., 2011).

- Patients should be kept on a strict oral hygiene protocol. They should be educated and encouraged to maintain the highest possible level of good oral hygiene. The importance of maintaining good oral hygiene is to be enforced pretreatment and during subsequent appointments. A periodontist may often be involved while treating adult patients with DM, for pretreatment and subsequent periodontal evaluation when the treatment progresses.

Table 15.3 Clinical manifestations of thyroid disorders.

Hypothyroidism	Hyperthyroidism
Salivary gland enlargement Mouth breathing and thick lips Delayed bone resorption and tooth eruption Macroglossia and glossitis Anterior openbite Enamel hypoplasia in primary and permanent dentitions	Increased bone turnover and accelerated tooth eruption Increased susceptibility to dental caries Increased susceptibility to periodontal disease Maxillary and mandibular osteoporosis Enhanced risk of development of connective tissue disorders such as Sjögren syndrome or systemic lupus erythematosus (SLE)

Thyroid disorders

Hypo- and hyperthyroidism are caused by unregulated thyroid hormone synthesis by the follicular cells of the thyroid gland. The orthodontist often sees patients with thyroid disorders who present with various clinical manifestations (Pinto and Click, 2002; Chandna and Bathla, 2011; Table 15.3).

Orthodontic Implications

- The treating physician/endocrinologist should be consulted before the commencement of orthodontic care.
- The risk of root resorption is high in patients with hypothyroidism, so regular radiographic evaluation is a must

before and during comprehensive orthodontic treatment (Maheshwari et al., 2012).

- In patients with hyperthyroidism, an effective stress reduction protocol must be followed. Early-morning appointments are preferred.
- For pain management during orthodontic care, nonsteroidal anti-inflammatory drugs (NSAIDs) and aspirin are usually avoided; instead, other groups of analgesics are preferred (Pinto and Click, 2002).
- In hyperthyroid patients the rate of tooth movement is increased, so judicious application of orthodontic force and selection of mechanics are musts (Maheshwari et al., 2012).

Infectious diseases

Human immunodeficiency virus and hepatitis B and C

The most relevant infectious diseases an orthodontist comes across are blood borne and include human immunodeficiency virus (HIV) and hepatitis B (HBV) and C (HCV). The risk of viral transmission after percutaneous exposure is highest for HIV, followed by HCV and HBV (Laheij et al., 2012). The risk of transmission through saliva is minimal in most cases unless the saliva is contaminated with blood.

Orthodontic implications

- The orthodontist and his/her support team should be immunized with the HBV vaccine, and postvaccination blood tests should be done at regular intervals for assessment of the adequate level of immunization.
- Universal cross-infection precautions should be followed at the orthodontic office for every patient, irrespective of health status.
- Implementing a sharp equipment disposal protocol and infection control policy should align with the best practice guidance of infection control agencies.

- All instruments and equipment should be sterilized adequately.
- In the case of percutaneous exposure, incidence should be reported to the appropriate authorities, and follow-up should be done as per the established guidelines.

COVID-19

Recently, COVID-19 infection has caused havoc worldwide and is caused by a nonsegmented positive-sense RNA virus (SARS-CoV-2) encapsulated by a lipid bilayer envelope. This virus tends to affect the cells of the nasopharynx, alveolus, and gastrointestinal tract. Transmission of SARS-CoV-2 among humans is predominantly from the respiratory tract via droplets or, indirectly, fomites, and to a lesser extent via aerosol. By the nature of their profession, orthodontists are always at high risk of infection from patients, mainly the asymptomatic ones. Therefore, it is imperative to have details of travel history along with the details of medical history to rule out COVID-19 infection. Patients who present with any of the symptoms of COVID-19 must be advised to get the appropriate test done. Apart from that, patients' COVID-19 vaccination details must be recorded, and if they have not taken the full course of the vaccine they should advised to complete it (Sharan et al., 2020).

Orthodontic Implications

- During the active phase of COVID-19 infection, the patient and treating orthodontist should use teledentistry for supervision of the ongoing orthodontic treatment and guidance in minimizing any complications (Sharan et al., 2022).
- Short-term management of various orthodontic emergencies under the guidance of a treating orthodontist is mentioned in Table 15.4.

Table 15.4 Short-term management of various orthodontic emergencies under the guidance of a treating orthodontist.

Orthodontic emergency situations	Things for the patient to do under the supervision of the orthodontist
Ulcer of the lip/cheek from orthodontic wire and brackets	Apply a small amount of rolled soft orthodontic relief wax over the bracket/wire Apply local anesthesia/antiseptic gel over the ulcer Avoid oily, spicy, and hot food for a week or till the ulcer has healed
Loose or broken brackets, bands, and wires	If the band or bracket is broken yet still attached to the wire, it is better to leave it like that if it is not causing any discomfort until the next orthodontic appointment If it is causing irritation/discomfort to the adjacent soft tissue, put relief wax on the loose bracket Do not put any elastic on the broken band or bracket If the bracket or band is broken off, keep it in a safe place and bring it to the orthodontic clinic for the next appointment
Elastic "O" ring/ligature came out during brushing or eating	The elastic "O" ring/ligature can be placed back on the bracket using clean tweezers Or it can be removed with the help of tweezers if the patient thinks he/she cannot place it back
Stainless steel ligature become loose and/or is irritating soft tissues	A loose ligature can be removed with clean tweezers if it is not coming out, or using nail clippers it can be cut and taken out
Loose/broken elastic chain	This can be taken out with clean

	tweezers or cut with nail clippers
Food caught between the teeth and brackets or soft tissue leading to discomfort	Advise the patient to maintain optimal oral hygiene Interproximal brushes, toothpicks, or a Waterpik can be used to dislodge food caught between the teeth and bracket or soft tissue
Poking/protruding wire at the end of brackets	The wire can be pushed from the back with clean tweezers to bring it flush with a band/bracket If it is due to slipping away from the wire, then reposition the wire with clean tweezers and make sure it is equally and symmetrically positioned If the wire is causing extreme discomfort, it can be cut with clean nail clippers; before cutting the wire, place a small clean gauze near the area to minimize accidental swallowing or soft tissue piercing
The patient has swallowed a piece of the band/bracket/orthodontic appliance	If the orthodontic accessory is small and has been swallowed, reassure the patient it will pass through the gastrointestinal tract and there is nothing to worry about The patient should make sure there are no acute respiratory symptoms associated with the swallowing (such as a cough or sneeze) or acute abdominal pain/colic. If such symptoms are present, the patient should visit the emergency department of a hospital for clinical examination or, if required, radiological assessment
Broken bonded lingual/palatal (BLR) retainers	If a BLR has come out from one or two teeth with or without resin pads, it should be trimmed or cut with clean

	nail clippers Where the whole BLR is loose and the patient is unable to come to the orthodontic clinic, it is advisable to take the whole BLR out carefully In both these scenarios, the patient is advised to use removable retainers, if provided, until the next appointment
Broken/loose-fitting transpalatal arch (TPA), translingual holding arch (TLA), or maxillary expanders	If the TPA becomes loose or broken and is still in the patient's mouth close to its original position, and the patient cannot visit the orthodontic clinic, it should be placed back. For an expander, no further activation/expansion is advised until the next visit to the orthodontist If the TPA, TLA, or expander has fallen out completely, the patient should keep it safe and bring it to the orthodontic clinic in the next visit
Orthodontic appliance is embedded in the soft tissue, leading to severe pain and infection	This is one a true emergency; ideally, the patient should be seen by the orthodontist provided the patient clears the triage questionnaire with respect to COVID-19. Proper infection control protocols have to be followed while treating the patient If the patient is unable to be personally seen by the orthodontist at the clinic, then the patient or home care provider is advised to use a clean and sterile clippers and cut the orthodontic wire, if it is attached to the broken or loose part, and remove the broken part of the orthodontic appliance from the mouth using clean tweezers. If required, tell the patient to send photos through WhatsApp. If

	needed, antibiotic and analgesic can be prescribed to the patient digitally, and the information saved in the treatment file
Edges of the aligner poking out	If the patient feels the aligner margin is biting on his or her gum, it can be smoothed with a nail file or the previous set of aligners should be used
Broken or nonfitting removable retainer/functional appliance	Avoid using the broken/distorted appliance Keep the removal/functional appliance in water
Broken fixed functional appliance	The patient is advised to send photos via WhatsApp • If asymptomatic → nothing to be done till next appointment • If mild pain/discomfort → warm saline rinses 3–4 times/day for a week • If moderate to severe pain and discomfort → emergency care at the orthodontic clinic*

* Adapted from American Association of Orthodontists (2020), COVID-19 Resource for Orthodontists 2020 (www1.aaoinfo.org/covid-19).

A patient who is on home quarantine can get emergency oral/orthodontic care when he or she fulfills these criteria:

- Afebrile for past three or more days without any medications or more than seven days since initial symptoms.
- Two negative laboratory tests (which have been done 24 h apart), afebrile without medication, and near-normal respiratory functions.

Skeletal system problems

Ankylosing spondylitis

Ankylosing spondylitis (AS) is an autoimmune disease that affects the spine and sacroiliac joints (Arora et al., 2013). The common signs and symptoms of AS are described in Table 15.5. Depending on the severity of the disease, various NSAIDs, anti-tumor necrosis factor-α (anti-TNF-α), corticosteroids, and bisphosphonates are used for treatment. A compromised inflammatory response against oral infection results in poor gingival and periodontal health.

Table 15.5 Clinical characteristics of ankylosing spondylitis and medication-related osteonecrosis of the jaws.

Ankylosing spondylitis	Severe and progressive back pain, enthesitis, morning stiffness, and fatigue. (Mehdizadeh and Mir, 2012) Uncomfortable for the patient to sit in the dental chair for a long period (Arora et al., 2013) Increased risk of periodontal diseases and temporomandibular joint dysfunction in an advanced stage of the disease (Arora et al., 2013)
Medication-related osteonecrosis of the jaws	Nonhealing exposed bone, jaw pain, and neuropathy (Akashi et al., 2018) Loose teeth, mucosal swelling, erythema, suppuration, and nonhealing extraction sockets (Sharma et al., 2013) Paresthesia or numbness in the jaw and bad breath (Akashi et al., 2018)

Orthodontic implications

- The orthodontic appointment should be short.
- Extension and flexion of the neck and spine should be minimal.
- Patients should be motivated for optimum oral hygiene.

Medication-related osteonecrosis of the jaws

Medication-related osteonecrosis of the jaws (MRONJ) is a condition in which severe bone loss of the maxillary–mandibular region occurs, without any history of radiation exposure or obvious metastatic diseases affecting the jaws (Rosella et al., 2016). Patients with various types of cancers, bisphosphonate use (>5 years), and receiving intravenous bisphosphonate with or without systemic glucocorticoids are at maximum risk for MRONJ development. The clinical characteristics of MRONJ are highlighted in Table 15.5.

Orthodontic implications

- It should be explained to the patient that the duration of orthodontic treatment is longer as bisphosphonate affects bone turnover and reduces the rate of orthodontic tooth movement.
- Care should be taken to avoid any trauma to the soft tissues.
- Use of stainless steel ligatures is to be avoided.
- A nonextraction treatment plan should be chosen.
- Any type of oral surgical plan should be avoided.
- The risks associated with temporary anchorage devices have not been established.

Gastrointestinal disorders

Inflammatory bowel diseases (IBD) include autoimmune conditions that mostly result in acute, chronic, and recurrent inflammation of the terminal ileum and colon (Feuerstein and Cheifetz, 2014). Crohn's disease and ulcerative colitis are two main varieties of IBD. The oral manifestations of IBD are described in Table 15.6. Steroids like prednisolone and hydrocortisone and immunosuppressants like methotrexate are commonly used to treat IBD (Patel and Patel, 2018). Also, in a few patients bowel surgery is performed.

Table 15.6 Oral manifestations of inflammatory bowel diseases.

Mucosal tags, granulomatous cheilitis, diffuse swellings in the lips and cheeks, and cobblestones (Johannsen et al., 2015; Tan et al., 2016)
Mucogingivitis, deep linear granulations, aphthous stomatitis, gingivitis, periodontitis, glossitis, candidiasis, pyostomatitis vegetans, altered taste sensation, halitosis, and gingival hyperplasia (Johannsen et al., 2015; Tan et al., 2016)
Multiple missing teeth and temporomandibular joint arthritis (Johannsen et al., 2015; Tan et al., 2016)

Orthodontic implications

- Injury to the soft tissues is to be avoided.
- Patients should be motivated to maintain optimum oral hygiene.
- For the management of aphthous ulcers, topical anesthetic agents and steroids can be used.
- Use of stainless steel ligatures is to be avoided.
- Bonded retainers are preferred.

Respiratory system problems

Asthma

Asthma is one of the most common causes of death in young adults (Gullach et al., 2015). Intermittent wheezing, dyspnea, cough, and chest tightness are the common clinical characteristics. Table 15.7 highlights the oral manifestations of asthma. The treatment involves inhalation of various bronchodilators along with corticosteroids. The long-term use of corticosteroids results in osteoporosis (Gibson and Ferguson, 2004). Also, prolonged use of inhalers containing steroids leads to xerostomia, increasing the risk of enamel demineralization and periodontal problems (Patel et al., 2009). There is a high risk of external root resorption during orthodontic treatment in patients with asthma (Patel et al., 2009; Yassir et al., 2021).

Table 15.7 Oral manifestations of asthma and cystic fibrosis.

Asthma	Reduced salivary flow, poor periodontal health, candidiasis, stomatitis, gingival hyperplasia, and increased calculus formation (Patel et al., 2009) Discoloration of the tongue (Patel et al., 2009) Osteoporosis of bones in the long run (Patel et al., 2009)
Cystic fibrosis	Facial pain due to chronic sinusitis (Harrington et al., 2016) Delayed teeth eruption (Harrington et al., 2016) Osteopenia and osteoporosis (Harrington et al., 2016) Black hairy tongue and xerostomia secondary to prolonged use of oral antibiotics (Harrington et al., 2016)

Orthodontic implications

- The treating physician must be consulted before the start of orthodontic treatment.
- Appointments for orthodontic treatment must be fixed in the morning (Sonis, 2004).
- Orthodontic treatment appointments should be short (Sonis, 2004).
- Stress and anxiety to the patient should be minimal.
- A supine position of the patient during orthodontic treatment should be avoided (Sonis, 2004).
- All emergency drugs must be made available in the clinic.
- The patient should have an inhaler in case of a sudden attack of asthma (Maheshwari et al., 2012).
- Care should be taken not to elicit a gag reflex while making impressions and using suction for moisture control (Maheshwari et al., 2012).
- Patients must be motivated to maintain strict oral hygiene (Sonis, 2004).
- Acetaminophen should be preferred over NSAIDs for pain management (Khattri and Bhardwaj, 2012).

Cystic fibrosis

Cystic fibrosis is a life-threatening autosomal recessive disease of the exocrine glands. Chronic infection of the chest leads to progressive damage to the lungs and bronchiectasis. Submandibular glands are commonly affected. It is common among Caucasians, with an incidence of 1 : 2500 live births (Jaffe and Bush, 1999). There is no sex predilection for cystic fibrosis (Slutsky and Greenberg, 2011). The use of long-term steroids, malabsorption of various nutrients, and deficiency of vitamin D result in osteopenia and osteoporosis (Harrington et al., 2016). The oral signs and symptoms of cystic fibrosis are mentioned in Table 15.7.

Orthodontic implications

- The patient's treating physician must be consulted first to identify the status and severity of the disease.
- The risk–benefit ratio of the orthodontic treatment must be evaluated first. If the orthodontic treatment is to be started, it has to be customized according to the patient's needs.
- The use of general anesthesia should be avoided. Local anesthesia, along with inhalation sedation, may be used for minor surgical procedures.
- Reduction of the saliva flow increases the risk of enamel decalcification (van Venrooy and Proffit, 1985), so proper oral hygiene and the use of fluoride supplements are crucial.
- Consecutive treatment of many cystic fibrosis patients in the same clinic should be avoided as it can increase the chance of drug resistance and lung infection spread among the patients.

Nervous system disorders

Epilepsy

Epilepsy is a medical condition characterized by sudden abnormal electrical signals generated by the cerebral neurons, leading to

recurring seizures. Various anti-epileptic drugs affect the functions of various organs like bone marrow and the liver and an individual's behaviors (Aragon and Burneo, 2007). Many patients also develop various intraoral symptoms, primarily due to side effects of the drugs used to treat epilepsy (Table 15.8). Comprehensive orthodontic treatment exacerbates gingival hyperplasia among subjects taking phenytoin (Figure 15.2). Intraoral traumas like tongue biting, tooth fracture, temporomandibular joint subluxation, and maxillofacial injuries are very frequent in patients with generalized "tonic–clonic" seizures (Sheller, 2004; Michelotti and Iodice, 2010).

Orthodontic implications

- Consultation with the patient's treating physician is a must to know the status of the epilepsy.
- Orthodontic treatment should not be started if the epilepsy is not well controlled (Sheller, 2004).

Table 15.8 Various intraoral features of epilepsy, multiple sclerosis, and schizophrenia.

Epilepsy	Gingival hyperplasia, xerostomia, and oral ulcerations (Aragon and Burneo, 2007) Osteopenia (Aragon and Burneo, 2007) Impaired wound healing and increased chance of postoperative infection and glossitis (Aragon and Burneo, 2007)
Multiple sclerosis	Pain and numbness in the face and mouth (Gibson and Ferguson, 2004) Poor oral hygiene due to tremors and loss of coordination (Gibson and Ferguson, 2004) Xerostomia increased the risk of oral superinfections, mucositis, and ulcerative stomatitis among subjects receiving monoclonal antibodies (Gibson and Ferguson, 2004) Increased risk of osteoporosis and candida infection among subjects using steroids for a prolonged period (Fischer et al., 2009)
Schizophrenia	Dental caries (Yang et al., 2018) Missing teeth (Yang et al., 2018) Gingivitis and periodontitis (Yang et al., 2018)

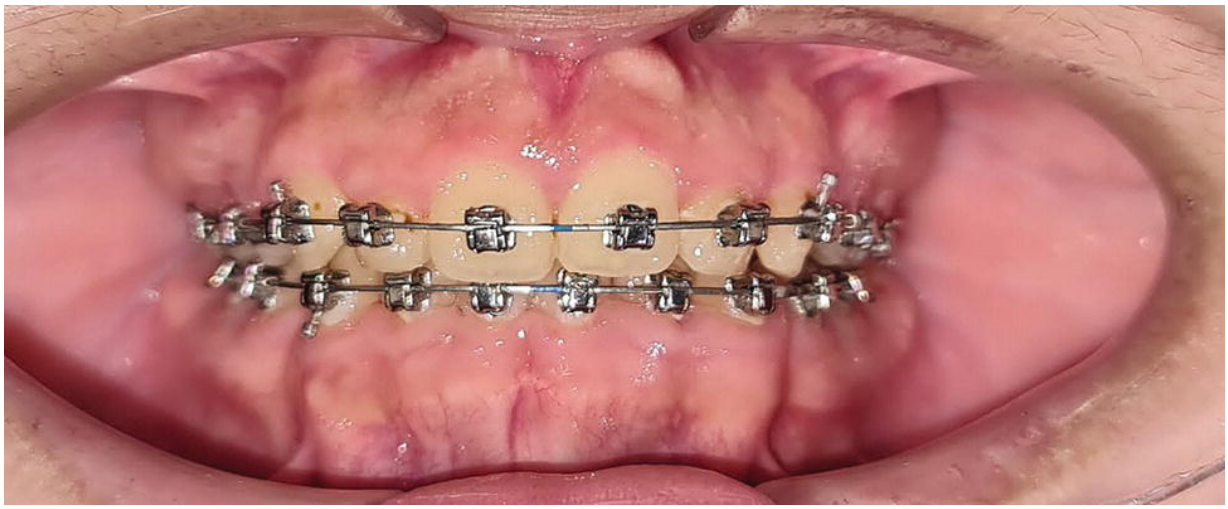

Figure 15.2 Aggravation of the gingival hyperplasia by comprehensive orthodontic treatment in a patient taking phenytoin for the treatment of epilepsy.

- The possible tooth and soft tissue injuries if seizures occur during orthodontic treatment should be explained to the patient.
- The use of removable orthodontic appliances should be avoided, as the dislodgment of appliances during epilepsy may cause trauma to the soft tissues and pose a risk of appliance aspiration. If removable appliances are to be used, they should have multiple retentive clasps for adequate retention and be made from high-impact acrylic (Fiske and Boyle, 2002).
- Fixed orthodontic appliances can produce artifacts on magnetic resonance imaging (MRI). Ceramic, plastic, or titanium brackets or aligners can be used to overcome this problem. Sometimes removal of the bonded metallic appliances and retainers may be needed to get an acceptable image.
- The margin of the clear aligner and bonded retainers should not touch the margins of the gingiva.
- If an epileptic attack occurs during orthodontic treatment, the orthodontist should be prepared to provide appropriate emergency treatment to manage the epileptic seizure.

Multiple sclerosis

Multiple sclerosis is a demyelinating disease due to chronic central nervous system inflammation. Common symptoms include tremors, weakness, and paresthesia of the limbs, trunk, jaws, lips, tongue, head, and speech. The symptoms of multiple sclerosis are aggravated by emotion and stress. Loss of coordination and tremor makes it difficult to maintain adequate oral hygiene. An MRI of the brain is routinely done for the diagnosis of multiple sclerosis. Xerostomia is the common side effect of various antidepressant drugs used for its treatment. The common oral symptoms of multiple sclerosis are mentioned in Table 15.8.

Orthodontic implications

- The treating physician must be consulted first to identify the prognosis of the disease.
- Orthodontic treatment should be delayed until the disease is in the remission phase.
- A power toothbrush should be advised for oral hygiene maintenance.
- Assistance may be needed to insert and remove intra- and extraoral elastics.
- Proper oral hygiene and fluoride supplements are important to maintain adequate periodontal health and prevent enamel demineralization.

Schizophrenia

Schizophrenia is a severe mental disorder that manifests as delusions, hallucinations, inability to pay attention, social withdrawal, loss of sense of pleasure, abnormal voluntary activities, cognitive defects, and poor quality of life (Neeley et al., 2006; Yang et al., 2018). Various antipsychotic drugs are used for its management, and their common side effect is xerostomia. The common oral problems of schizophrenia are mentioned in Table 15.8.

Orthodontic implications

- The treating physician must be consulted first to identify the status of the disease.
- Orthodontic treatment should be avoided unless the disease is well controlled.
- Lack of patient cooperation during orthodontic treatment is a major concern.
- Involuntary movements of body parts make it difficult for the patient to wear removable orthodontic appliances (Neeley et al., 2006).

Renal disorders

Chronic renal failure or renal transplantation

Patients with renal transplantation or dialysis are susceptible to enamel demineralization, bone loss, and resorption of periapical tissue (Cazzolla et al., 2018). The susceptibility to oral infection is high in patients using immunosuppressant drugs. Also, bone metabolism and tooth movements are affected to a great extent by various drugs (Santos et al., 2012). Gingival hyperplasia is often found in patients using cyclosporine. Various intraoral signs and symptoms in patients with chronic renal failure or renal transplantation are highlighted in Table 15.9.

Table 15.9 Intraoral signs and symptoms of chronic renal failure or in renal transplantation patients.

Enamel demineralization (Walker et al., 2007)
Periodontal bone loss and resorption of periapical tissue (Walker et al., 2007; Cazzolla et al., 2018)
Increased susceptibility to oral infection (Walker et al., 2007; Cazzolla et al., 2018)
Gingival hyperplasia (Walker et al., 2007; Cazzolla et al., 2018)
Abnormal bone metabolism and tooth movements (Walker et al., 2007; Cazzolla et al., 2018)

Orthodontic implications

- Consultation with the treating nephrologist/physician is important to identify the current status and prognosis of the disease.
- Orthodontic treatment should be initiated only when the disease is well controlled (Patel et al., 2009).
- In kidney transplant subjects, orthodontic treatment should be started at least six months after surgery when the patient is stable and without the risk of transplant rejection (Georgakopoulou et al., 2011).
- Orthodontic treatment should be customized to reduce the duration of treatment.
- The treating nephrologist/physician must be consulted before prescribing any analgesic.
- Orthodontic force should be light, and adjustment of the appliance should be more frequent, as prolonged use of immunosuppressants accelerates the rate of orthodontic tooth movement (Patel et al., 2009; Santos et al., 2012).
- Strict oral hygiene is important to prevent excessive gingival hyperplasia. Chlorhexidine gluconate (0.2%) mouthwash may be advised in addition to routine mechanical plaque control methods.
- Gingivectomy may be needed before and during comprehensive orthodontic treatment (Maheshwari et al., 2012).
- Small and low-profile brackets should be preferred.
- Cemented bands should be avoided.
- Excessive composite around the brackets and tubes should be removed.
- All attachments on the tooth surface should be away from the gingival margin.
- A bonded retainer should be avoided. Essix retainers can be used, but their margins should be kept away from the gingival

margin (Patel et al., 2009).

- Gingival overgrowth often leads to the need for frequent adjustment of removable appliances.
- A nonextraction treatment plan should be preferred, as excessive gingival overgrowth may interfere with extraction space closure.

Allergy reactions

Latex allergy

Allergy to natural rubber (latex) can occur during orthodontic treatment. Substances such as residual proteins and various chemicals like thiurams, carbamates, and benzothiazoles used during the vulcanization process result in sensitivity reactions. Powdered gloves are the main source of latex allergy. In orthodontics, latex is commonly present in gloves, elastomeric modules, elastics, and separators. Latex allergy occurs in <1% of the general population, 5–15% of healthcare workers, and 24–60% of spina bifida patients (Poley and Slater, 2000). Latex allergy is predominant among occupationally exposed subjects, and is also very high among subjects with a history of asthma, hay fever, and eczema (Cullinan et al., 2003). Hypersensitivity to certain foods like papaya, potatoes, bananas, chestnuts, and avocados increases the risk of latex allergy (Cullinan et al., 2003). Latex allergy can be a type I and type IV hypersensitive reaction. Its symptoms are described in Table 15.10. Harmless and effective orthodontic treatment depends on recognizing the susceptible subjects while effectively managing their allergy.

Table 15.10 Clinical signs and symptoms of latex, nickel, and acrylic allergic reactions.

Latex allergy	Itching, redness, and rash or hives Itchy nose, throat, or eyes Nausea and abdominal cramps Difficulty breathing, including a runny nose, sneezing, coughing, or wheezing Anaphylaxis reaction characterized by drop in blood pressure, difficulty breathing, and/or swelling of throat, tongue, and nose
Nickel allergy	Gingivitis, gingival hyperplasia, angular cheilitis, stomatitis, and multiple erythemas (Namikoshi et al., 1990)
Acrylic allergy	Edema, erythema, burning sensations, and chronic urticaria (Lunder and Rogl-Butina, 2000)

Orthodontic implications

- Appropriate medical history should be recorded to identify a patient with latex allergy.
- In suspected patients, the presence of circulating antibodies to latex should be identified by doing an epicutaneous skin test.
- An early-morning appointment should be given to a patient with a known latex allergy. This can avoid exposure to air-borne latex particles.
- Nitrile, polychloroprene, elastin, and vinyl gloves should be used.
- Kesling springs should be used in place of elastomeric separators.
- Latex-free intra- and extraoral elastics should be used. However, in the first 24 hours, latex-free elastics have shown more force decay compared to latex elastics (40% vs. 25%; Russell et al., 2004)

- Latex-free headgear components and band remover tips should be used.
- Stainless steel ligatures should be used in place of elastomeric ligatures.
- Self-ligating brackets can be the preferred choice.
- Latex-free consumables and disposables must be stored in a separate place.
- All emergency drugs and resuscitation equipment must be in place. The resuscitation equipment should be latex free (Field and Longman, 2004).

Nickel allergy

The incidence of nickel allergy in orthodontic practice is about 0.3–0.4% (Schuster et al., 2004). Intraoral nickel allergy symptoms occur in approximately 0.1–0.2% of orthodontic patients (Menne, 1994). Nickel allergy is more frequent among females and patients with asthma (Alawsi et al., 2020). In orthodontic patients, nickel induces delayed hypersensitive (type IV) reactions. The average release of nickel from orthodontic appliances is about 40 μg, which is negligible to induce cytotoxicity, but it may be significant for a patient who is highly sensitive to nickel (Park and Shearer, 1983). The hypersensitive reaction linked to an inflammatory response is secondary to the release of nickel ions from corrosion of orthodontic appliances. Persons who are sensitive to metals are more susceptible to nickel allergy (Janson et al., 1998). The concentration of nickel ions in saliva and serum is significantly higher following the initial stage of orthodontic treatment (Nayak et al., 2015) or insertion of orthodontic appliances (Agaoglu et al., 2001). The release of nickel ions is higher from nickel–titanium archwires than stainless steel archwires (Hussain et al., 2016). The increased risk of nickel allergy in orthodontic patients may be due to wearing nickel-containing jewelry at an early age (McDonagh et al., 1992). The clinical manifestations of nickel allergy are highlighted in Table 15.10. The clinical symptoms usually manifest at least 24 hours after exposure (Al-Tawil et al., 1981). Symptoms of allergic reactions to nickel, as

shown in Figure 15.3 after a short period following insertion of orthodontic appliances, may be an alarming sign for an orthodontist.

Orthodontic implications

- Appropriate history and proper observation of clinical signs and symptoms are important.
- In suspected patients like industrial workers and employees who report for orthodontic treatment, sensitivity to nickel must be evaluated by a patch test (5% nickel sulfate in petroleum jelly; Menne et al., 1987).

Figure 15.3 Symptoms of nickel allergy in a patient undergoing comprehensive orthodontic treatment.

- Nickel-free alloys should be used in orthodontic appliances. Nickel–titanium (Ni-Ti) alloy should be replaced with titanium–molybdenum alloy (TMA), stainless steel, resin/plastic-coated Ni-Ti, pure titanium, or ion-implanted Ni-Ti archwires (Toms, 1988; Kim and Johnson, 1999). Fiber-reinforced composite wire and gold-plated archwires can also be used. A sectional Ni-Ti archwire can be used initially for a few days in sensitive patients to monitor the patient's response to nickel allergy.

- Stainless steel brackets are usually well tolerated by nickel allergy patients as these are resistant to corrosion and thus prevent the release of nickel (Rahilly and Price, 2003). Ceramic, polycarbonate, pure titanium, and gold brackets should be used in highly sensitive patients.
- For patients needing headgear, plastic-coated headgear studs are an alternate option. Also, temporary anchorage devices can be used in place of headgear for anchorage preservation.
- Plastic aligners can be used.
- Nickel allergy might be a causative factor for excessive apical root resorption (Nishioka et al., 2006).

Acrylic allergy

The leaching of residual monomers into the oral cavity from methyl methacrylate–based acrylic resins can induce type IV hypersensitive reactions (Devlin and Watts, 1984). The oral manifestations of acrylic allergy reactions are described in Table 15.10.

Orthodontic implications

- In suspected patients, a skin patch test for acrylic allergy should be done.
- Bonded retainers or clear aligners can be used in place of acrylic-based removable retainers.
- Acrylic-based removable appliances should be avoided.

Conclusion

Early diagnosis and quality treatment have improved the quality of life and increased the life expectancy of adult patients with various systemic diseases. The demand for orthodontic treatment is high among patients with well-controlled systemic diseases. An orthodontist needs to understand the present status and prognosis of the disease. Consultation with the treating physician is essential prior to beginning orthodontic treatment. Each patient must have

explained to them the risks and benefits of orthodontic treatment, and informed consent must be obtained prior to the start of treatment. Orthodontic treatment must be customized for the best benefit of the patient. The orthodontist and supporting staff must have up-to-date knowledge to handle any emergency that might happen during orthodontic treatment.

References

Abu Alhaija, E.S., Aldaikki, A., Al-Omairi, M.K. et al. (2010). The relationship between personality traits, pain perception and attitude toward orthodontic treatment. *Angle Orthodontist* 80: 1141–1149.

Agaoglu, G., Arun, T., Izgu, B. et al. (2001). Nickel and chromium levels in the saliva and serum of patients with fixed orthodontic appliances. *Angle Orthodontist* 71: 375–379.

Akashi, M., Kusumoto, J., Takeda, D. et al. (2018). A literature review of perioperative antibiotic administration in surgery for medication-related osteonecrosis of the jaw. *Oral and Maxillofacial Surgery* 22: 369–378.

Alawsi, F., Sawbridge, D., and Fitzgerald, R. (2020). Orthodontics in patients with significant medical co-morbidities. *Journal of Orthodontics* 47: 4–24.

Al-Tawil, N., Marcusson, J., and Moller, E. (1981). Lymphocyte transformation test in patients with nickel sensitivity: An aid to diagnosis. *Acta Dermato-Venereologica* 61: 511–515.

American Association of Orthodontists (2020). COVID-19 resource for orthodontists. www1.aaoinfo.org/covid-19.

American Diabetes Association (2018). Classification and diagnosis of diabetes: Standards of medical care in diabetes. *Diabetes Care* 41: S13–S27.

Aragon, C.E., and Burneo, J.G. (2007). Understanding the patient with epilepsy and seizures in the dental practice. *Journal of the*

Canadian Dental Association 73: 71–76.

Arora, P., Amarnath, J., Ravindra, S.V. et al. (2013). Temporomandibular joint involvement in ankylosing spondylitis. *BMJ Case Reports* 2013: bcr2013009386.

Batista, M.J., Lawrence, H.P., and Sousa, M.L.P. (2018). Oral health literacy and oral health outcomes in an adult population in Brazil. *BMC Public Health* 18: 60.

Baymest, H.W. (2015). Classification, pathophysiology, diagnosis and management of diabetes mellitus. *Journal of Diabetes and Metabolism* 6: 5.

Braga, S.M., Taddei, S.R., Andrade, I., Jr. et al. (2011). Effect of diabetes on orthodontic tooth movement in a mouse model. *European Journal of Oral Sciences* 119: 7–14.

Cazzolla, A., Zhurakivska, K., Ciavarella, D. et al. (2018). Primary hyperoxaluria: Orthodontic management in a pediatric patient: A case report. *Special Care in Dentistry* 38: 259–265.

Chandna, S., and Bathla, M. (2011). Oral manifestations of thyroid disorders and its management. *Indian Journal of Endocrinology and Metabolism* 15(Suppl 2): S113–S116.

Cullinan, P., Brown, R., Field, A. et al. (2003). Latex allergy. A position paper of the British Society of Allergy and Clinical Immunology. *Clinical and Experimental Allergy* 33: 1484–1499.

Dahllöf, G., and Huggare, J. (2004). Orthodontic considerations in the pediatric cancer patient: A review. *Seminars in Orthodontics* 10: 266–276.

Devlin, H., and Watts, D.C. (1984). Acrylic “allergy”? *British Dental Journal* 157: 272–275.

Feuerstein, J.D., and Cheifetz, A.S. (2014). Ulcerative colitis: Epidemiology, diagnosis, and management. *Mayo Clinic Proceedings* 89: 1553–1563.

Field, E.A., and Longman, L.P. (2004). *Guidance for the Management of Natural Rubber Latex Allergy in Dental Patients and Dental Health Care Workers*. London: Faculty of General Dental Practitioners.

Fischer, D.J., Epstein, J.B., and Klasser, G. (2009). Multiple sclerosis: An update for oral health care providers. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* 108: 318–327.

Fiske, J., and Boyle, C. (2002). Epilepsy and oral care. *Dental Update* 29: 180–187.

Franceshi, C., Garogani, P., Morsiani, C. et al. (2018). The continuum of aging and age-related diseases: Common mechanisms but different rates. *Frontiers in Medicine* 5: 61.

Georgakopoulou, E.A., Achtari, M.D., and Afentoulide, N. (2011). Dental management of patients before and after renal transplantation. *Stomatologija* 13: 107–112.

Gibson, N., and Ferguson, J.W. (2004). Steroid cover for dental patients on long-term steroid medication: Proposed clinical guidelines based upon a critical review of the literature. *British Dental Journal* 197: 681–685.

Gullach, A.J., Risgaard, B., Lynge, T.H. et al. (2015). Sudden death in young persons with uncontrolled asthma—a nationwide cohort study in Denmark. *BMC Pulmonary Medicine* 15: 35.

Harrington, N., Barry, P.J., and Barry, S.M. (2016). Dental treatment for people with cystic fibrosis. *European Archives of Paediatric Dentistry* 17: 195–203.

Hussain, H.D., Ajith, S.D., and Goel, P. (2016). Nickel release from stainless steel and nickel-titanium archwires: An in vitro study. *Journal of Oral Biology and Craniofacial Research* 6: 213–218.

Jaffe, A., and Bush, A. (1999). Cystic fibrosis: A management update. *Prescribers' Journal* 39: 91–96.

Janson, G.R., Dainesi, E.A., Consolaro, A. et al. (1998). Nickel hypersensitivity reaction before, during and after orthodontic therapy. *American Journal of Orthodontics and Dentofacial Orthopedics* 113: 655–660.

Jena, A.K., Duggal, R., Mathur, V.P. et al. (2004). Orthodontic care for medically compromised patients. *Journal of Indian Orthodontic Society* 37: 160–171.

Johannsen, A., Fored, M.C., Hakansson, J. et al. (2015). Consumption of dental treatment in patients with inflammatory bowel disease, a register study. *PLoS One* 10: e0134001.

Khan, O., Shafi, A.M.A., and Timmis, A. (2016). International guideline changes and the incidence of infective endocarditis: A systematic review. *Open Heart* 3: e000498.

Kharbanda, O.P., and Wadhawan, N. (2012). Orthodontic diagnosis and treatment planning: Collaborating with medical and other dental specialists. In: K. Vinod and Z. Devidovitch (eds.), *Integrated Clinical Orthodontics*. Chichester: Wiley Blackwell, pp. 37–67.

Khattri, S., and Bhardwaj, M. (2012). Orthodontic management in medically compromised patients. *International Journal of Dental Clinics* 4: 26–29.

Kim, H., and Johnson, J. (1999). Corrosion of stainless steel, nickel-titanium, coated nickel-titanium and titanium orthodontic wire. *Angle Orthodontist* 69: 39–44.

Laheij, A.M.G.A., Kistler, J.O., Belibasakis, G.N. et al. (2012). Healthcare-associated viral and bacterial infections in dentistry. *Journal of Oral Microbiology* 4: 17659.

Lee, E.J., and Lee, A.I. (2016). Thrombocytopenia. *Primary Care: Clinical in Office Practice* 43: 543–557.

Lunder, T., and Rogl-Butina, M. (2000). Chronic urticaria from an acrylic dental prosthesis. *Contact Dermatitis* 43: 232–233.

Maheshwari, S., Verma, S.K., Ansar, J. et al. (2012). Orthodontic care of medically compromised patients. *Indian Journal of Oral Sciences* 3: 129–137.

McDonagh, A.J., Wright, A.L., Cork, M.J. et al. (1992). Nickel sensitivity: The influence of ear piercing and atopy. *British Journal of Dermatology* 126: 16–18.

Mehdizadeh, M., and Mir, P. (2012). Surgical orodental implications in ankylosing spondylitis. *Dental Research Journal* 9: 807–811.

Menne, T. (1994). Quantitative aspects of nickel dermatitis. Sensitization and eliciting threshold concentrations. *Science of the Total Environment* 148: 275–281.

Menne, T., Brandup, F., Thestrup-Pedersen, K. et al. (1987). Patch test reactivity to nickel alloys. *Contact Dermatitis* 16: 255–259.

Michelotti, A., and Iodice, G. (2010). The role of orthodontics in temporomandibular disorders. *Journal of Oral Rehabilitation* 37: 411–429.

Mituś, M.K., Łoboda, M., Marcinkowska-Mituś, A. et al. (2015). Orthodontic treatment in oncological patients. *Przegląd Lekarski* 72: 243–245.

Namikoshi, T., Yoshimatsu, T., Suga, K. et al. (1990). The prevalence of sensitivity to constituents of dental alloys. *Journal of Oral Rehabilitation* 17: 377–381.

Nayak, R.S., Khanna, B., Pasha, A. et al. (2015). Evaluation of nickel and chromium ion release during fixed orthodontic treatment using inductively coupled plasma-mass spectrometer: An in vitro study. *Journal of International Oral Health* 7: 14–20.

Neeley, W.W., II, Kluemper, G.T., and Hays, L.R. (2006). Psychiatry in orthodontics, part 1: Typical adolescent psychiatric disorders and their relevance to orthodontic practice. *American Journal of Orthodontics and Dentofacial Orthopedics* 129: 176–184.

Nishioka, M., Ioi, H., Nakata, S. et al. (2006). Root resorption and immune system factors in the Japanese. *Angle Orthodontist* 76:

103–108.

Park, H.Y., and Shearer, T.R. (1983). In-vitro release of nickel and chromium from simulated orthodontic appliances. *American Journal of Orthodontics* 84: 156–159.

Patel, A., Burden, D.J., and Sandler, J. (2009). Medical disorders and orthodontics. *Journal of Orthodontics* 36: 1–21.

Patel, D., and Patel, V. (2018). Pharmacology: MRONJ risk factor. *British Dental Journal* 224: 198.

Petersen, P.E., Bourgeois, D., Bratthall, D. et al. (2005). Oral health information systems—towards measuring progress in oral health promotion and disease prevention. *Bulletin of World Health Organisation* 83: 686–693.

Pinto, A., and Click, M. (2002). Management of patients with thyroid disease Oral health considerations. *Journal of American Dental Association* 133: 849–858.

Poley, G.E., Jr., and Slater, J.E. (2000). Latex allergy. *Journal of Allergy and Clinical Immunology* 105: 1054–1062.

Rahilly, G., and Price, N. (2003). Current products and practice: Nickel allergy and orthodontics. *Journal of Orthodontics* 30: 171–174.

Rosella, D., Papi, P., Giardino, R. et al. (2016). Medication-related osteonecrosis of the jaw: Clinical and practical guidelines. *Journal of International Society of Preventive and Community Dentistry* 6: 97–104.

Russell, K.A., Milne, A.D., Khanna, R.A. et al. (2004). In-vitro assessment of the mechanical properties of latex and non-latex orthodontic elastics. *American Journal of Orthodontics and Dentofacial Orthopedics* 126: 65–70.

Santos, R.L., Lacerda, M.C.M., Gonçalves, R.T. et al. (2012). Immunosuppressants: Implications in orthodontics. *Dental Press Journal of Orthodontics* 17: 55–61.

Schuster, G., Reichle, R., Bauer, R.R. et al. (2004). Allergies induced by orthodontic alloys: Incidence and impact on treatment. *Journal of Orofacial Orthopedics* 65: 48–59.

Sharan, J., Barhare, U., and Jena, A.K. (2022). Teledentistry: Our experience during the Covid pandemic at a tertiary care hospital. *International Journal of Applied Dental Science* 8: 157–162.

Sharan, J., Chanu, N.I., Jena, A.K. et al. (2020) COVID-19: Orthodontic care during and after the pandemic: A narrative review. *Journal of Indian Orthodontic Society* 54: 352–365.

Sharan, J., Mohapatra, S., Chhabra, G. et al. (2022). Gingival hyperplasia: Initial oral manifestation of acute myeloid leukemia (a case report). *Journal of Indian Society of Periodontology* 27(2): 201–206.

Sharma, D., Ivanovski, S., Slevin, M. et al. (2013). Bisphosphonate-related osteonecrosis of jaw (BRONJ): Diagnostic criteria and possible pathogenic mechanisms of an unexpected anti-angiogenic side effect. *Vascular Cell* 5: 1.

Sheller, B. (2004). Orthodontic management of patients with seizure disorders. *Seminars in Orthodontics* 10: 247–251.

Sheller, B., and Williams, B. (1996). Orthodontic management of patients with hematologic malignancies. *American Journal of Orthodontics and Dentofacial Orthopedics* 109: 575–580.

Slutsky, H., and Greenberg, J.R. (2011). Orthodontic and prosthetic treatment of a patient with cystic fibrosis and agenesis of maxillary lateral incisors. *Compendium of Continuing Education in Dentistry* 32: E80–E85.

Sonis, S.T. (2004). Orthodontic management of selected medically compromised patients: Cardiac disease, bleeding disorders, and asthma. *Seminars in Orthodontics* 10: 277–280.

Sugiura, T., Yamamoto, K., Murakami, K. et al. (2018). Immune thrombocytopenic purpura detected with oral hemorrhage: A case report. *Journal of Shiraz University Medical Sciences* 19: 159–163.

Tan, C.X.W., Brand, H.S., de Boer, N.K.H. et al. T (2016). Gastrointestinal diseases and their oro-dental manifestations: Part 1: Crohn's disease. *British Dental Journal* 221: 794–799.

Toms, A.P. (1988). The corrosion of orthodontic wire. *European Journal of Orthodontics* 10: 87–97.

Tosato, M., Zamboni, V., Derrini, A. et al. (2007). The aging process and potential interventions to extend life expectancy. *Clinical Interventions in Aging* 2: 401–412.

United Nations Department of Economic and Social Affairs (2021). Global population growth and sustainable development. https://www.un.org/development/desa/pd/sites/www.un.org.development.desa.pd/files/undesa_pd_2022_global_population_growth.pdf.

van Venrooy, J.R., and Proffit, W.R. (1985). Orthodontic care for medically compromised patients: Possibilities and limitations. *Journal of American Dental Association* 111: 262–266.

Walker, M.R., Lovel, S.F., and Melrose, C.A. (2007). Orthodontic treatment of a patient with a renal transplant and drug-induced gingival overgrowth: a case report. *Journal of Orthodontics* 34(4): 220–228.

Wilson, W., Gewitz, M., Lockhart, P.B. et al. (2021). Prevention of viridans group Streptococcal infective endocarditis. A scientific statement from the American Heart Association. *Circulations* 143: e963–e978.

Yang, M., Chen, P., He, M.-X. et al. (2018). Poor oral health in patients with schizophrenia: A systematic review and meta-analysis. *Schizophrenia Research* 201: 3–9.

Yassir, Y.A., McIntyre, G.T., and Bearn, D.R. (2021). Orthodontic treatment and root resorption: An overview of systematic reviews. *European Journal of Orthodontics* 43(4): 442–456.

Part IV
Orthodontics and Other Dental Specialties

16

Comprehensive Periodontal Evaluation of the Orthodontic Patient: The Role of a Periodontist in Orthodontic Practice

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Summary

Periodontal diseases represent inflammatory conditions initiated by oral biofilms. Outcomes from studies in humans have indicated that elimination of the bacterial infection and institution of plaque control regimes result in almost all cases in periodontal health. This condition forms the basis for further corrections, including orthodontic therapy. Apart from periodontal considerations leading to orthodontic treatment, the intervention path can be observed in the opposite direction. Pathological tooth migration is defined as tooth displacement that occurs as a consequence of periodontal disease. It often occurs in periodontal patients and represents one of the most obvious changes causing adult patients to seek orthodontic treatment as a first step. This chapter highlights the need for a thorough assessment and tight collaboration between periodontists and orthodontists in a common treatment plan. The comprehensive periodontal evaluation of the orthodontic patient is described along with relevant clinical cases.

Periodontal diseases represent inflammatory conditions initiated by oral biofilms. From a clinical point of view, redness and swelling of the gingiva as well as increased pocket probing depths (PPD) with tendency to bleeding on probing (BoP) are common characteristics of patients suffering from periodontitis. Moreover, periodontitis may be recognized in radiographs by moderate to severe loss of alveolar bone.

Patients with stage IV periodontitis (Tonetti et al., 2018) are affected by the presence of severe periodontal lesions extending to the apical portion of the roots, resulting in tooth hypermobility, bite collapse, and drifting. In such cases, proper control of periodontitis and adequate orthodontic and prosthetic rehabilitation represent the only ways to restore masticatory function and reduce the risk of loss of the entire dentition.

Outcomes from studies in humans have indicated that elimination of the bacterial infection and institution of plaque control regimes

result in almost all cases in periodontal health. This condition forms the basis for further corrections, including orthodontic therapy. This is corroborated by the fact that outcomes of experimental studies in dogs indicated that in biofilm-free dentitions orthodontic tooth movement (i.e. tilting and bodily movements) neither jeopardized periodontal health nor induced loss of the attachment apparatus, even under reduced but healthy periodontal tissue conditions (Ericsson and Thilander, 1978; Polson et al., 1984). Apart from periodontal considerations leading to orthodontic treatment, the intervention path can be observed in the opposite direction in usual clinical practice.

Pathological tooth migration

Pathological tooth migration (PTM) is defined as tooth displacement that occurs as a consequence of periodontal disease. It often occurs in periodontal patients and represents one of the most obvious changes causing adult patients to seek orthodontic treatment as a first step. PTM commonly occurs in the anterior region, may affect one or more teeth, and often involves facial flaring, extrusion, rotations, over-eruption, and diastema/spacing formation at teeth with alveolar bone loss. The position of a tooth is determined by an equilibrium that is the result of forces from the occlusion, the periodontium, and the pressure from soft tissues, including tongue, lips, and cheeks (Proffit, 1978). Typical forms of PTM are associated with an imbalance between the facial muscles and the tongue when the periodontal support is reduced, as the tongue pressure may be higher than the pressure from the facial muscles. The reported prevalence of PTM varies from 9.4% (Brunsvold et al., 1999) to 55.8% (Martinez-Canut et al., 1997). Towfighi et al. (1997) reported a prevalence of 30% in patients with moderate and severe periodontitis. This is in line with Demetriou et al. (1991), who reported tooth migration in 36.9% of 330 periodontal patients.

The etiology of PTM is not yet fully elucidated, although several factors have been suggested as part of the causative pathway. The likelihood of tooth migration increased from 2.23- to 7.97-fold when substantial bone loss and tooth loss had occurred and when gingival inflammation was present (Martinez-Canut et al., 1997). This is in

line with a study including 100 periodontitis patients, with an association observed between bone loss, increased probing depth, and PTM, although no correlation between parafunction such as clenching or bruxism and PTM was seen (Rathod et al., 2013).

The change in positioning of the center of resistance (CR) of the affected tooth, which becomes more apical as the alveolar bone height is reduced, and the pressure produced from the inflamed tissue within the periodontal pocket are also considered important. Costa et al. (2004) analyzed periodontal destruction in migrated and nonmigrated anterior teeth in 32 patients suffering from generalized chronic periodontitis. Facial flaring occurred most frequently (34.8%), followed by diastema formation. Extrusion was found in only 4.3% of this group of participants. Notably, severe bone loss (BL; 59%) and significant clinical attachment loss (CAL; 8.42 mm) were observed in extruded teeth, followed by teeth with facial flaring (45% BL and 6.07 mm CAL loss). Rotated and tilted teeth showed less bone reduction. Overall, migrated teeth exhibited greater BL and loss of CAL (40% BL and 5.1 mm) than nonmigrated teeth (31% BL and 4.1 mm; Costa et al., 2004). Other studies reported attachment loss of migrated teeth to be greater than for nonmigrated control teeth (4.79 ± 0.28 mm vs. 3.21 ± 0.18 mm, $p < 0.001$; Towfighi et al., 1997). These results point to the fact that the destruction of periodontal tissue plays a significant role in PTM.

Development of severe PTM is often a major esthetic concern for patients and is central in decisions about dental and orthodontic treatment. Among patients undergoing periodontal therapy, the presence of PTM was the main reason for 9% of them, while 25% reported different esthetic problems (Brunsvold et al., 1999). Spontaneous correction after periodontal treatment can be expected in mild PTM (less than 1 mm). Orthodontic correction may be considered to treat more severe PTM and the existing malocclusion during the remission of active periodontitis. Traditionally, periodontal treatment is performed before the start of orthodontic treatment to safeguard movement of periodontally compromised teeth in noninflamed periodontal tissues. Interestingly, a recent randomized clinical trial did not show differences in periodontal status after orthodontic treatment between patients treated

traditionally and in parallel with orthodontic treatment (Zasčiurinskienė et al., 2019).

Orthodontic correction of PTM helps to obtain optimal tooth alignment in the dental arches, well-balanced occlusion, and normal tooth contacts. Improvement in the smile esthetics can be an important motivation for a patient with periodontitis to maintain the result of the combined periodontal and orthodontic treatment. During orthodontic treatment it is mandatory to carefully plan force levels and biomechanical set-ups in view of the reduced bone support associated with the periodontally compromised dentition.

The increasing demand for combined periodontal and orthodontic treatment is obvious in a contemporary clinical therapeutical process. This highlights the need for a comprehensive assessment and tight collaboration between periodontists and orthodontists in a common treatment plan (Kloukos et al., 2022).

Treatment plan

A comprehensive treatment plan for patients diagnosed with stages I–IV periodontitis (Tonetti et al., 2018), including orthodontic problems such as tilting, malpositioning, and tooth migration, should include the following four steps (Sanz et al., 2020).

Step 1: Implementation of behavioral changes

Implementation of behavioral changes followed by supragingival biofilm, gingival inflammation, and risk factor control. The three main risk factors for periodontal diseases include (i) insufficient biofilm control; (ii) tobacco consumption; and (iii) uncontrolled diabetes mellitus (Kinane et al., 2006).

Step 2: Delivery of supra- and subgingival instrumentation with/without adjunctive therapies

This step, also called cause-related therapy, aims to achieve infection-free conditions in the oral cavity through removal of all

supra- and subgingival soft and hard deposits. At the end of the healing time following this step (i.e. 3–6 months), a re-evaluation with a periodontal chart allows the need for further therapies to be determined.

Step 3: Performance of periodontal surgical interventions

The main goal of this step is to address the sequelae of periodontal tissue destruction. It includes therapies such as periodontal and implant surgery and delivery of prosthetic reconstructions.

Step 4: Delivery of supportive periodontal therapy

The aim of this step is the prevention of reinfection and disease recurrence. This step includes repeated assessments of residual PPD >5 mm, BoP, and suppuration around teeth and implants, as well as the evaluation of furcation involvement. It is established that self-performed biofilm control in conjunction with regular attendance at supportive periodontal therapy (SPT) visits following active periodontal treatment represented effective means of controlling gingivitis and periodontitis and limiting tooth mortality over a 30-year period (Axelsson et al., 2004).

In addition, regular control of prosthetic reconstructions with respect to loss of retention and tooth vitality is crucial following abutment tooth preparation (Bergenholtz and Nyman 1984; Lang et al., 2004; Lulic et al., 2007). Finally, bitewing radiographs should be incorporated at regular intervals in order to detect early carious lesions.

Goals of periodontal therapy

The following clinical parameters should be assessed at the end of active periodontal therapy:

- Reduction of periodontal tissue inflammation as measured by BoP. A full-mouth mean BoP ≤25% should be achieved (Matuliene et al., 2008).
- Reduction in PPD measured in mm. Absence of residual pockets with PPD >5 mm should be achieved (Matuliene et al., 2008).
- Control of furcation involvement of multirooted teeth not exceeding degree I (Salvi et al., 2014).
- Absence of pain and discomfort.

Comprehensive periodontal examination

Basic periodontal examination

The screening of each tooth or implant is performed by means of a periodontal probe. At least two sites per tooth/implant (i.e. mesio-buccal and disto-buccal) are probed using a light force (i.e. 0.2 N) in each sextant of the dentition. The highest score in each sextant is used.

The aim of the basic periodontal examination (BPE) is to identify patients with:

- Healthy or marginally inflamed (i.e. gingivitis) periodontal conditions in need of long-term preventive measures.
- Periodontitis in need of periodontal therapy.

The BPE scores are classified as follows:

- *Score 0*: PPD ≤3 mm, BoP negative, absence of calculus or overhanging fillings.
- *Score 1*: PPD ≤3 mm, BoP positive, absence of calculus or overhanging fillings.
- *Score 2*: PPD ≤3 mm, BoP positive, presence of supra- and/or subgingival calculus and/or overhangs.
- *Score 3*: PPD 4–5 mm.

- *Score 4*: PPD ≥6 mm.

Patients with BPE scores of 0, 1, or 2 belong to the periodontally healthy or gingivitis group, respectively. Patients exhibiting a sextant with BPE scores of 3 or 4 belong to the periodontitis group and should undergo a comprehensive periodontal examination.

Periodontal chart

The comprehensive periodontal examination is carried out by performing a full-mouth periodontal chart. In conjunction with the comprehensive periodontal examination, the patient's oral hygiene practices must be evaluated.

This examination includes measurement of the following parameters at six sites around each tooth/implant:

- Pocket probing depth
- Bleeding on probing
- Clinical attachment level
- Furcation involvement
- Tooth mobility
- Plaque index

Radiographic evaluation

The radiographic evaluation by means of periapical radiographs or orthopantomograms (OPGs) provides information on both the height and configuration of the interproximal bone level. The evaluation of the radiographs allows the extension of horizontal bone loss and/or presence of angular (i.e. vertical) bony defects to be estimated. For periodontal diagnostic purposes it is important to visualize the interdental alveolar bone height. Therefore, periapical radiographs taken with a long-cone paralleling technique are recommended (Updegrave, 1951; Leonardi Dutra et al., 2016).

Pretherapeutic periodontal prognosis

Based on the results of the clinical and radiographic evaluation, a pretherapeutic prognosis for each tooth can be made. The following three questions may be addressed with respect to the pretherapeutic prognosis:

- Which tooth is secure (good)?
- Which tooth is doubtful (insecure)?
- Which tooth is irrational to treat?

The goal of this classification is to identify doubtful teeth before therapy and to change their prognosis into that of secure teeth. Teeth with a secure prognosis will require relatively simple periodontal therapy and may be considered as abutments for function.

Teeth with a doubtful periodontal prognosis may be identified on the basis of the following criteria:

- Furcation involvement degrees 2 and 3
- Angular (i.e. vertical) bony defects
- Horizontal bone loss affecting >2/3 of the root

Teeth considered “irrational to treat” should be extracted during Step 2 of therapy.

Based on the comprehensive periodontal examination and pretherapeutic prognosis, patient-based diagnoses will be made indicating how to carry out Steps 1–3 of periodontal treatment. During and following active periodontal therapy, repeated examinations prior to and following orthodontic therapy will have to be performed.

Case presentations

The case presentations illustrate the various steps of the comprehensive treatment plan and therapy, including periodontal re-evaluations to assess further treatment needs.

Case 1

A 27-year-old systemically healthy and nonsmoking female patient was examined with respect to her periodontal conditions: gingival sites displaying signs of BoP were identified, PPDs were measured, the periodontal attachment level was calculated, furcation involvements were graded, tooth mobility was assessed, and periapical radiographs were analyzed to determine the height and outline of the alveolar bone crest. Based on these findings, each tooth in the dentition was given a diagnosis of either gingivitis or periodontitis and a pretherapeutic prognosis. In addition to examination of the periodontal conditions, detailed assessments of primary and secondary caries were made for all teeth in the dentition. Finally, the patient was examined with respect to endodontic and occlusal problems as well as temporomandibular joint dysfunctions. See Figures 16.1–16.16.

Diagnosis

This patient was diagnosed with periodontitis Stage III Grade C with furcation involvement (Tonetti et al., 2018). In addition, caries was diagnosed at teeth 16 and 26.

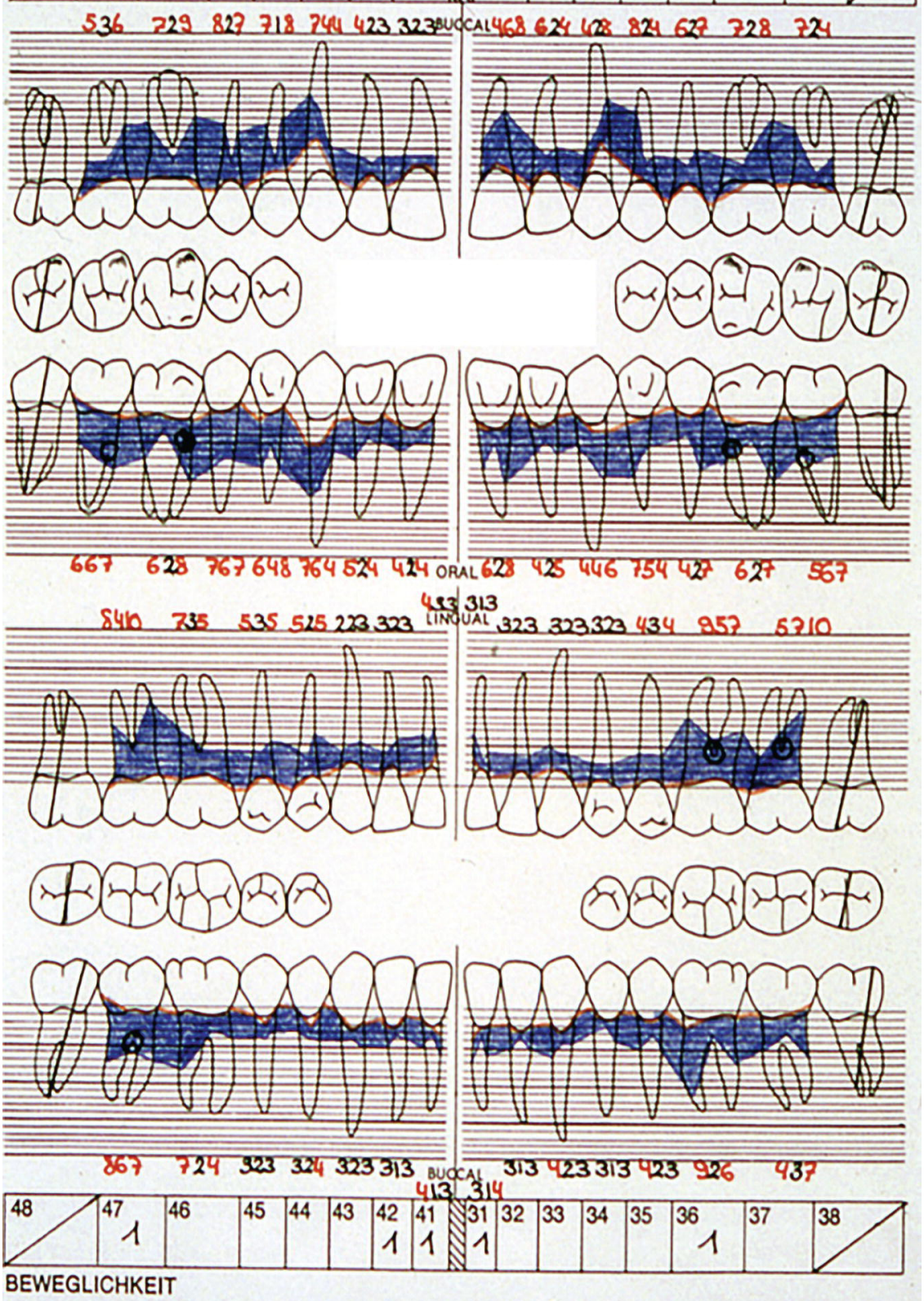
Treatment sequence

Based on the fact that the patient was systemically healthy and a nonsmoker, no medical examination and smoking cessation counselling were required. Steps 1 and 2 included patient motivation to improve oral hygiene measures and subsequent assessments and reinstructions, supra- and subgingival mechanical debridement under local anesthesia, treatment of carious lesions at 16 and 26, and endodontic treatment of tooth 46.

Figure 16.1 (a–d) Smile line and clinical characteristics of the patient at baseline.

BEWEGLICHKEIT

18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
	1		1	2	1	1		1		1	1	1			



48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38
	1					1	1	1					1		

BEWEGLICHKEIT

Figure 16.2 The baseline periodontal chart indicates generalized increased probing depths, furcation involvement, and increased tooth mobility.

Re-evaluation after non-surgical periodontal therapy

Following nonsurgical mechanical instrumentation with adjunctive delivery of systemic antimicrobials, a re-evaluation of the patient's periodontal conditions was performed. The results of this re-evaluation built the basis for additional surgical interventions (i.e. Step 3). Following completion of nonsurgical periodontal therapy, the patient was enrolled in a recall system aiming at preventing the recurrence of periodontitis and caries.

Additional surgical therapy (i.e. Step 3)

Based on the fact that the patient displayed low full-mouth plaque and BoP scores (Lindhe and Nyman, 1975), Step 3 of therapy could be carried out, including surgical interventions by means of open-flap debridement in the maxillary left and right quadrants as well as in the mandibular molar regions. Guided tissue regeneration (GTR) by means of a resorbable barrier membrane was performed at the mesial aspect of tooth 36. Following completion of periodontal surgery, a re-evaluation including a periodontal chart was performed.

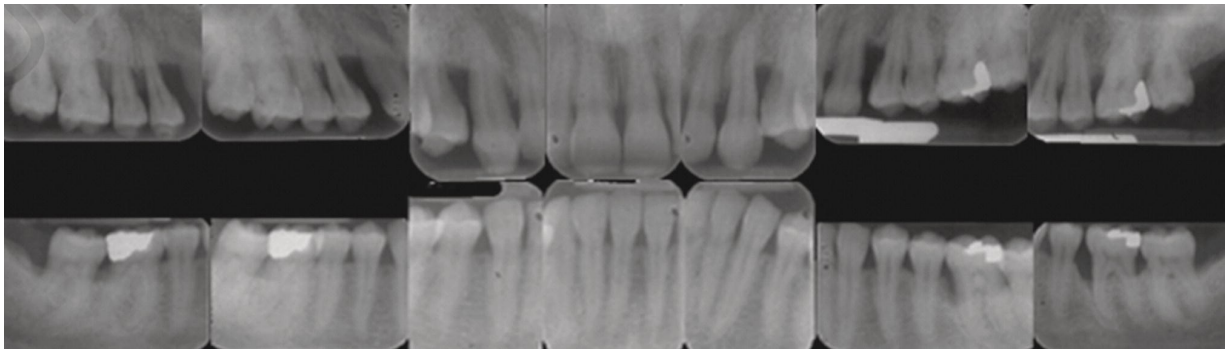


Figure 16.3 The baseline periapical radiographic status indicates generalized horizontal bone loss and localized advanced bony defects at teeth 14, 15, 23, 36, and 47.

	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
Irrational to treat																
Doubtfull (insecure)			x	x	x	x					x	x		x	x	
Secure (good)							x	x	x	x			x			
Secure (good)				x	x	x	x	x	x	x	x	x	x			
Doubtful (insecure)		x	x											x	x	
Irrational to treat																
	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38

Figure 16.4 Pretherapeutic single-tooth prognosis. Assessed as Irrational to treat/Doubtful (insecure)/Secure (good).

(a) (b) (c)

Figure 16.5 (a–c) Clinical views of the patient at re-evaluation following nonsurgical periodontal therapy

Orthodontic treatment

Orthodontic therapy by means of fixed appliances was performed in the upper anterior area to correct tooth malpositioning and improve the esthetic appearance.

Re-evaluation 20 years following active therapy

Delivery of individually tailored supportive periodontal therapy (Axelsson et al., 2004) coupled with excellent compliance of the patient was successful in maintaining the entire dentition of this challenging case for at least 20 years.

Case 2

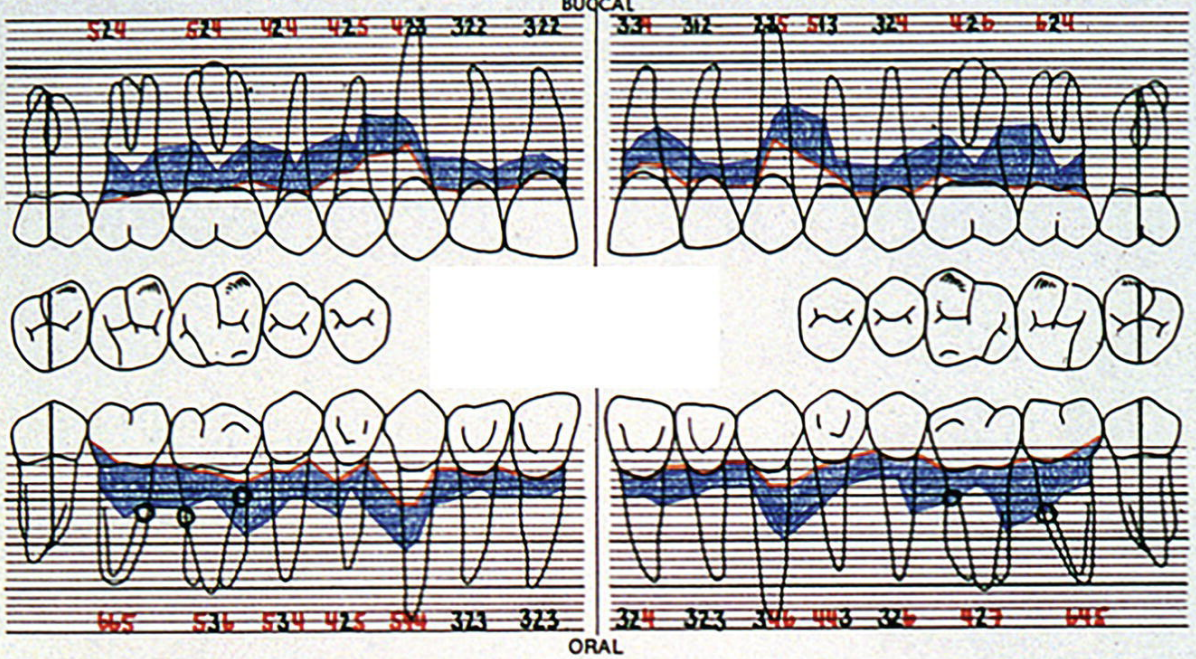
This case describes in detail the different steps of comprehensive treatment including periodontal therapy (i.e. Steps 2–3), oral rehabilitation with an implant-supported single unit crown (SUC), orthodontic therapy, and supportive periodontal care (SPC).

A 49-year-old systemically healthy and nonsmoking female patient was referred to the Department of Periodontology of the University of Bern and consequently examined with respect to her periodontal conditions: gingival sites displaying signs of BoP were identified, PPDs were measured, the CAL was calculated, furcation involvements were graded, tooth mobility was assessed, and periapical radiographs were analyzed to determine the height and outline of the alveolar bone crest. Based on these findings, each tooth in the dentition was given a diagnosis of either gingivitis or periodontitis and a pretherapeutic prognosis. Furthermore, a detailed assessment was performed of primary and secondary caries, endodontic and occlusal problems, as well as temporomandibular joint dysfunctions. See Figures 16.17–16.30.

BEWEGLICHKEIT

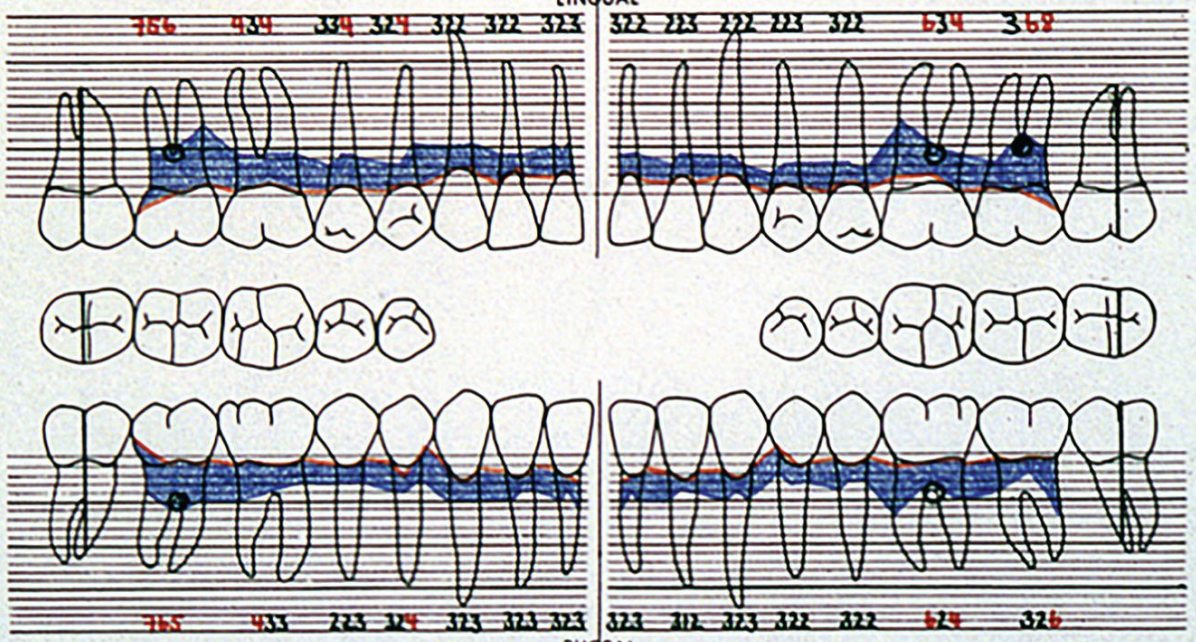
18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
	0	0	1	1/2	0	0	0	1	0/1	0/1	0/1	0	0	0	

BUCCAL



ORAL

LINGUAL



BUCCAL

48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38
	0/1	0	0	0	0	0/1	0/1	0/1	0/1	0	0	0	0/1	0	

BEWEGLICHKEIT

Figure 16.6 Periodontal chart at re-evaluation following nonsurgical periodontal therapy.

(a) (b) (c)

Figure 16.7 (a–c) Intrasurgical views of the mandibular and maxillary left quadrants.

(a) (b)

Figure 16.8 (a, b) Clinical lateral views at re-evaluation following periodontal surgery.

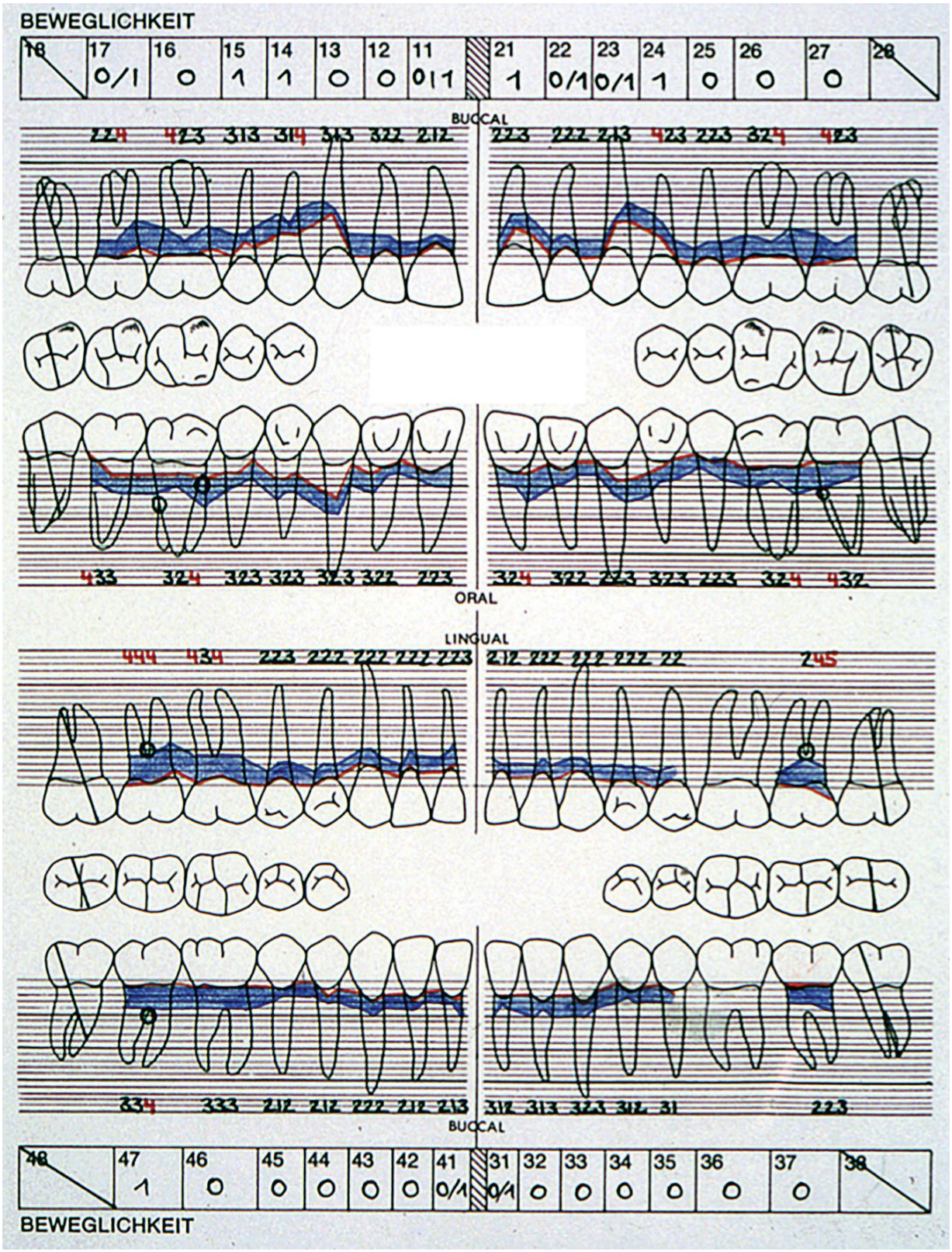
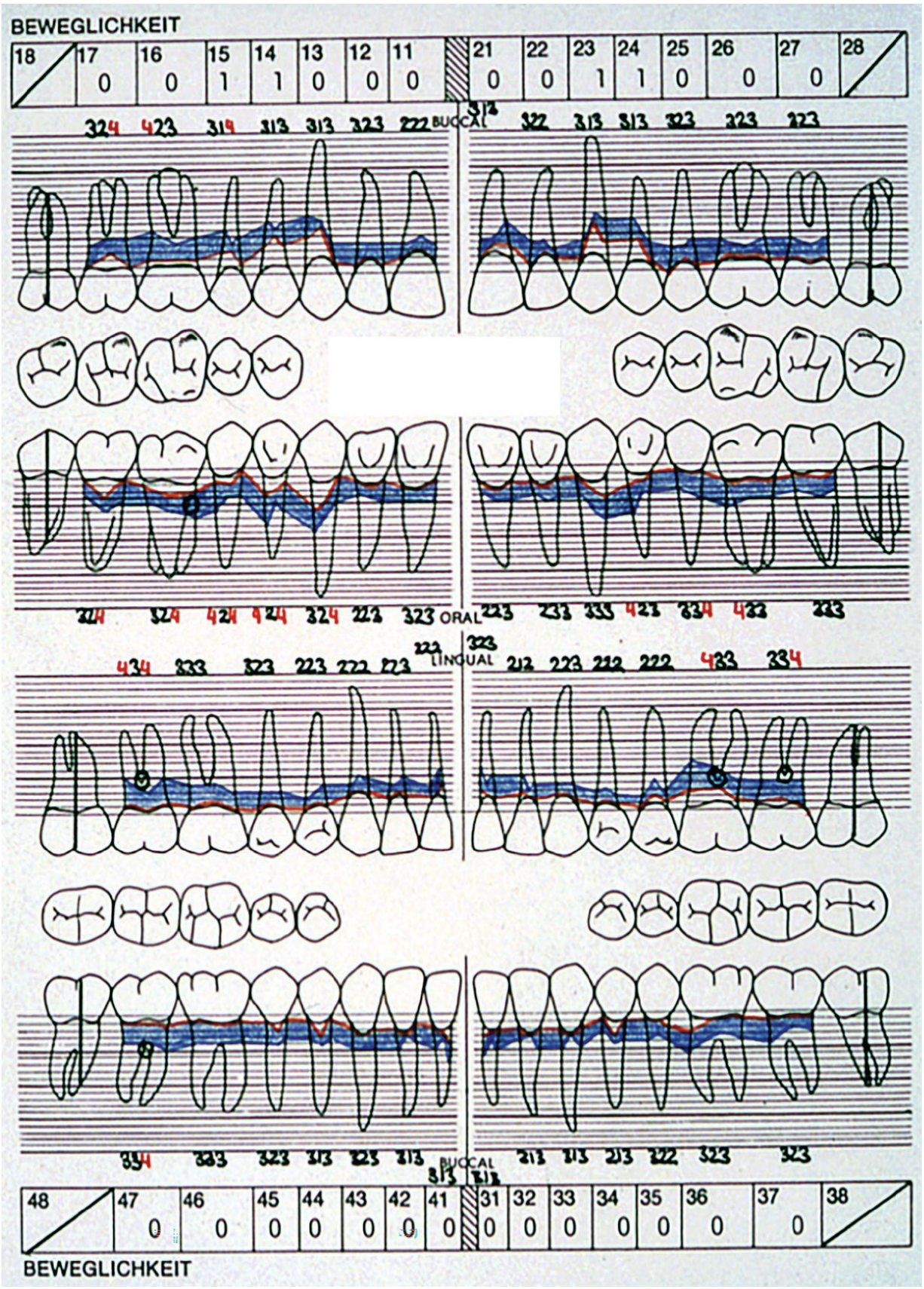


Figure 16.9 Periodontal chart at re-evaluation following periodontal surgery.

Figure 16.10 (a–c) Clinical frontal and lateral views during orthodontic therapy of the upper anterior area.

Figure 16.11 (a–c) Clinical frontal and lateral views at the final re-evaluation. In order to improve the esthetic outcome, the upper anterior teeth were restored with composite fillings.


BEWEGLICHKEIT
18 17 16 15 14 13 12 11
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0 0 1 1 0 0 0
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0 0 0 0 0 0 0
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Figure 16.12 Periodontal chart at the final re-evaluation following completion of periodontal, orthodontic, and restorative therapy.

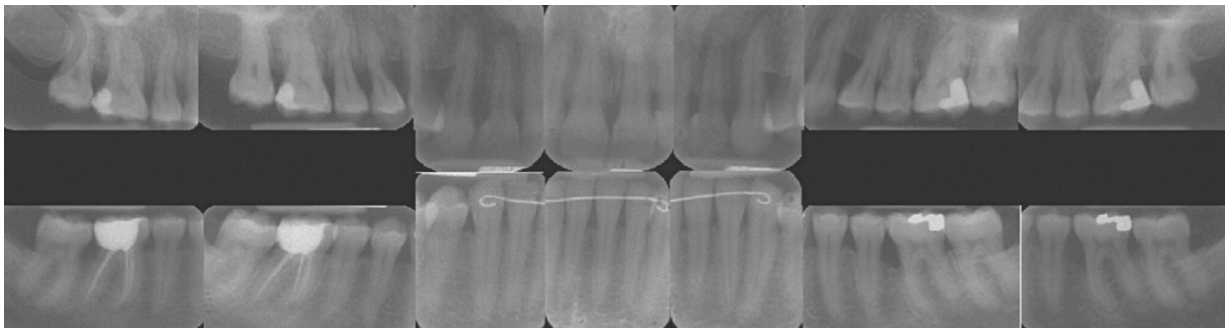


Figure 16.13 Periapical radiographic status following completion of periodontal, orthodontic, and restorative therapy.

Figure 16.14 Clinical frontal and lateral views 20 years following completion of active therapy.

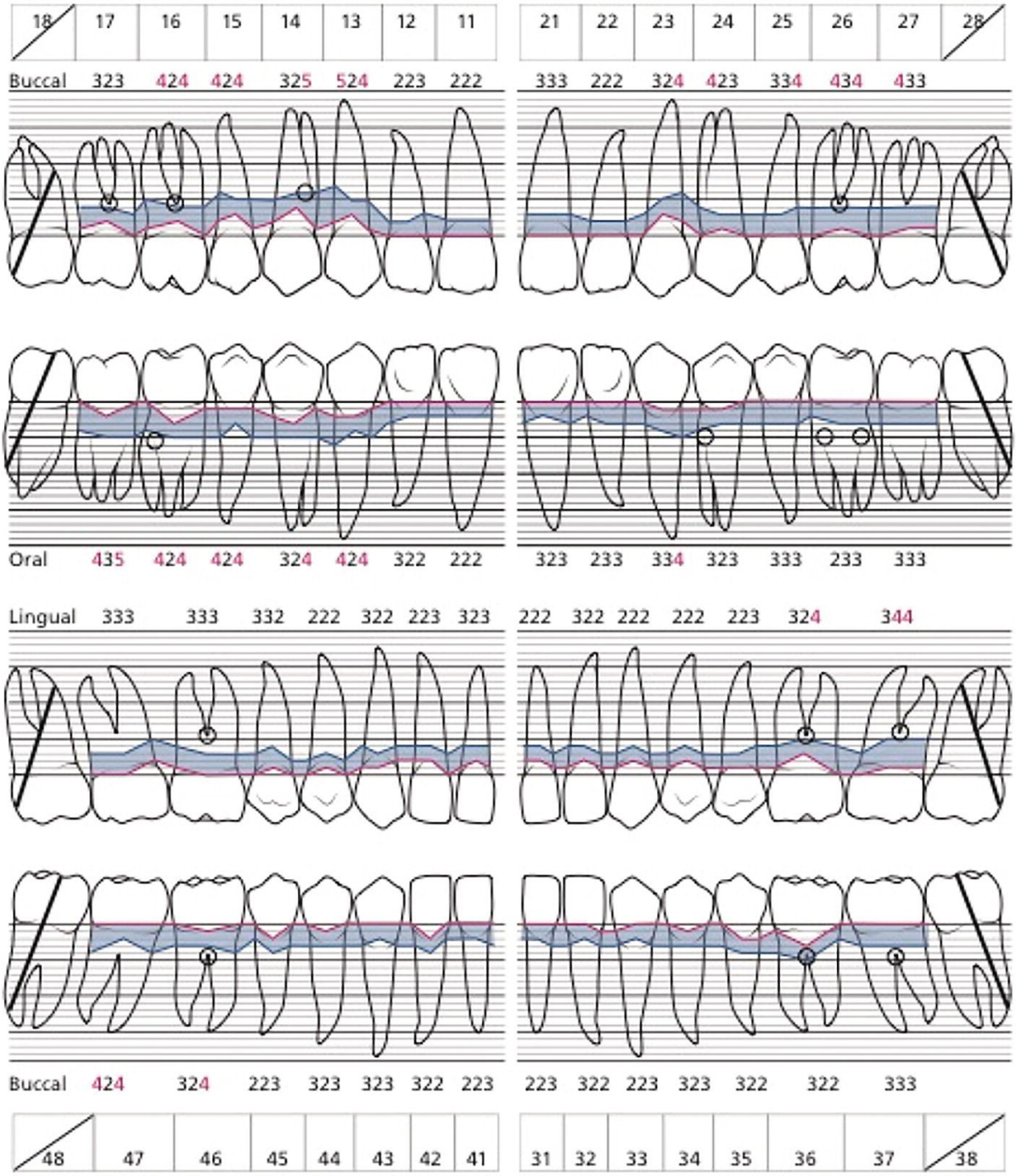


Figure 16.15 Periodontal chart 20 years following completion of active therapy.

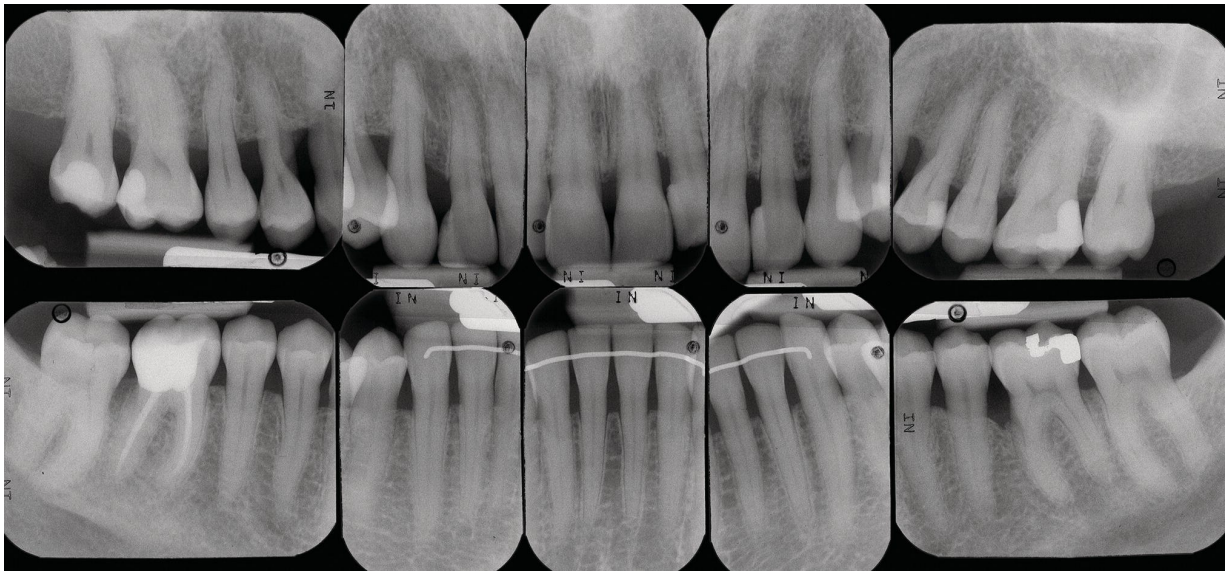
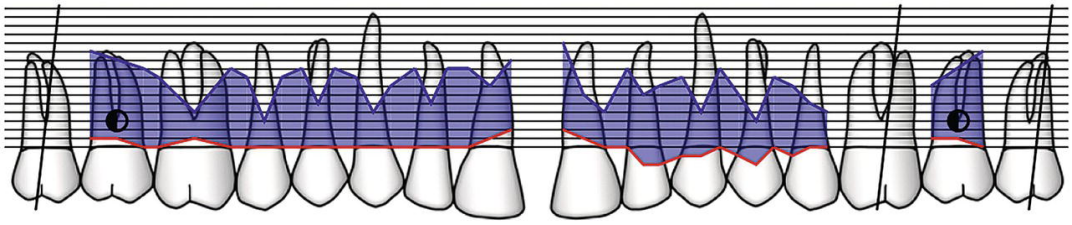


Figure 16.16 Periapical radiographic status 20 years following completion of active therapy.

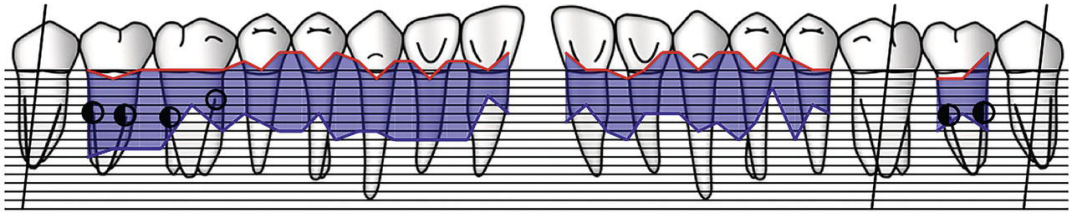
Figure 16.17 (a–d) Smile line and clinical characteristics of the patient at baseline.

	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
Beweglichkeit		2	1	0	0	0	1	1	1	1	0	0	0		2	
Implantat																
Furkation		◐													◐	
Bluten auf Sondieren		■ ■ ■	■ ■ ■	■ ■ ■	■ ■ ■	■ ■ ■	■ ■ ■	■ ■ ■	■	■ ■ ■	■ ■	■	■ ■ ■		■ ■ ■	
Plaque																
Margo Gingivae		-1 -1 0	0 -1 0	0 0 0	0 0 0	0 0 0	0 0 0	0 -1 -2	-2 -1 0	0 2 2	1 1 0	1 2 0	1 0 0		-1 -1 0	
Sondierungstiefe		10 9 9	8 3 9	8 3 8	9 5 9	8 4 7	9 5 9	9 6 8	10 5 4	9 8 9	9 5 9	7 5 8	8 5 4		6 8 11	

Bukkal



Palatinal

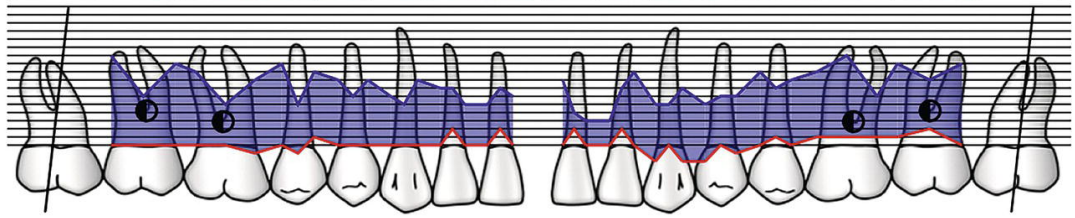


Margo Gingivae		0 -1 0	0 0 0	1 0 2	2 0 2	1 -1 1	1 -1 1	1 0 2	2 0 0	-1 0 2	2 0 2	2 0 2	1 0 0		-1 -1 2	
Sondierungstiefe		10 8 9	9 4 7	6 6 9	9 5 10	8 6 9	9 7 9	9 3 7	8 4 7	7 5 7	7 7 8	10 6 4	9 4 5		6 4 9	
Plaque																
Bluten auf Sondieren		■ ■ ■	■ ■ ■	■ ■ ■	■ ■ ■	■ ■ ■	■ ■ ■	■ ■ ■	■ ■	■ ■ ■ ■	■ ■ ■ ■	■ ■	■ ■		■ ■ ■	
Furkation	|	◐ | ◐	◐ | ○		|						|		|	◐ | ◐	|
Bemerkung				Pus	Pus			Pus	Pus			Pus			Pus	

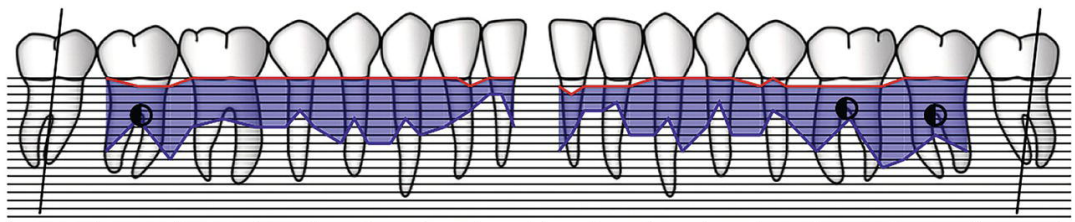
Durchschn. Sondierungstiefe = **6.8** mm Durchschn. Attachmentniveau = **-6.8** mm **0** % Plaque **88** % Bluten auf Sondieren

Bemerkung		Pus							Pus		Pus	Pus	Pus	Pus	Pus	
Furkation		◐	◐											◐	◐	
Bluten auf Sondieren		■ ■ ■	■ ■ ■	■ ■ ■	■ ■ ■	■ ■ ■	■ ■ ■	■ ■ ■	■	■	■ ■ ■	■ ■ ■	■ ■ ■	■ ■ ■	■ ■ ■	
Plaque																
Margo Gingivae		0 0 0	0 0 1	0 1 -1	0 0 0	0 0 0	0 -2 0	0 -2 0	0 -2 0	0 -2 0	2 0 2	2 0 1	0 -1 0	-1 -1 -1	-1 -2 0	
Sondierungstiefe		11 6 10	9 5 9	10 6 8	8 6 8	6 5 8	7 5 5	5 5 6	8 2 3	3 5 9	7 5 9	7 6 7	9 6 8	8 10 5	9 6 10	

Lingual



Bukkal



Margo Gingivae		0 -1 -1	0 0 0	0 0 0	0 0 0	0 0 0	0 0 -1	0 0 0	-1 -2 -1	-1 -1 -1	0 0 0	0 0 0	-1 0 -1	-1 -1 -1	0 0 0	
Sondierungstiefe		9 4 9	6 5 6	6 4 6	8 5 8	8 5 7	6 5 3	2 2 6	8 5 3	3 2 6	7 5 9	6 3 7	6 4 4	8 4 10	10 7 9	
Plaque																
Bluten auf Sondieren		■ ■ ■	■ ■ ■	■ ■	■ ■	■ ■	■ ■ ■	■	■ ■		■ ■ ■ ■	■ ■ ■ ■	■ ■ ■ ■	■ ■ ■	■ ■ ■	
Furkation		◐												◐	◐	
Implantat																
Beweglichkeit		2	1	0	0	0	0	0	0	0	0	0	0	1	2	
	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38

Figure 16.18 The baseline periodontal chart revealed generalized increased probing depths, furcation involvement, increased tooth mobility, and bleeding on probing of 88%.

Source: Department of Periodontology, University of Bern, Switzerland.

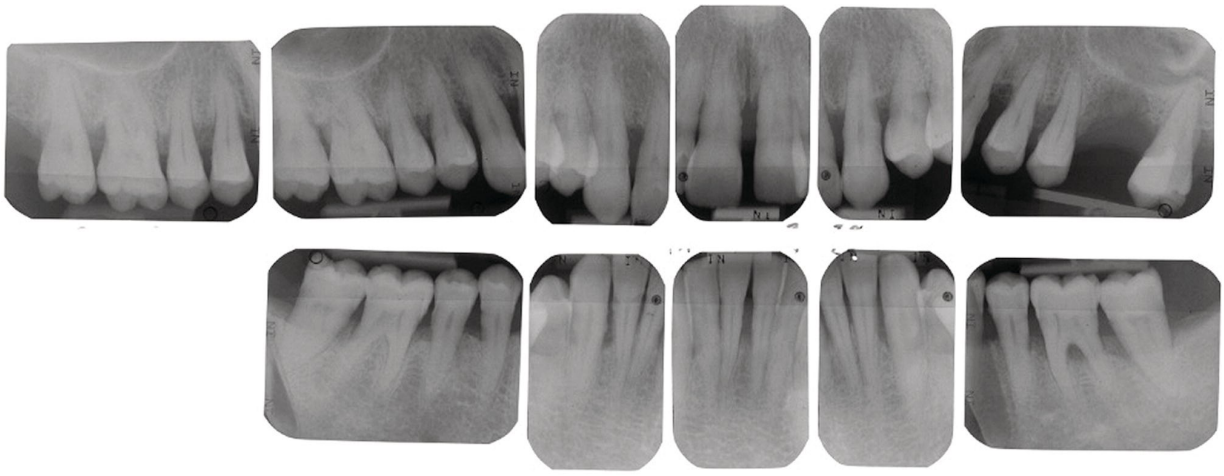


Figure 16.19 The baseline periapical radiographic status indicates generalized horizontal bone loss, localized intrabony defects at teeth 11 and 24, and radiographic evidence of furcation involvement at tooth 36. Tooth 27 has an endo-periodontal lesion without root damage (i.e. Grade 3) and a caries on the buccal surface. Subgingival calculus deposits are detectable at teeth 14, 11, 21, 23, 25, 41, and 45.

	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
Irrational to treat															x	
Doubtful		x	x	x	x	x	x	x	x	x	x	x	x			
Secure																
Secure																
Doubtful		x	x	x	x	x	x	x	x	x	x	x	x	x	x	
Irrational to treat																
		47	46	45	44	43	42	41	31	32	33	34	35	36	37	

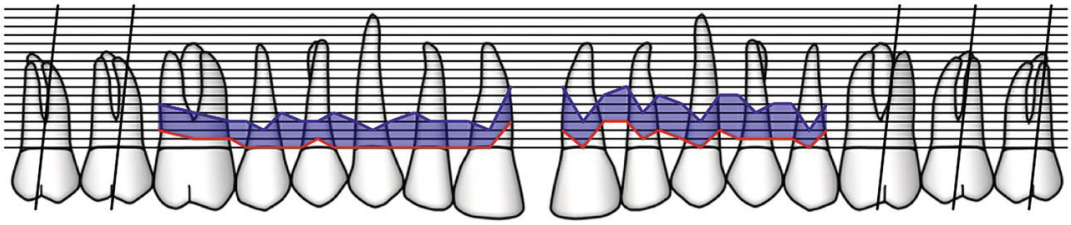
Figure 16.20 Pretherapeutic single-tooth prognosis. Assessed as Irrational to treat/Doubtful (insecure)/Secure (good).

(a) (b) (c)

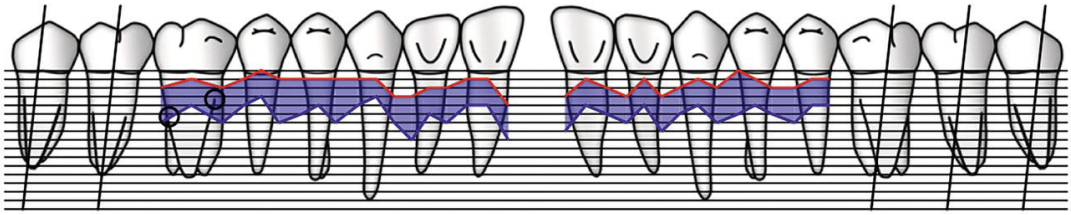
Figure 16.21 (a–c) Clinical appearance of the patient at re-evaluation following Steps 1 and 2 of periodontal therapy.

	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
Beweglichkeit			0	0	0	0	0	0	0	1	0	0	0			
Implantat																
Furkation																
Bluten auf Sondieren			■				■■		■	■						
Plaque																
Margo Gingivae			-2 -1 -1	0 0 0	0 -1 0	0 0 0	0 0 0	0 0 -3	-2 0 -3	-3 -1 -2	-1 0 -2	-1 -1 -1	-1 0 -2			
Sondierungstiefe			3 3 2	3 2 4	3 2 4	3 2 3	4 3 3	3 2 4	5 3 3	4 3 4	4 3 4	5 3 4	4 2 3			

Bukkal



Palatinal

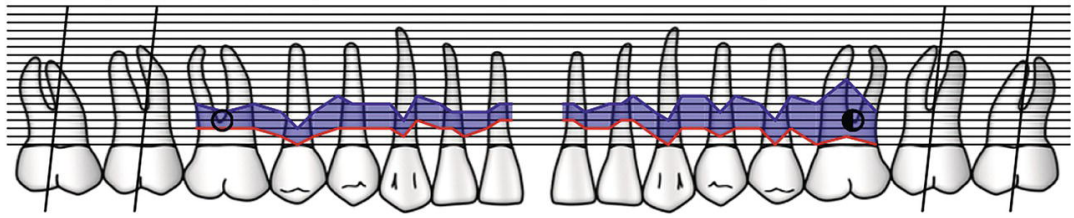


Margo Gingivae			-2 -1 -2	-1 0 -1	-1 -1 -1	-1 -1 -3	-3 -2 -2	-1 -1 -4	-3 -1 -2	-3 -1 -3	-2 -1 -2	0 -1 -2	-2 -1 -1			
Sondierungstiefe			4 3 4	3 3 5	4 3 5	3 2 3	5 3 4	3 3 4	4 3 3	3 3 4	3 3 4	5 3 3	4 3 3			
Plaque																
Bluten auf Sondieren			■		■		■■			■		■■				
Furkation	|	|	○ | ○		|						|		|	|	|
Bemerkung																

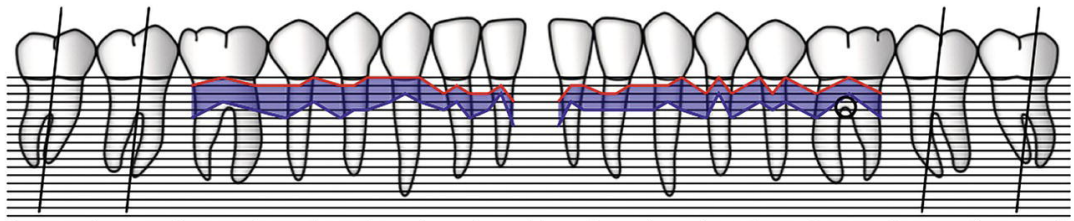
Durchschn. Sondierungstiefe = **3.1** mm Durchschn. Attachmentniveau = **-4.4** mm **0** % Plaque **14** % Bluten auf Sondieren

Bemerkung																
Furkation			○									◐				
Bluten auf Sondieren					■		■			■	■					
Plaque																
Margo Gingivae			-2 -2 -2	-1 0 -1	-2 -2 -2	-2 -1 -3	-2 -2 -1	-2 -3 -3	-3 -3 -2	-2 -3 -3	-1 0 -2	-2 -1 -2	-2 0 -2	0 -1 0		
Sondierungstiefe			3 2 3	3 2 3	4 3 3	3 2 3	3 2 3	2 2 2	2 2 2	3 2 3	3 3 4	4 3 4	3 3 4	5 7 4		

Lingual



Bukkal



Margo Gingivae			-1 0 -1	-1 -1 0	-1 -1 0	0 0 0	-2 -1 -2	-2 -1 -3	-3 -1 -1	-2 -2 -1	-1 -1 0	-2 0 -2	0 -2 0	-2 0 -2		
Sondierungstiefe			4 3 3	4 3 3	4 3 4	3 2 3	2 2 3	2 1 3	3 2 3	2 2 3	3 2 4	3 2 3	3 2 3	3 2 3		
Plaque																
Bluten auf Sondieren			■ ■									■		■		
Furkation														○		
Implantat																
Beweglichkeit			0	0	0	0	0	0	0	0	0	0	0	0		
	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38

Figure 16.22 Periodontal chart at re-evaluation following Steps 1 and 2 of the periodontal therapy.

Source: Department of Periodontology, University of Bern, Switzerland.

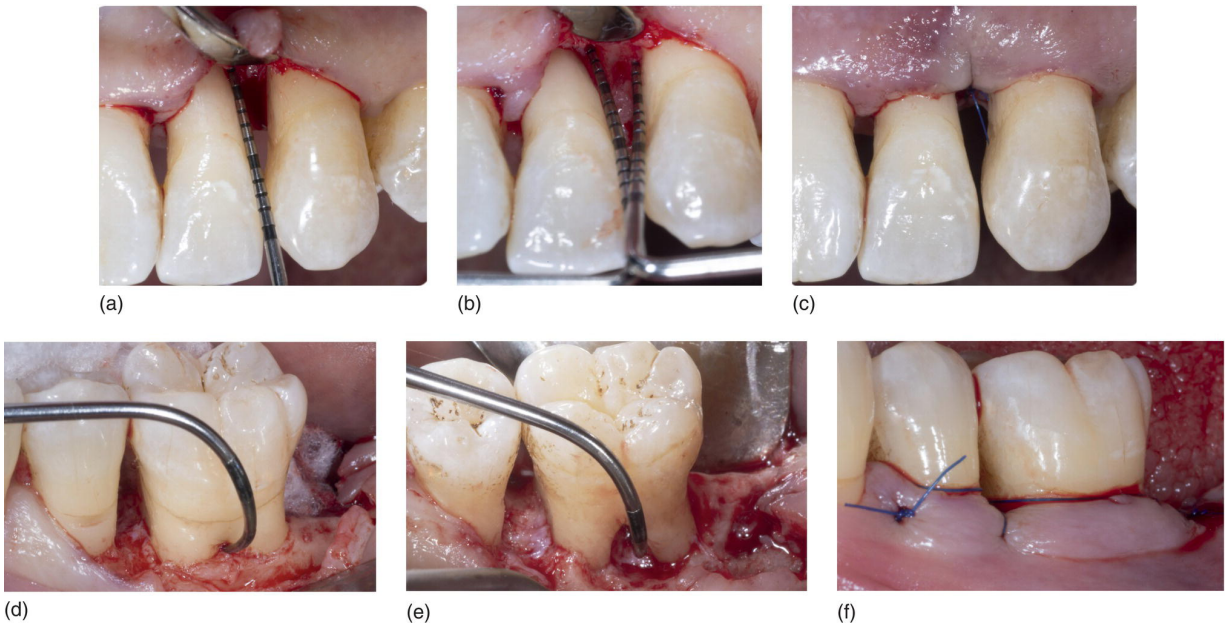


Figure 16.23 (a–f) Intrasurgical views of the maxillary and mandibular left quadrants.

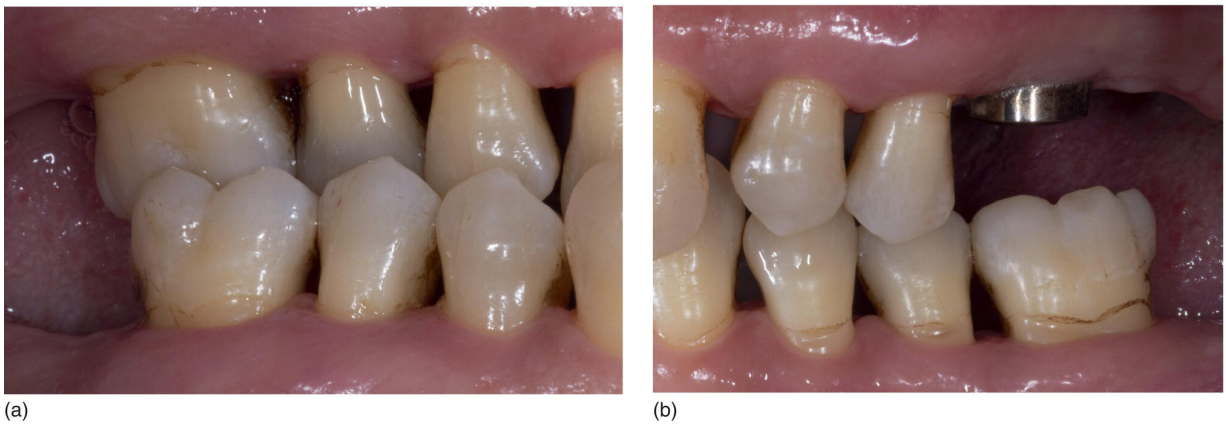


Figure 16.24 (a, b) Clinical lateral views at re-evaluation following Step 3 of periodontal therapy.

Diagnosis

This patient was diagnosed with periodontitis Stage IV Grade C with furcation involvement (Tonetti et al., 2018). In addition, tooth 27

had an endo-periodontal lesion without root damage (i.e. Grade 3; Herrera et al., 2018) and a caries on the buccal surface.

Treatment sequence

Since the patient was systemically healthy and a nonsmoker, no medical examination or smoking cessation counselling was required.

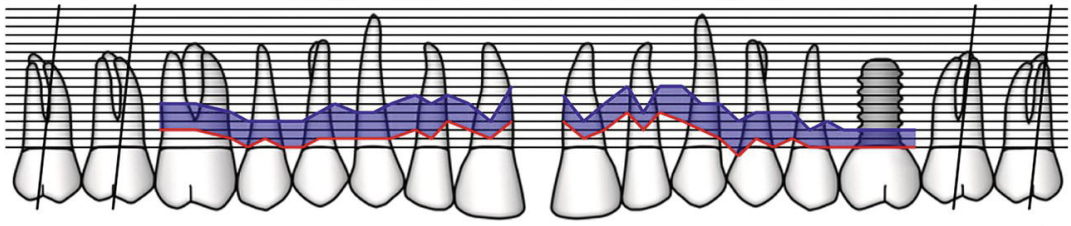
Steps 1 and 2 included patient motivation to improve oral hygiene measures and subsequent assessments and reinstructions, supra- and subgingival mechanical debridement under local anesthesia, and extraction of teeth 17, 27, 37, and 47.

Re-evaluation after nonsurgical periodontal therapy (i.e. Steps 1–2)

Following nonsurgical mechanical instrumentation without adjunctive delivery of systemic antibiotics, a re-evaluation of the patient's periodontal conditions was performed. The results of this re-evaluation pointed out the need for additional surgical interventions (i.e. Step 3). Following completion of nonsurgical periodontal therapy, the patient was enrolled in a tailored SPC program aimed at preventing the recurrence of periodontitis.

	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
Beweglichkeit			0	0	0	0	0	0	0	0	0	0	0	0		
Implantat														■		
Furkation																
Bluten auf Sondieren							■ ■									
Plaque																
Margo Gingivae			-2 -2 -1	0 -1 0	0 -1 -1	-1 -1 -1	-2 -1 -3	-2 -1 -3	-3 -1 -2	-4 -2 -4	-3 -2 -1	1 -1 0	-1 0 0	0 0 0		
Sondierungstiefe			3 3 3	3 2 3	3 3 4	3 3 4	4 4 3	3 2 4	3 2 3	3 2 3	4 3 4	4 3 4	3 2 3	2 2 2		

Bukkal



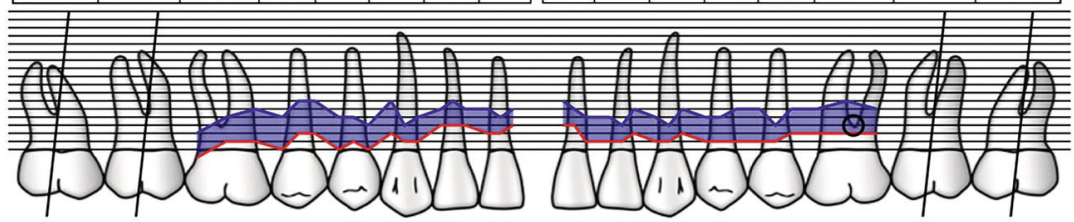
Palatinal

Margo Gingivae			0 -1 -1	0 0 -1	0 -1 0	-1 -1 -1	0 -2 -2	0 -1 -4	0 -1 -2	-4 -2 -5	-4 -2 -3	0 -1 0	-2 -1 -1	0 0 0		
Sondierungstiefe			3 3 4	4 3 4	4 3 4	4 3 4	4 3 4	3 3 3	2 2 2	3 2 3	3 3 4	4 3 3	3 2 3	3 3 4		
Plaque																
Bluten auf Sondieren					■		■ ■						■	■		
Furkation	|	|	|		|							|	|	|	|
Bemerkung																

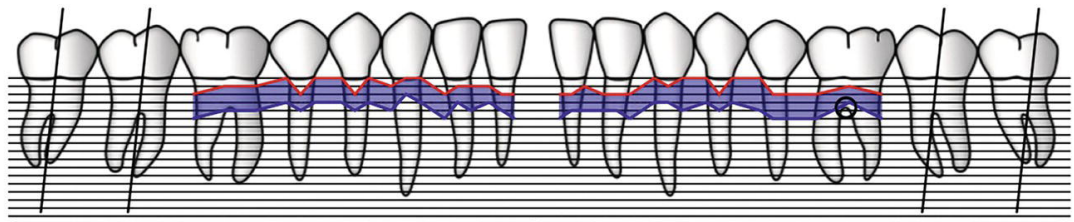
Durchschn. Sondierungstiefe = **3** mm Durchschn. Attachmentniveau = **-4.3** mm **0** % Plaque **8** % Bluten auf Sondieren

Bemerkung																
Furkation														○		
Bluten auf Sondieren			■									■				
Plaque																
Margo Gingivae			1 -1 -1	0 -2 -2	0 -1 0	-2 -1 -1	-3 -3 -3	-2 -2 -3	-3 -3 -1	-1 -1 -2	-1 -1 -2	-1 -1 -1	-1 -1 -2	-2 -2 -2		
Sondierungstiefe			3 3 4	4 4 4	4 3 3	4 2 3	2 3 2	3 2 2	3 2 3	3 2 3	3 2 3	3 3 4	4 2 3	3 4 3		

Lingual



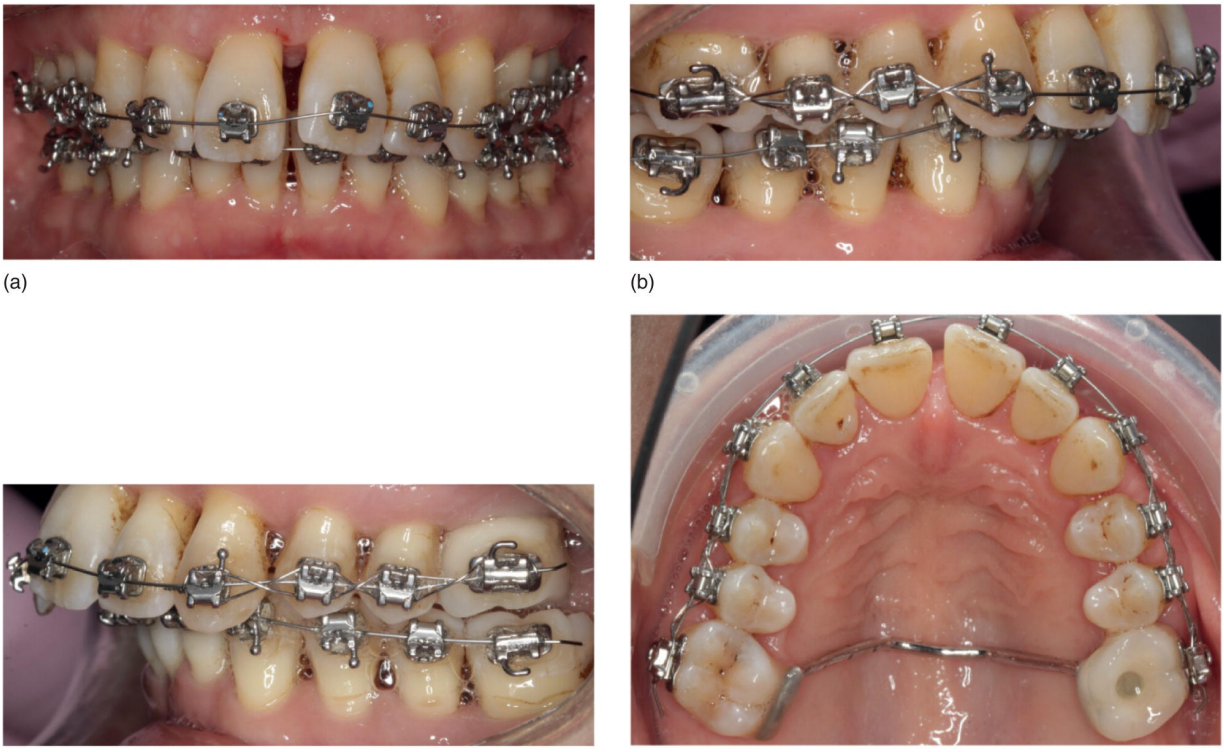
Bukkal



Margo Gingivae			-2 -1 -1	0 -2 0	0 -2 0	-1 0 0	-2 -1 -1	-1 -2 -2	-2 -2 -1	-2 -2 -2	0 -1 0	0 -2 0	0 -2 -2	-2 -1 -2		
Sondierungstiefe			3 3 3	3 2 3	3 2 3	3 2 3	3 2 3	2 2 3	3 2 3	2 2 3	3 2 4	3 2 3	4 3 3	3 2 3		
Plaque																
Bluten auf Sondieren			■				■		■							
Furkation														○		
Implantat																
Beweglichkeit			0	0	0	0	0	0	0	0	0	0	0	0		
	48	**47**	**46**	**45**	**44**	**43**	**42**	**41**	**31**	**32**	**33**	**34**	**35**	**36**	**37**	**38**

Figure 16.25 Periodontal chart at re-evaluation following periodontal surgery and implant placement (i.e. Step 3).

Source: Department of Periodontology, University of Bern, Switzerland.



(a) (b) (c) (d)

Figure 16.26 (a–d) Clinical frontal, lateral, and occlusal views during orthodontic therapy of both jaws.

(a) (b) (c)

Figure 16.27 (a–c) Clinical frontal and lateral views at the end of the orthodontic therapy.

Figure 16.28 (a–d) Smile line and clinical characteristics of the patient at the final re-evaluation following completion of periodontal, orthodontic, and restorative therapy.

Additional surgical therapy (i.e. Step 3)

Following assessment of the patient's optimal full-mouth plaque and BoP scores (i.e. 7% and 14%, respectively; Lindhe and Nyman 1975), Step 3 of therapy was carried out, including surgical interventions by means of open-flap debridement with bone recontouring in the maxillary left as well as in the mandibular left molar region. At the end of the healing phase following periodontal surgery, a dental implant was placed in region 26 after internal sinus lift floor elevation. A re-evaluation including a periodontal chart was performed.

Orthodontic treatment

Orthodontic therapy by means of fixed appliances was performed in the upper anterior area using the implant placed in region 26 as skeletal anchorage. Treatment goals were tooth mispositioning

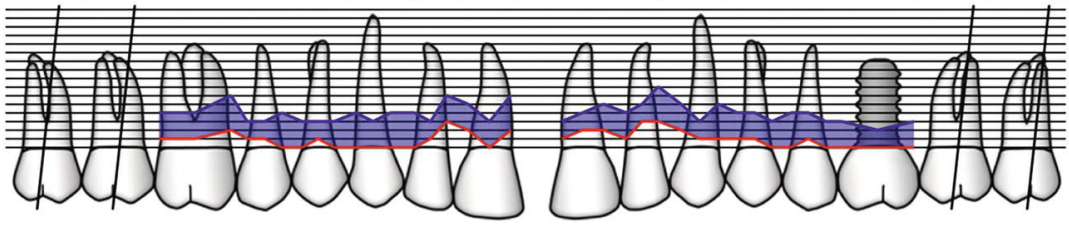
correction, overjet reduction, creation of the interproximal contact points, and improvement of the esthetic appearance.

Acknowledgments

The authors thank Dr. med. dent. Manuel Tacchi for performing the orthodontic treatment in these cases.

	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
Beweglichkeit			0	0	0	0	0	0	0	0	0	0	0	0		
Implantat														■		
Furkation																
Bluten auf Sondieren							■	■	■	■						
Plaque																
Margo Gingivae			-1 -1 -2	-1 -1 0	0 -1 0	0 0 0	0 -1 -3	-2 0 -2	-1 -2 -2	-1 -3 -3	-2 -1 -1	-1 -1 0	0 -1 0	0 0 0		
Sondierungstiefe			3 3 4	2 2 4	3 2 3	4 3 4	4 2 3	3 3 4	2 2 3	3 2 4	3 2 4	3 3 3	4 3 3	3 2 3		

Bukkal



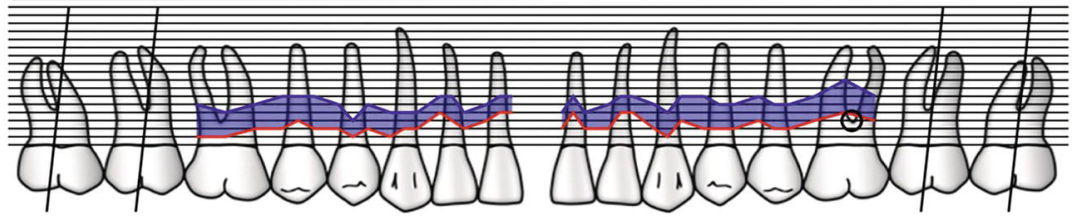
Palatinal

Margo Gingivae			-1 -1 -1	-2 -2 -2	-2 -1 -1	-1 -2 -1	0 -2 -4	-1 -2 -3	-2 -2 0	-4 -2 -4	-3 0 -2	0 0 -1	0 -1 0	0 0 0		
Sondierungstiefe			4 4 4	3 2 3	2 3 4	4 4 4	3 4 3	3 3 3	4 3 3	4 3 3	3 4 3	3 3 3	3 3 3	3 2 2		
Plaque																
Bluten auf Sondieren			■		■		■	■						■		
Furkation			○ ○													
Bemerkung																

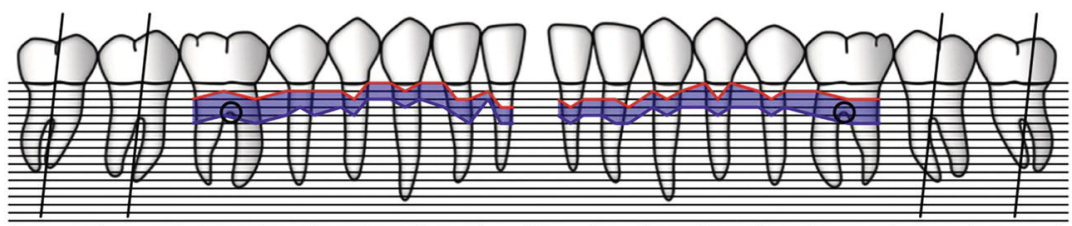
Durchschn. Sondierungstiefe = **2.8** mm Durchschn. Attachmentniveau = **-4.4** mm **0** % Plaque **10** % Bluten auf Sondieren

Bemerkung																
Furkation														○		
Bluten auf Sondieren							■							■		
Plaque																
Margo Gingivae			-1 -1 -2	-2 -3 -2	-2 -1 -2	-1 -2 -2	-4 -3 -2	-3 -4 -4	-2 -4 -2	-2 -4 -4	-2 -1 -3	-2 -2 -2	-3 -2 -2	-3 -4 -3		
Sondierungstiefe			4 3 3	4 3 4	3 2 3	3 2 2	2 3 2	2 2 2	2 2 2	3 2 2	3 3 3	4 3 3	3 3 3	3 4 3		

Lingual



Bukkal



Margo Gingivae			-2 -1 -2	-1 -1 -1	-1 -2 0	0 -1 0	0 -2 -2	-1 -3 -3	-2 -3 -2	-2 -2 -3	-1 -2 -1	0 -2 0	-1 -2 -1	-1 -2 -2		
Sondierungstiefe			3 3 3	3 2 3	2 2 2	2 2 2	3 2 3	1 2 2	2 2 2	2 3 2	2 2 2	3 2 3	2 2 2	3 3 3		
Plaque																
Bluten auf Sondieren			■			■							■			
Furkation			○											○		
Implantat																
Beweglichkeit			0	0	0	0	0	0	0	0	0	0	0	0		
	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38

Figure 16.29 Periodontal chart at the final re-evaluation following completion of periodontal, orthodontic, and restorative therapy.

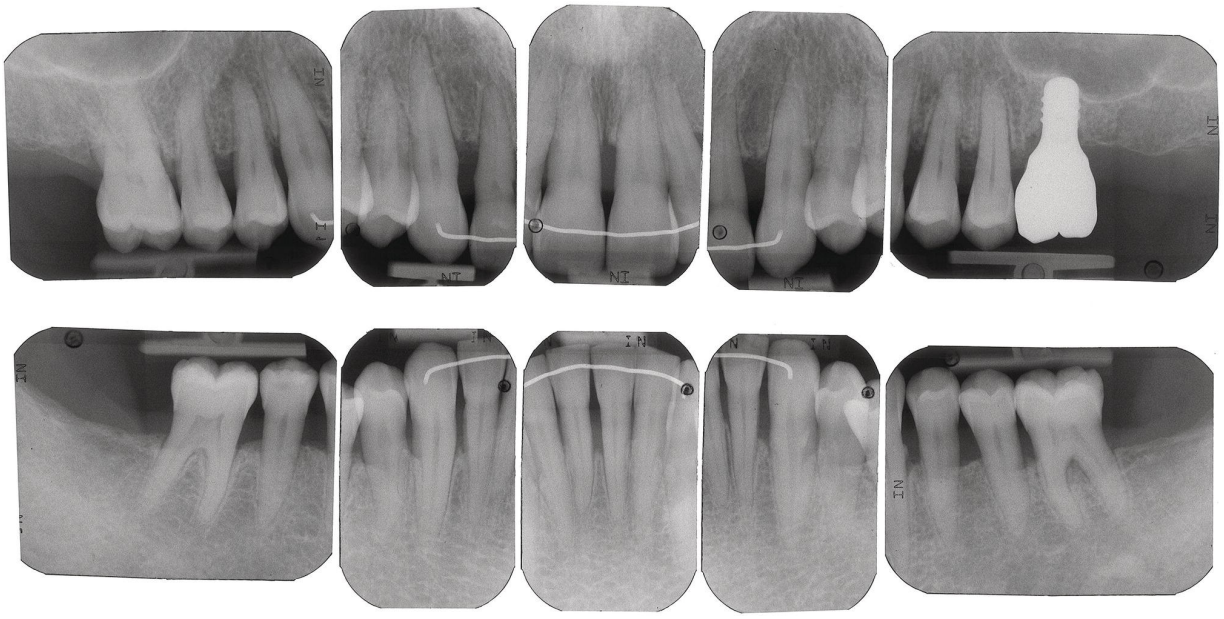


Figure 16.30 Periapical radiographic status following completion of periodontal, orthodontic, and restorative therapy.

References

Axelsson, P., Nyström, B., and Lindhe, J. (2004). The long-term effect of a plaque control program on tooth mortality, caries and periodontal disease in adults. Results after 30 years of maintenance. *Journal of Clinical Periodontology* 31: 749–757.

Bergenholtz, G., and Nyman, S. (1984). Endodontic complications following periodontal and prosthetic treatment of patients with advanced periodontal disease. *Journal of Periodontology* 55: 63–68.

Brunsvold, M.A., Nair, P., and Oates, T.W., Jr. (1999). Chief complaints of patients seeking treatment for periodontitis. *Journal of the American Dental Association* 130(3): 359–364.

Costa, M.R., Silverio, K.G., Rossa, C.J. et al. (2004). Periodontal conditions of teeth presenting pathologic migration. *Brazilian Oral Research* 18(4): 301–305.

Demetriou, N., Tsami-Pandi, A., and Parashis, A. (1991). [Is it possible for periodontal patients to recognize periodontal disease]. *Stomatologia (Athenai)* 47: 284–295.

Ericsson, I., and Thilander, B. (1978). Orthodontic forces and recurrence of periodontal disease. An experimental study in the dog. *American Journal of Orthodontics* 74(1): 41–50.

Herrera, D., Retamal-Valdes, B., Alonso, B. et al. (2018). Acute periodontal lesions (periodontal abscesses and necrotizing periodontal diseases) and endo-periodontal lesions. *Journal of Periodontology* 89(Suppl 1): S85–S102.

Kinane, D.F., Peterson, M., and Stathoupoulou, P.G. (2006). Environmental and other modifying factors of the periodontal diseases. *Periodontology 2000* 40: 107–119.

Kloukos, D., Roccuzzo, A., Stähli, A. et al. (2022). Effect of combined periodontal and orthodontic treatment of tilted molars and of teeth with intra-bony and furcation defects in stage-IV periodontitis patients: A systematic review. *Journal of Clinical Periodontology* 49(Suppl 24): 121–148.

Lang, N.P., Pjetursson, B.E., Tan, K. et al. (2004). A systematic review of the survival and complication rates of fixed partial dentures (FPDs) after an observation period of at least 5 years. II. Combined tooth-implant supported FPDs. *Clinical Oral Implants Research* 15: 643–653.

Leonardi Dutra, K., Haas, L., Porporatti, A.L. et al. (2016). Diagnostic accuracy of cone-beam computed tomography and conventional radiography on apical periodontitis: A systematic review and meta-analysis. *Journal of Endodontics* 42(3): 356–364.

Lindhe, J., and Nyman, S. (1975). The effect of plaque control and surgical pocket elimination on the establishment and maintenance of periodontal health. A longitudinal study of periodontal therapy in cases of advanced disease. *Journal of Clinical Periodontology* 2: 67–79.

Lulic, M., Brägger, U., Lang, N.P. et al. (2007). Ante's (1926) law revisited. A systematic review on survival rates and complications of fixed dental prostheses (FDPs) on severely reduced periodontal tissue support. *Clinical Oral Implants Research Suppl* 3: 63–72.

Martinez-Canut, P., Carrasquer, A., Magan, R. et al. (1997). A study on factors associated with pathologic tooth migration. *Journal of Clinical Periodontology* 24(7): 492–497.

Matuliene, G., Pjetursson, B.E., Salvi, G.E. et al. (2008). Influence of residual pockets on progression of periodontitis and tooth loss: Results after 11 years of maintenance. *Journal of Clinical Periodontology* 35: 685–695.

Polson, A., Caton, J., Polson, A.P. et al. (1984). Periodontal response after tooth movement into intrabony defects. *Journal of Periodontology* 55(4): 197–202.

Proffit, W.R. (1978). Equilibrium theory revisited: Factors influencing position of the teeth. *Angle Orthodontist* 48(3): 175–186.

Rathod, S.R., Kolte, A.P., and Chintawar, S. (2013). The dynamic relationship between pathological migrating teeth and periodontal disease. *Journal of the Indian Society of Periodontology* 17(6): 762–764.

Salvi, G.E., Mischler, D.C., Schmidlin, K. et al. (2014). Risk factors associated with the longevity of multi-rooted teeth. Long-term outcomes after active and supportive periodontal therapy. *Journal of Clinical Periodontology* 41: 701–707.

Sanz, M., Herrera, D., Kebschull, M. et al. (2020). Treatment of stage I–III periodontitis: The EFP S3 level clinical practice guideline. *Journal of Clinical Periodontology* 47(Suppl 22): 4–60.

Tonetti, M.S., Greenwell, H., and Kornman, K.S. (2018). Staging and grading of periodontitis: Framework and proposal of a new classification and case definition. *Journal of Clinical Periodontology* 45(Suppl 20): S149–S161.

Towfighi, P.P., Brunsvold, M.A., Storey, A.T. et al. (1997). Pathologic migration of anterior teeth in patients with moderate to severe periodontitis. *Journal of Periodontology* 68(10): 967–972.

Updegrave, W.J. (1951). The paralleling extension-cone technique in intraoral dental radiography. *Oral Surgery, Oral Medicine, and Oral Pathology* 4: 1250–1261.

Zasčiurinskienė, E., Lund, H., Lindsten, R. et al. (2019). Outcome of periodontal-orthodontic treatment in subjects with periodontal disease. Part II: A CBCT study of alveolar bone level changes. *European Journal of Orthodontics* 41(6): 565–574.

17

The Restorative Dentist and Orthodontist: Orthodontic Implications of Dental Caries, Tooth Fracture, Exposed Dental Pulp, and Esthetic Improvements

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Summary

For the past 15–20 years, social scientists and observers of contemporary life have been commenting on the dramatic change in the way business is done in both the public and private sectors. The change that has attracted so much attention and commentary is a significant increase in teamwork and collaborative efforts: people with different views and perspectives are coming together, putting aside their narrow self-interests, and discussing issues openly and supportively to solve a larger problem or achieve a broader goal. Teams come together for several different reasons, but their goals are the same – to achieve peak performance and experience success. We as dental specialists share the same goal. We want to have happy and satisfied patients with acceptable, even better, facial and dental esthetics, with healthy, functional, and stable occlusions. In a beauty-addicted society where a good smile is a powerful weapon, the demand for orthodontic treatment is increasingly rising, and in challenging situations input from a number of dental disciplines is required to construct detailed treatment plans. This chapter comprises a comprehensive review of topics requiring interactive cooperation or teamwork between the orthodontist, endodontist, pediatric dentist, and restorative dentistry specialist. Topics such as the key points affecting the orthodontic treatment plan and the healthy prognosis of the dentition will be discussed in detail, including caries risk assessment considering demineralization around orthodontic attachments, pulpal reactions, root resorption and invasive cervical resorption, and special considerations about dental trauma. The chapter also covers restorative esthetic touch-ups after the orthodontic treatment.

Primum non nocere.

(Hipoccrates, c.460–c.377 BCE)

An increase in desire for improved facial esthetics and dental appearance is the key motivating factor for orthodontic treatment in every population. These appearance-conscious patients and/or their

families request esthetic treatment plans that usually require a comprehensive interactive approach. Coordinated orthodontic, endodontic, and restorative treatments, with careful consideration of patients' and their families' expectations and requests, are critical for successful outcomes and patient satisfaction (Vitale et al., 2004). Clearly, it is the orthodontist's responsibility to take a proactive role in forming close cooperation between the disciplines to reach the ultimate goal of achieving healthy esthetics and function, while at the same time limiting undesirable consequences and risks of mechanotherapeutics.

Optimized treatment outcomes necessitate close collaboration between the disciplines to evaluate, diagnose, and resolve problems at the following stages of the treatment life cycle:

- Pretreatment evaluation of prognostic factors and the early stages of the orthodontic treatment.
- Orthodontic treatment.
- Emergency orthodontic treatment in trauma cases.
- Immediate postorthodontic period.
- Restorative and/or esthetic touch-ups.

This chapter reviews and summarizes the need for and benefit of interactions between orthodontists, endodontists, pediatric dentists, and/or restorative dentistry specialists according to these stages of orthodontic treatment.

Pretreatment evaluation and early stages of the orthodontic treatment

Successful orthodontic therapy relies on the accurate assessment of the pretreatment dental and gingival health status with the aid of other dental disciplines. The assessment should include a determination of systemic and/or local factors and obtaining a detailed history of previous trauma to the oral tissues. The initial clinical examination should precede basic radiographic evaluation, which will help the clinician to decide on precautions to minimize the

undesirable effects of orthodontic mechanics. It should not be forgotten that every patient is unique and demands and merits a unique treatment plan customized for his or her specific needs.

Initial caries risk assessment: Can the dental team tailor an interdisciplinary approach to end up with a healthy smile?

The orthodontist should take a proactive role throughout the treatment, not only from his or her own perspective, but also from that of the other disciplines, making sure to achieve a healthy, functional, and esthetic smile. The possibility of an increased incidence of caries (i.e. the number of new cavitated or incipient lesions) during a certain time period like orthodontic treatment, or the likelihood of a change in the size or activity of lesions already present, is determined by caries-risk assessment (CRA; American Academy of Pediatric Dentistry, 2021). Being able to forecast whether new carious lesions may appear in the future will help orthodontists make better decisions, especially when it comes to preventive interventions. It will also help the clinician construct personalized treatment and preventive strategies that are tailored to the needs of each patient. Furthermore, CRA approaches could be employed as an effective health education tool to improve patients‘, parents’, and caregivers’ attitudes and actions toward maintaining excellent oral hygiene and nutritional habits (Bratthall and Petersson, 2005). This is especially important for patients who are receiving orthodontic treatment. Various CRA models have been presented over the years (Twetman and Fontana, 2009). These models vary in many aspects, from the age group to which they can be applied to the risk and protective factors that they include.

The CRA tools basically work on a reasoning-based model (CAT, CAMBRA, and ADA model) or an algorithm-driven model (Cariogram, NUS-CRA, and PreViser). In the first group the clinician takes a brief history and matches that with intraoral findings, then correlates this knowledge with the CRA model’s criteria. In the algorithm-driven model, computer-assisted work is done.

Caries Risk Assessment Tool (CAT)

The CAT, from the American Academy of Pediatric Dentistry (AAPD) for patients ≥6 years old, is utilized by answering the following with yes or no:

- *Risk factors (social/biological)*: poverty, low health literacy, frequent exposure (>3 times/day) to between-meal sugar-containing snacks, being a recent immigrant, a patient with special healthcare needs.
- *Protective factors*: optimally fluoridated drinking, fluoridated toothpaste, topical toothpaste, topical fluoride, the patient has dental home/regular dental care.
- *Clinical findings*: ≥1 interproximal caries lesions, active noncavitated (white spot) caries lesions or enamel defects, low salivary flow, defective restorations, patient wears an intraoral appliance.

Caries Risk Management by Risk Assessment (CAMBRA)

The CAMBRA philosophy was developed in California and has been used for 14 years in the teaching clinics of the School of Dentistry at the University of California San Francisco (UCSF). The items used in the caries risk assessment for patients aged 6 years through adult were grouped into the following:

- *Disease indicators (clinical observations*): aproximal caries on the radiograph, past caries experience –3 years – and white spot lesions.
- *Biological risk factors (expanded to pathological factors)*: visible plaque, snack habits, saliva deficiencies, reactional drug use.
- *Protective factors*: fluoridated toothpaste/mouthrinse use, fluoridated community.

Accordingly, low, moderate, high, and extreme risk levels are assigned. Extreme is defined as a combination of high risk and

hyposalivation, as determined by visual inspection, medical history, and, if in question, salivary flow rate testing.

American Dental Association (ADA)

- *Contributing conditions*:
  - Fluoride exposure.
  - Sugary foods or drinks.
  - Caries experience of mother, caregiver, and/or other siblings (no carious lesions in last 24 months, carious lesions in last 7–23 months, carious lesions in last 6 months).
  - Dental home: receiving regular dental care in a dental office.
- *General health conditions*:
  - Special healthcare needs (developmental, physical, medical, or mental disabilities that prevent or limit the performance of adequate oral healthcare by patient or caregivers).
  - Chemo/radiation therapy.
  - Eating disorders.
  - Medications that reduce salivary flow.
  - Drug/alcohol abuse.
- *Clinical considerations*:
  - Cavitated or noncavitated carious lesions or restorations, visually or radiographically evident (last 36 months considered).
  - Teeth missing due to caries (in past 36 months).
  - Visible plaque.
  - Unusual tooth morphology that compromises oral hygiene.
  - Interproximal restorations – 1 or more.
  - Exposed root surfaces present.
  - Restorations with overhangs and/or open margins; open contacts with food impaction.

- Dental/orthodontic appliances (fixed or removable).
- Severe dry mouth (xerostomia).

Cariogram

Cariogram is an interactive computer program, first developed by Bratthall in 1996 and further refined in 1997 for better understanding of the multifactorial nature of dental caries. It illustrates the "caries risk" and possible interactions between caries-related factors (Bratthall 1996). The patient is examined and data are obtained for various parameters that are directly associated to caries, as bacteria, nutrition, and susceptibility. The computer program assigns a score to each factor/variable based on a specified scale. It generates a pie diagram with bacteria in the red sector, diet in the dark blue sector, and susceptibility-related factors in the light blue sector, according to its built-in formula. Furthermore, some situations are depicted as a yellow sector. The four sectors divide their shares, leaving a green sector that reflects the possibility of preventing caries. The software is available on both Android and IOS platforms for purchasing (Singh et al., 2018: 26–31).

National University of Singapore Caries Risk Assessment Tool (NUS-CRAT)

Similar to the Cariogram, the NUS-CRAT classifies children's caries risk into five risk levels and is expressed as "chance (%) to avoid caries." NUS-CRAT considers 11 risk factors (6 items in the community-screening version) and the risk level is program generated based on a predetermined algorithm. The evaluated risk factors include ethnicity, family socioeconomic status, infant feeding history, diet, fluoride, dental attendance, oral hygiene, past caries, systemic health, and *Mutans streptococci* and *Lactobacilli* (Christian et al., 2019).

Effectiveness of caries risk assessment models

A recent systematic review concluded that the evidence for the effectiveness of existing CRA models in assessing and predicting caries lesions is limited (Cagetti et al., 2018); even though Cariogram was used in a few high-quality studies in children and adults, there is

insufficient evidence to conclude that the method is effective in caries assessment and prediction. Other CRA models, such as CAT, CAMBRA, NUS-CRAT, and PreViser, may be effective in clinical settings; however, there is limited scientific evidence to date. Christian et al. (2019) systemically compared several CRA models including CAMBRA, Cariogram, AAPD, and a few more for patients aged <6 years. Due to the results of this review, only the NUS-CRAT received a high degree of evidence for criterion validity and responsiveness, as well as individual sensitivity and specificity values of at least 75% and 85%, respectively. The limited evidence for CRA tools was mentioned by Twetwan (2016), who underlined that there is no clearly superior method for predicting future caries and no evidence to support the use of one model, program, or technology over any other. On the other hand, the article concluded that multivariate models display better accuracy than the use of single predictors and this is especially true for preschool children. Twetman (2016) emphasized the fact that there is a great need for methods that more accurately reflect the activity in the biofilm.

With all this in mind, the authors recommend the following in order to increase CRA tool effectiveness (Cagetti et al., 2018):

- A caries risk assessment should be carried out at the patient's first dental visit and reassessments should be done during treatment.
- The risk category should be linked to appropriate preventive care, with recall intervals based on individual need.
- In preschool children CRA tools including socioeconomic and sociodemographic information, baseline caries, and etiological factors resulted in moderate/good accuracy, with sensitivity >80% and specificity >70% (Mejàre et al., 2014). In general, similar models were less accurate in school children and adolescents, who are the vast majority of orthodontic patients.

Indicators of past dental caries experience remain the strongest predictors of risk of dental caries among school children and older adult populations. In addition, dental caries in the primary teeth are a strong predictor of future dental caries experience (Swedish Council on Technology Assessment in Health Care, 2008). If an

orthodontic patient has an active lesion or treated carious teeth, this patient should receive professional preventive measures along with orthodontic therapy.

When the limited evidence regarding the effectiveness of CRA is evaluated, the adoption of CRA tools can be viewed as a tool for patient health education, as it identifies the risk variables implicated in illness onset (Cagetti et al., 2018). These tools are particularly important in patients undergoing orthodontic treatment, as the nature of the treatment may increase caries susceptibility.

In addition to evaluating the child's status, the orthodontist should also evaluate the family, which plays a great role in children's oral health. Families, as the smallest social unit with which children interact, play a critical role in shaping a child's oral health behavior (Fisher-Owens et al., 2007; Abbasoglu and Kuvvetli, 2021). The psychosocial factors of a parent are major determinants of children's oral health behavior. These factors influence a child's oral health via parent–child relationships and are also a reflection of mother–father relationships in a child's behavior. For example, the cognitive qualities of the mother, such as knowledge of healthy oral behaviors, are significantly related to a child's proclivity to establish oral hygiene routines. A recent survey conducted on 8446 families revealed that parents with higher education levels have better oral health knowledge and benefit from preventive measures such as pit and fissure sealants. Furthermore, children of higher-educated parents have better dental hygiene routines (Chen et al., 2020). Eating a lot of sweets, using the wrong brushing method, starting brushing at later ages (after the first year of life), and not brushing regularly are major risk factors for early childhood caries. Emphasizing oral health knowledge to parents and guardians, using proper brushing methods, and limiting frequent sweets intake are all important factors in the prevention of dental caries (Sun et al., 2017).

Nonrestorative or minimally invasive approaches and fighting cavities for good

The notion of active surveillance (prevention therapies and close monitoring) of enamel lesions is based on the idea that treatment of

disease is only necessary if it progresses, and that caries can be stopped without therapy.

Minimal-intervention dentistry is a holistic approach to caries care that combines caries lesion control with minimal surgical intervention. Tissue preservation is the major goal, which includes early caries identification and nonoperative therapy, as well as minimally invasive restorative methods (Frencken et al., 2012; Machiulskiene et al., 2020). The following are short descriptions of noninvasive or minimally invasive approaches that can be performed easily during orthodontic treatment. One should keep in mind that for clinical success, all of these techniques should be combined with good oral hygiene and proper diet, as well as sugar intake restriction.

Nonrestorative/nonoperative cavity treatment

This approach makes the cavitated caries lesions accessible to tooth cleaning by removal of overhanging enamel margins (Machiulskiene et al., 2020).

Silver diamine application

Silver diamine fluoride (SDF; 38%) is a clear liquid that contains a high concentration of fluoride ions (44,800 ppm) and combines the antibacterial effects of silver with the remineralizing effects of fluoride (Crystal and Niederman, 2019). SDF is employed as a promoter of the arrest and remineralization of active carious lesions, but it stains teeth black. The clinician should inform the patient that this discoloration is permanent (Horst et al. 2016). SDF is also effective for arresting active dentinal lesions and for teeth with exposed root surfaces that cause dentinal hypersensitivity, and may also be beneficial for permanent molar teeth with molar–incisor hypomineralization (MIH), since plugging the dentinal tubules may lessen sensitivity. As for safety, one drop of SDF contains 2.24 mg of fluoride (a typical dose of 5% fluoride varnish contains 11.3 mg fluoride). Thus, it is considered that biannual application of dental fluorides should not be a risk in children (Seifo et al., 2020; Figure 17.1).

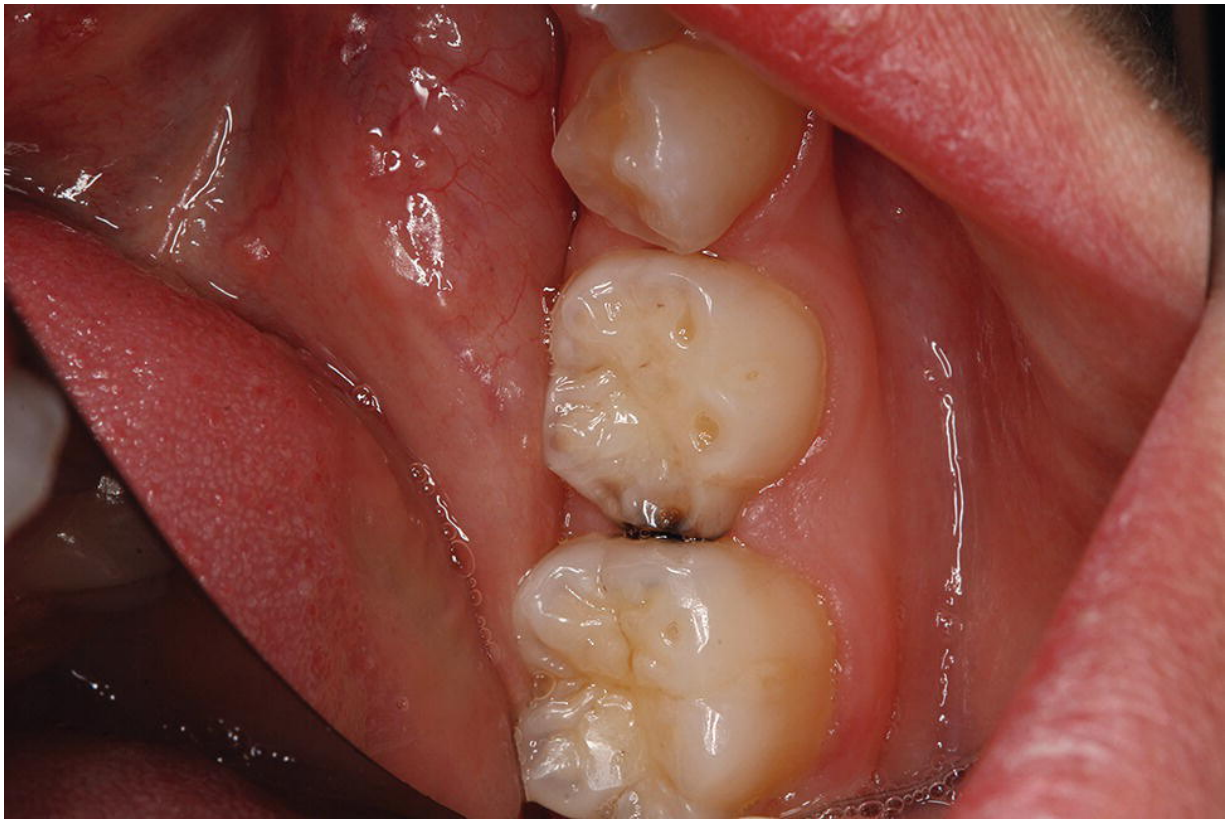


Figure 17.1 Silver diamine fluoride application on the distal surface of the second primary molar.

Atraumatic restorative treatment

Atraumatic restorative treatment is a caries management approach that uses hand instruments for opening caries cavities and removing decomposed carious dentine, followed by restoration with a high-viscosity glass ionomer. The technique can be tooth saving in small children and class I lesions.

Ultraconservative caries therapy

Ultraconservative caries therapy describes the approach of bonded and sealed restorations placed directly over frank cavitated carious lesions extending into dentine (Machiulskiene et al., 2020).

Evaluation of the prognostic factors of the existing dentition

The decision of whether or not to extract tooth/teeth is an important step in designing concrete orthodontic treatment procedures. If the orthodontist judges a case as one requiring extraction, the next step will be the decision regarding which tooth/teeth to extract (Yagi et al., 2009). There may be multiple options and choosing one of the potential teeth requires consideration of parameters that might require a consultation with specialists from other disciplines. For example, a history of root canal treatment or the presence of periapical lesions, restorations, and carious teeth complicates the decision about the site of extraction. In such cases, the decision should be the one that optimizes the orthodontic treatment prognosis with less invasive operative intervention (Figure 17.2).

Teeth with deep or extremely deep caries: Restorative strategies

Facing teeth with deep caries lesions presents challenge to every orthodontist, leading to hesitation about incorporating this uncertain prognosis into the game plan. Cariology experts (Innes et al., 2016) and the European Society of Endodontology (ESE; European Society of Endodontology developed by:, Duncan et al., 2019) reached a consensus and clarified a distinction between deep and extremely deep caries. The ESE defined deep caries as “Caries reaching the inner quarter of dentine, but with a zone of hard or firm dentine between the caries and the pulp with a risk of pulp exposure during operative treatment” and extremely deep caries as “the carious demineralized dentine penetrating the entire thickness of the dentine, without a radiopaque zone separating the lesion from the pulp with microorganism penetrating into the critical zone of tertiary dentine including the pulp” (Bjørndal 2018). However, the diagnosis of the exact extent of the disease is challenging for many experienced orthodontists, restorative dentistry specialists, and endodontists, compromising choice of the most appropriate treatment strategy. Evaluation of the radiographic image is inevitably not sufficient to make an exact diagnosis of the proximity of the lesion to the pulp

(Bjørndal et al., 2019). Likewise, the relation between clinical symptoms and the histopathological state of the pulp has presented contradictory findings where asymptomatic teeth may have presented pulpal involvement (Iwamoto et al., 2006; Iqbal et al., 2007).

As our biological conceptualization of pulpal response to caries has evolved, management strategies have shifted from traditional invasive techniques to contemporary philosophies that aim at arresting caries progression, remineralization of caries-affected dentine by bioactive materials, and maintenance of the pulp's developmental, defensive, and proprioceptive functions in the light of minimally invasive dentistry (Smith, 2002; Edwards et al., 2021).

The decision making for a deep or extremely deep lesion mostly relies on comprehensive evaluation of the patient with a detailed history of signs and symptoms, and appropriate radiographic and clinical assessment (Allison et al., 2020). Even so, identification of reversible and irreversible pulpitis clinically has been shown to be both erratic and subjective (Villa-Chávez et al., 2013; Jespersen et al., 2014). Thus, a new classification system to judge the true repair potential of the pulp is proposed by Wolters et al. (2017). This new classification system eliminates the terms "reversible" and "irreversible," suggesting that the inflammatory process is a continuum from initial to mild, moderate, and severe inflammation. With the advent of conservative treatment options, bacterial invasion of the pulp may be prevented and severe pulpal inflammation, necrosis, root canal treatment, and even extraction may be avoided or at least postponed.

The initial step of conservative treatment of deep and extremely deep caries lesions begins from the carious tissue removal stage. The International Caries Consensus Collaboration reached a consensus that complete excavation of carious tissue to hard dentine is overtreatment and favored selective or stepwise removal techniques (Schwendicke et al., 2016).

Stepwise caries removal technique involves nonselective removal of carious tissue in two sessions. In the first session, all carious dentin is removed, including the most necrotic and contaminated dentin on the pulp wall, leaving some soft tissue nearest to the pulp, with

temporary sealing for 2–6 months to give the pulp the chance to remineralize and reduce the risk of pulpal exposure by stimulating the deposition of tertiary dentin (Maltz et al., 2012). In the second session the cavity is reopened, the softened remaining carious tissue is removed, and the final restoration is performed. However, the need for a revisit, possible failure of the temporary restoration, and the possibility of iatrogenic pulpal exposure in the second visit are the basic pitfalls of the stepwise technique (Maltz et al., 2018). To overcome these pitfalls, and as a result of debates about the temporization and reopening of the restoration, a selective caries removal technique is proposed. This technique is less invasive and utilizes nonselective removal of carious tissue from the surrounding cavity walls, allowing remineralization of the affected dentin in the pulpal wall, and restoring the tooth definitively (Maltz et al., 2018; Casagrande et al., 2017). The ultimate goal of both techniques is to reduce the bacterial load by removing the infected dentin to preserve pulp vitality (Reeves and Stanley, 1966). Thus, the dentin–pulp complex can continue reactionary and reparative dentinogenesis to reduce the likelihood of further injury (Duncan et al., 2019; European Society of Endodontology developed by:, Duncan et al., 2019).

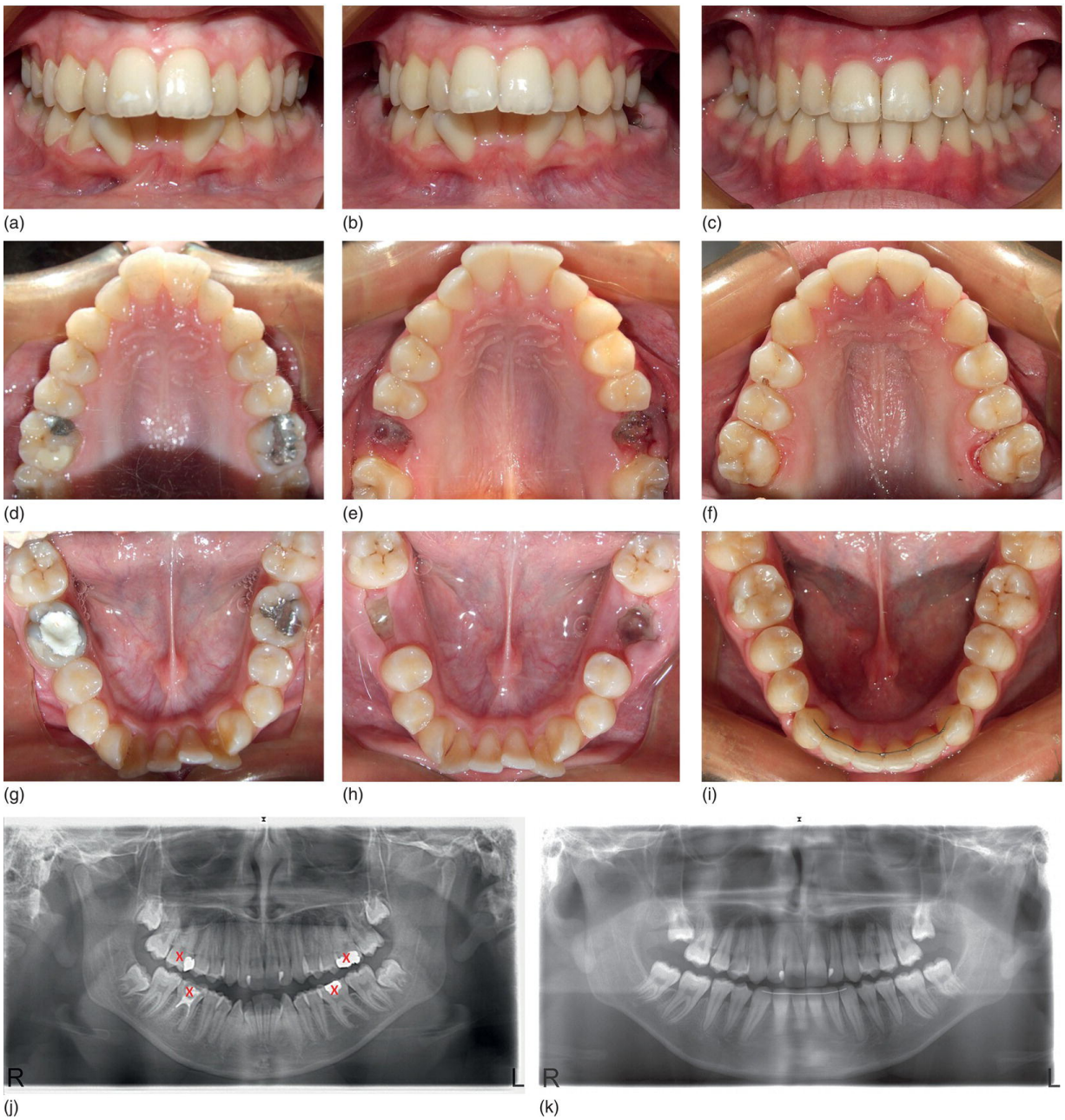


Figure 17.2 (a–j) Heavily restored four first permanent molars were extracted instead of premolars due to poor prognosis of the molar teeth in order to correct the Class II malocclusion. Crosses represent missing teeth. (k) The lower third molars erupted and replaced the second molars.

In 2019, ESE updated the definition of indirect pulp capping to "application of a biomaterial onto a thin dentine barrier in a one-stage carious-tissue removal technique generally to hard dentine"

(European Society of Endodontology developed by:, Duncan et al., 2019). The emphasis on application of a biomaterial is the backbone of vital pulp therapy, which refers to avoiding monomer and bacterial ingress stimulating dentin formation. In fact, the previous version was a “procedure in which a pulp is covered with a protective dressing or cement placed over a thin partition of remaining dentine” (European Society of Endodontology, 2006).

Following stepwise or selective caries removal, a bioactive material should be placed before definitive restoration. Calcium silicate cements – mineral trioxide aggregate (MTA) or Biodentine™ (Septodont, New Castle, DE, USA) or glass ionomer cement (GIC) may be placed in this therapeutic approach. The “tricalcium silicate-based dentin replacement and repair material” Biodentine (Malkondu et al., 2014) shows promising results on biocompatibility as well as bioactivity-inducing proliferation of pulp stem cells (Luo et al., 2014; Laurent et al., 2012) and mineralization (Loison-Robert et al., 2018). Evidence is currently equivocal between the use of GIC and calcium silicate cements or conventional MTA, as at present there is an absence of long-term studies (Hashem et al., 2019). However, the superiority of calcium silicate cements over calcium hydroxide liners is proven (Petrou et al., 2014).

A recent systematic review and meta-analysis reported selective caries removal to be superior than the stepwise technique (Barros et al., 2020). Furthermore, a Cochrane systematic review also reported reduced risk of pulp exposure (Ricketts et al., 2013). Bjørndal et al. (2017), in a randomized clinical trial, pointed out that the stepwise carious removal group had a significantly higher proportion of pulps with sustained vitality without apical radiolucency versus nonselective carious removal of deep carious lesions in adult teeth at five-year follow-up.

Pulpotomy, the removal of all the coronal pulp tissue, has been recommended as an alternative treatment to pulp capping where appropriate (Asgary and Eghbal, 2010; Simon et al., 2013). The histologically based idea beneath this philosophy is that the limited inflammation in the coronal part of the pulp tissue may be removed without interfering with the roots (Ricucci et al., 2014). This technique is routinely accomplished in pediatric dentistry to allow

the radicular process and apexogenesis, and may be a promising approach for mature teeth (Simon et al., 2013; Taha et al., 2017). In the future, practical issues surrounding coronal pulpotomy will also need investigation, including the lack of response to pulp sensibility testing and the likelihood of pulp canal obliteration, which will compromise potential reentry.

Immature permanent teeth with pulp necrosis and apical periodontitis

The American Association of Endodontics Clinical Considerations for Endodontic Regenerative Procedures (REPs) identifies three goals for the success of REPs: symptom relief and observation of bone healing; increased root wall thickness and/or a desirable, though not necessary, root length increase; and finally a positive response to cold test and electric pulp tests. However, it is impossible to achieve all these goals at once, and often only one of them is achieved (Chen et al., 2012; Natera and Mukherjee, 2018). REPs were accelerated in the early 2000s with the publication of two remarkable case studies (Iwaya et al., 2001; Banchs and Trope, 2004) and nowadays REPs are becoming the preferred treatment option for immature permanent teeth with pulp necrosis and apical periodontitis (Garcia-Godoy and Murray, 2012; Kim et al., 2012; Lin et al., 2014; Natera and Mukherjee, 2018).

It is important to consider that complete closure of the root apex occurs approximately three years after a tooth erupts in the oral cavity, and the loss of pulp vitality during this time stops further root development. Immature teeth diagnosed with pulp necrosis have been conventionally treated with apexification methods using long-term calcium hydroxide therapy (Cvek, 1992) or immediate placement of an MTA apical plug (Witherspoon et al., 2008). Although these treatments usually end with resolution of the disease symptoms, they provide little or no benefit for continued root growth (Bose et al., 2009). The root closure process includes root elongation, apical closure, and further thickening of the root. REPs have been described as biological methods created to stimulate apical maturation and thicken dentinal walls (Murray et al., 2007).

In orthodontic dental treatment, reshaping or resorption of the apical part of the root during the movement of the tooth is effective (Hamilton and Gutmann, 1999). However, there is no study that has negative views on orthodontic treatment in patients undergoing REP. In a case report followed for four years, it was shown that a tooth treated with REP responded to orthodontic treatment in a similar way to teeth that were not treated with REP. Therefore, REP probably does not have a negative effect on orthodontic treatment (Natera and Mukherjee, 2018; Figure 17.3).

Survival of hypomineralized teeth (molar–incisor hypomineralization)

Molar–incisor hypomineralization (MIH) is defined as demarcated, qualitative developmental enamel defects of systemic origin in at least one permanent molar with or without incisors being affected (Weerheijm et al., 2003; Weerheijm 2004). Research revealed that the demarcated defects that are present on molars and incisors with MIH have also been present on other teeth such as primary molars. This phenomenon is called hypomineralized second primary molars (HSPM). Thus, HSPM can be considered a predictor for MIH (Elfrink et al., 2015).

MIH is considered a worldwide clinical problem with a global prevalence of 14.2%, ranging from 0.5% to 40.2% according to different studies (Kusku et al., 2008; Padavala and Sukumaran, 2018). The condition is associated with significantly increased dental treatment needs, especially in severe cases. Giuca et al. (2020) states that children with MIH undergo dental treatment nearly 10 times more than unaffected children. Restorative treatment is initiated with preventive measures and ends with extractions in severe cases. The preventive measures include casein phosphopeptide–amorphous calcium phosphate (CPP-ACP), glass ionomer sealants, topical application of fluoride varnish, tricalcium phosphates, and more recently, SDF application.

Figure 17.3 A 14-year-old female patient with deep/extremely deep caries lesions on molar and premolar teeth. Regenerative endodontic treatment of the lower left second molar tooth. (a) A periapical radiograph depicting periapical radiolucency associated with tooth # 37 with an immature apex. (b) Placement of white mineral trioxide aggregate below the cementoenamel junction and a coronal seal with composite. (c) Thirteen-month follow-up periapical radiograph of the tooth shows a decrease in the size of the periapical radiolucency, periapical healing, and root maturation.

Figure 17.4 (a) Molar–incisor hypomineralization (MIH) treated with silver diamine and glass ionomer. (b) MIH treated with stainless steel crown and resin composite. (c) Untreated MIH.

The remineralization function of the active molecule, CPP-ACP crème, has been well documented in the literature in the treatment of hypomineralized white spot lesions (WSL), with calcium and phosphate levels recovering to nearly that of normal, mature enamel at the three-year mark (Baroni and Marchionni, 2011). The product is also effective in treating hypersensitivity in MIH. In a clinical study conducted on 40 patients aged from 8 to 13 years old who had a molar with MIH hypersensitivity, the use of CPP-ACP resulted in a significant improvement in dental sensitivity (Pasini et al., 2018). Recently, Kumar et al. (2022) compared daily single application of CPP-ACP cream and professional application of fluoride varnishes

every three months on enamel slabs prepared from MIH-affected teeth *in situ*. The intergroup comparison revealed no significant differences between the two groups at either baseline or six months after intervention. The usage of this innovative product is also discussed in the "Immediate postorthodontic period" section of this chapter.

Even if clinicians initiate preventive measures along with early detection of the phenomenon, in moderate to severely affected cases they still may face many complications like enamel breakdown, caries occurrence, restoration failure, need for endodontic treatment, or the need for extraction. The permanent first molars (PFMs) severely affected with MIH are vulnerable to pulpal inflammation even in the very early stages of their presence in the mouth, which in turn complicates the endodontic treatment due to open apices (Lygidakis et al., 2010; Rodd et al., 2007; Figure 17.4).

Another problem with MIH-affected PFMs is that these teeth are hypersensitive and treatments can be painful due to difficulties in anaesthetizing. As a consequence of repeated painful treatments, children with severe MIH have been reported to display more behavior management problems and anxiety during dental treatments (Jälevik and Klingberg, 2002). As a basic rule, PFMs should only be extracted if their preservation until the third decade of life seems unlikely (Schopf, 2008). The challenging and never-ending treatments of severely MIH cases are thereby good candidates for this rule. Thus, clinicians may prefer extraction over treatment in cases with poor prognosis.

Poor long-term prognosis of MIH-affected PFMs can be expected (Fayle, 2003; Jälevik and Klingberg, 2002) for molars with a severe and large-scale hypomineralization area that needs comprehensive restorative treatment, fast posteruptive breakdown and porosities reaching into the dentin, uncontrollable periodontal and/or endodontic problems, or repeatedly failed rehabilitations where patient cooperation is also lacking.

Orthodontic alignment in the postextraction period (i.e. without spontaneous alignment) is another issue in cases with MIH. Thilander and Skagius (1970) reported that the best timing for the extractions of PFMs was at 8–10 years of age. Kirschneck and Proff

(2016) reported that the appropriate timing for molar extraction – between 8 and 11.5 years of (dental) age – is critical for the efficacy of orthodontic extraction therapy in MIH. Early referral of children with MIH to an orthodontist, as well as an orthodontic evaluation in the early stages of mixed dentition, is therefore recommended to allow for proper scheduling of orthodontic extraction therapy and space closure in patients who would benefit from this treatment strategy.

One retrospective cohort study had evaluated extraction of MIH-affected PFMs and subsequent spontaneous alignment of the second molars (Jälevik and Möller, 2007). Overall 27 children aged 5.6–12.7 years at the time of extraction were evaluated. A median of 2.6 molars were extracted in each participant (overall number was 70 extracted molars). Seven participants (26%) had common malocclusions like crowding or crossbites; 79% of the extractions took place in a quadrant where a third molar was present; in three participants all third molars were missing, while in two participants two third molars were missing. The eruption of the second molars followed after a mean period of six years after extraction. In the maxilla 55% and in the mandible 47% of second molars aligned spontaneously and did not require orthodontic intervention. The authors stated that their study shows favorable spontaneous development of the permanent dentition after first molar extraction in the majority of cases. Unfortunately, that valuable study lacks information on influencing factors for alignment (like stage of second molar development or vertical skeletal dimension).

The other issue with MIH is coexisting dental anomalies, mainly hypodontia. A study by Walshaw et al. (2020) inspected children with MIH and reported that in total 29% of the patients had a dental abnormality. Coexisting hypodontia was found in 12% of cases, with lower second premolars being the most affected teeth. Concurrent ectopic first permanent molars were seen in 8% of cases, while infraocclusion of one or more primary molars was found in 9%. There was abnormal morphology in 9% of the teeth, including macrodont and microdont teeth.

Thus, the “take-home message” for the clinician should be that MIH-affected PFMs should be evaluated carefully early in the mixed

dentition by a pediatric dentist and an orthodontist. It is wise to remember that severe, even moderate cases may cause complications resulting in tooth loss. On the other hand, the clinical management of mild cases can be undertaken successfully with a deep knowledge of appropriate preventive materials.

Amelogenesis imperfecta

Amelogenesis imperfecta (AI) is an uncommon developmental defect of tooth enamel that occurs at a rate ranging from 1 in 4000 to 1 in 14,000 in Western cultures (Witkop, 1988; Kida et al., 2002). AI enamel is excessively thin, brittle, pitted, and/or discolored, causing considerable feeding problems and discomfort in individuals. It is also linked to bad social results, humiliation, and poor esthetics (Crawford et al., 2007).

AI is a hereditary condition characterized by mutations in genes *AMEL*, *ENAM*, *MMP20*, *KLK4*, and *FAM83H*, and characterized by a wide variety of phenotypes (Gadhia et al., 2012). The type of AI determines whether heredity is autosomal dominant, autosomal recessive, or X-linked. Although there are many kinds of AI, the main abnormality in each is hypoplasia, hypomaturation, or hypocalcification. The hypoplastic kind of enamel is thin, pitted, or fissured. The hypocalcified enamel is powdery, varies in color, and erodes easily.

Coexisting dental anomalies may include delayed tooth eruption, impacted teeth, congenitally missing teeth, open bite, pulpal calcifications, taurodontism, and root malformations, which may lead to resorption during orthodontic treatment (Witkop, 1988; Arkutu et al., 2012). Arkutu et al. (2012) described all the features of AI that may compromise orthodontic approaches in their review.

Like MIH, AI also needs an interdisciplinary approach for its treatment. Tight contact between the interdisciplinary team is required for treatment planning in the immediate, transitory, and long-term stages (Figure 17.5).

The major problem of weak and delicate enamel may be overcome with alternative approaches. If possible, choosing removable approaches would be in the best interest of the patient (Arkutu et al.,

2012). Traditional banded appliances are out of date, yet they may be utilized to solve some of the adhesion problems. With an AI patient, the orthodontist will face clear difficulties in attachment and bracket bonding. Because they are less reliant on micromechanical adhesion phenomena, GIC-based adhesives are expected to increase appliance retention and aid in the mitigation of future enamel demineralization. In AI, the use of sodium hypochlorite to eliminate excess protein around the enamel crystals and enhance etch quality has been documented (Sarıoğlu et al., 2006). However, since this study was done on primary teeth, the evidence for enhanced bracket retention with these approaches as well as increasing etch times in AI remains weak (Venezie et al., 1994; Hiraishi et al., 2008).

As for the problem of impacted teeth, even in the lack of clear supported data, preventive measures such as deciduous canine removal and space construction should be used (Parkin et al., 2009a). In addition, as for the taurodont and malformed roots, an endodontist should keep an eye on AI patients throughout the orthodontic treatment.

Figure 17.5 (a–k) Orthognathic surgical and restorative treatment of a patient with severe Class III open bite malocclusion and amelogenesis imperfecta. Successful bonding is a challenge in patients with amelogenesis imperfecta.

Endodontically treated teeth

Successful root canal treatment relies on adequate removal of microorganisms and prevention of recolonization or reinfection through the placement of a root canal filling that obliterates the

canal space and a restoration with a good coronal seal (Briggs and Scott, 1997). The benefits of root canal treatment are retention of the natural tooth in the dental arch and facilitation of the restoration to conserve the remaining crown and root structures, preservation of the alveolar bone and accompanying papillae, and maintenance of pressure and tension perception by paradental mechanoreceptors. However, such a retained tooth may be at risk of future root fracture and development of caries or periodontal disease after orthodontic treatment (Torabinejad et al., 2007). Epidemiological radiographic surveys have revealed a relatively low frequency of high-quality root canal fillings, ranging from 14% to 65% (Eriksen et al., 2002). Epidemiological studies of root canal–treated teeth in different groups performed outside of a university-sponsored clinic produced more adverse treatment results, with rates of highly insufficient root canal fillings and apical periodontitis (between 40 and 65%) related to endodontically treated teeth (Gillen et al., 2011).

Endodontic outcomes are difficult to predict, since nonendodontic factors such as the quality of the subsequent restoration and the remaining tooth structure contribute to the true prognosis. Whenever the decision has to be made about whether to perform endodontic treatment or to extract a tooth, orthodontists should consult with endodontists, taking into account pre-, intra-, and postoperative factors, such as the patient's age, socioeconomic class, vital or necrotic pulp, and presence of periapical infections (Travassos et al., 2003). It is important to realize that the presence of periapical lesions, increased age, and irregular canal anatomies, especially in molars, may compromise the endodontic outcome. Moreover, procedural errors during canal instrumentation, rinsing with irrigation solutions, and medicaments and fillings may play a crucial role in long-term prognosis. These factors should be evaluated based on good clinical judgment along with input from endodontists, so that the patient is provided with an optimized treatment plan that is at the same time cost-effective.

The time at which a tooth may be moved after completion of endodontic therapy is the most frequently asked question and presents uncertainties in orthodontic and endodontic clinical practice. Endodontically treated teeth can be moved orthodontically as readily as teeth with vital pulp. But the effects of orthodontic

treatment on endodontically treated teeth depend on a variety of factors such as the applied force, the seal of the canal, any previous history of trauma, and the patient's clinical symptoms (Consolaro and Consolaro, 2013; Consolaro et al., 2020). If teeth require root canal treatment during orthodontic movement, it is recommended that the root canals be cleaned, shaped, and an interim dressing of calcium hydroxide be placed. Canal obturation is accomplished after orthodontic treatment (Hamilton and Gutmann, 1999). If orthodontic treatment might take too long to finish, a gutta-percha filling should be placed in treatment, because the calcium hydroxide filling may make the tooth prone to fracture during this period.

Congenitally missing and peg-shaped laterals

Tooth agenesis (hypodontia) is the most commonly observed craniofacial developmental anomaly, which involves absence of at least one permanent tooth, excluding third molars, with a prevalence of 3.5–10% in the permanent dentition and exhibiting variable prevalence in different races or ethnic groups, with a modest preference for females (Krassnig and Fickl, 2011; Khalaf et al., 2014; Arte et al., 2017). The most frequent permanent missing teeth are the second premolars and maxillary lateral incisors (Rizos and Spyropoulos, 2004; Al-Ani et al., 2017). This form of hypodontia can be bilateral or unilateral; such a condition can occur with a contralateral small or peg-shaped lateral incisor, adding complexity to the restorative options (Mirabella et al., 2012). Bilateral agenesis of maxillary permanent lateral incisors occurs more often than unilateral agenesis (Polder et al., 2004).

Studies have shown that different dental and craniofacial characteristics accompany agenesis. Bimaxillary retrognathism, a Class III skeletal pattern, and reduced vertical and transverse dental arch dimensions may be skeletal companions (Vucic et al., 2016). Microdontia resulting in spacing and displacement of adjacent teeth (Hobkirk et al., 2010), taurodontism (Goodman et al., 1994), ectopic eruption (Peck et al., 1998), delayed eruption (Dhanrajani, 2002), ankylosis, and infraocclusion may be seen on a dento-alveolar level. In addition, hypodontia patients may display reduced alveolar bone development, which may be restricted to a particular region or

generalized to the whole alveolar process. These patients may have an older look as a sequelae of more prominent mandible and lips. Also, the freeway space may be increased, compromising esthetics and function.

Hypodontia can be classified as syndromic or nonsyndromic. Syndromes such as ectodermal dysplasia, Van der Woude syndrome, or Down syndrome and craniofacial microsomia are more commonly associated with severe hypodontia and can be either sporadic or familial, whereas in nonsyndromic conditions such as cleft lip and palate, hypodontia is more commonly seen in the permanent dentition and ranges in severity (Cobourne, 2007; Pagán-Collazo et al., 2014).

Familial hypodontia is complex and multifactorial, influenced by a combination of gene function, environmental interaction, and developmental stage (Lammi et al., 2004). Although congenital absence of teeth typically has a complex and poorly defined genetic background, since more than 200 genes are involved in tooth formation (De Coster et al., 2009), many affected individuals have a family history of developmental dental anomalies (Hobkirk et al., 1995). Genetic transmission of hypodontia has demonstrated variable penetrance, with reported polygenic, epigenetic, and environmental influences (Parkin et al., 2009b). Mutations in transcription factors (Javed et al., 2014) MSX1, PAX9, and AXIN 2 have been identified in families with an autosomal dominant oligodontia (Tallón-Walton et al., 2014). These mutations have been implicated in arresting tooth development at the bud stage (Mitsui et al., 2014).

Environmental factors that lead to arrested tooth development may include factors that cause failure of tooth bud cell proliferation from the dental lamina (Al-Ani et al., 2017). This may be due to infection (e.g. rubella, osteomyelitis), trauma in the dental region such as fractures, surgical procedures on the jaw and extraction of the preceding primary tooth, drugs (e.g. thalidomide), or chemotherapy or radiotherapy at a young age (Al-Ani et al., 2017).

The peg-shaped lateral phenotype has a strong genetic etiology, and peg-shaped laterals have been associated with tooth agenesis (Arte et al., 2001). The prevalence of peg-shaped laterals has been reported

to be 1.8% (Hua et al., 2013). The prevalence of bilateral and unilateral peg-shaped lateral incisors is the same, and the left side is more common than the right side (Hua et al., 2013). Peg-shaped lateral prevalence has been shown to be 7.5% in nonsyndromic cleft patients (Sæle et al., 2017).

Severe hypodontia with excessive spacing and compromised esthetics have been reported to cause functional and psychosocial burdens (Robertson and Mohlin, 2000), such as bullying in school, which led to depression, loneliness, anxiety, low self-esteem, and underachievement, especially during the sensitive adolescent period (Kavadia et al., 2011; Johal et al. 2021). Meaney et al. (2012) reported that adolescents become more aware of their esthetics as they grow up, and their primary motivation for treatment is esthetics.

A logical hierarchy of decisions should be followed to create a stable occlusion, periodontal health, and acceptable dental and facial esthetics after diagnosing agenesis (Cocconi, 2020). To design a custom treatment plan, it is of fundamental importance to analyze key factors such as the patient's age, type of sagittal malocclusion, presence or absence of crowding, profile type, shape and color of the canine, smile line, arch length, tooth size discrepancy, ridge thickness, existing occlusion, patient's expectation from treatment, and possible cooperation level of the patient (Silveira et al., 2016; Hsu and Lee, 2019).

In fact, the decision requires an interdisciplinary treatment plan that mostly involves restorative touch-ups, which will be discussed in the last section of this chapter under "Esthetic improvements."

Interactive collaboration during orthodontic treatment

Orthodontic treatment will succeed when its advantages outweigh any adverse sequelae. To prevent, minimize, and manage the iatrogenic effects of orthodontic mechanics, the clinician should examine both the hard and soft oral tissues that may be affected by the orthodontic treatment (Shaw et al., 1991), just like at the treatment planning stage before treatment initiation.

Cariogenic potential and white spot lesions

After the decision about the final treatment plan, before the full bond-up appointment, the clinician should take preventive measures against caries. Dental caries in the enamel is unique among other infective diseases in the human body, as enamel is both acellular and avascular; thus, enamel cannot heal itself by a cellular repair mechanism (Zero, 1999). In orthodontic patients, caries starts as decalcification areas adjacent to fixed orthodontic appliances. Several studies showed that orthodontic attachments caused an increase in occurrence of cariogenic *Streptococcus mutans*, and the number of bacteria was found to be four times higher compared with the number at the beginning of treatment (Ahn et al., 2007; Rosenbloom and Tinanoff, 1991). These acidogenic bacteria produce byproducts of organic acids in the presence of fermentable carbohydrates, further lowering the pH of the plaque. As the pH drops below the threshold for remineralization (pH = 4.5), enamel demineralization/decalcification occurs. The first clinical evidence of this demineralization is visualized as a WSL, which has been defined as “sub-surface enamel porosity from carious demineralization” that represents itself as “a milky white opacity” caused by the changes in enamel translucency and light scattering (Bishara and Ostby, 2008).

WSL development is a very rapid process and they may be apparent within four weeks after the orthodontic bond-up appointment (Ogaard et al., 1988). Their prevalence is reported to vary from 4.9% (Gorelick et al., 1982) to 84% (Mizrahi, 1982) of tooth surfaces. More than 50% of subjects may experience an increase in the number of WSLs with fixed orthodontic appliance therapy (Artun and Brobakken, 1986). Boersma et al. (2005) observed that 97% of all their subjects and on average 30% of the buccal surfaces in a person were affected. Again, on average, 40% of the surfaces in males and 22% in females showed WSLs. Briefly, any tooth in the mouth can be affected, with the common ones being the maxillary lateral incisors, maxillary canines, and mandibular premolars. Diagnosis, prevention, and treatment of WSLs are all crucial to prevent tooth decay as well as to minimize the tooth discoloration that could compromise the smile esthetics.

The acquired biofilm (the pellicle) in the intact enamel surface participates in dynamic physico-chemical equilibrium with the oral fluids (Zero, 1999; Ten Cate and van Loveren, 1999). When the pH of the oral fluids goes below the physiological norm, calcium and phosphate ions diffuse from the hydroxyapatite mineral in the enamel to the pellicle and into the oral cavity (demineralization). When the pH of the oral fluids rises to the norm, the calcium and phosphate ions in the supersaturated saliva are transmitted through the pellicle into the enamel following the laws of chemical equilibrium (remineralization). Within this cycle, destructive demineralization and restorative remineralization occur either simultaneously or alternately. If this cycle is not prevented and demineralization predominates, WSLs will be the result and, once they are established, it is extremely difficult, or sometimes impossible, to achieve complete remineralization.

Excess of bonding material around the attachment base may exacerbate the problem by creating retentive areas where the acidogenic bacteria can adhere and cause demineralization. Complicated appliance designs with loops, auxiliary archwires, springs, coils, and some Class II correctors create noncleanable areas even in highly motivated patients. In most cases, the lesions are small and restricted to forming narrow white bands around the bracket bases or in the areas between the brackets and the gingival margin (Ogaard, 2008). The demineralized enamel is porous and absorbs stains from the daily diet, representing esthetic challenges on the labial surfaces of the affected tooth. In some patients, who are noncompliant with oral hygiene and fluoride regimens, lesion development may be extensive and require premature debonding.

Cariogenic challenge between different orthodontic treatment modalities

On a basic level, the types of orthodontic treatment can be subgrouped into fixed orthodontic treatment and removable orthodontic treatment. In contemporary orthodontics, due to the esthetic demand, the variety of orthodontic appliances has increased, from lingual appliances to a diversity of fixed techniques and clear aligners as a type of a removable appliance. Even though these

appliances provide comfort in social life due to less or no visibility than conventional methods, their effects on plaque accumulation and oral flora need detailed investigation.

Significant changes occur in the microbial plaque mass at the metal surfaces and the adjacent tooth surface as early as one week after the insertion of fixed orthodontic appliances (Reichardt et. al., 2019). During orthodontic treatment, the areas that show the highest risk for demineralization are maxillary incisors and mandibular canines and premolars (Hu and Featherstone, 2005).

The use of elastomeric ligatures is frequently blamed for the increase of bacterial plaque around the brackets during fixed orthodontic treatment. Therefore, it is logical to assume that orthodontic brackets that do not need any type of a ligation, namely self-ligation brackets (SLB), can reduce the amount of bacterial plaque, and thus improve overall oral health. There are several studies that investigated the effects of SLB on oral health and the results of these studies are contradictory (Lucchese et al., 2018). One study showed an increase of *S. mutans* and *Lactobacillus* spp. at three months with the use of SLB compared to controls (Baka et al., 2013). Another study showed fewer *S. mutans* with SLB compared to conventional brackets (Perinetti et al., 2004a). These conflicting results may indicate that the variation in the number of cariogenic bacteria may be a result of the individual's behavior in terms of oral hygiene measures, and not the type of bracket used.

Lingual orthodontics is also a type of fixed orthodontic treatment technique. Food and plaque deposits on the lingual gingival margin of the teeth are more difficult to remove with standard oral hygiene procedures with respect to the labial side (Lombardo et al., 2013). Bilgin Yener and Polat Ozsoy (2020) measured the amount of biofilm formation on labial and lingual brackets using a quantitative image analysis. Their results showed that the amount of biofilm on debonded brackets was higher than in the labial bracket group. According to some retrospective (Sinclair et al., 1986; Artun, 1987) and prospective studies (Caniklioğlu and Öztürk, 2005; Stamm et al., 2005), wider lingual brackets cause a reduced interbracket distance and make oral hygiene procedures very difficult, leading to an increased risk for plaque accumulation and gingival problems.

Therefore, the use of adjunct cleaning aids such as sonic electric toothbrushes, interproximal brushes, chlorhexidine mouthwashes, fluoride mouthwashes, and regular professional cleaning should be recommended for patients with lingual fixed appliances. However, despite the evidence concerning the increased number of cariogenic bacteria in lingual orthodontics, Wiechmann et. al. (2015) showed that the incidence of WSLs was much less in lingual treatment compared to labial treatment. The reason behind this reduction could be the difference in saliva wetting between lingual and labial treatment. Moreover, lingual WSLs do not compromise smile esthetics due to their location on the lingual side of the teeth (Figure 17.6).

Figure 17.6 Caries lesion arising from the lingual bracket on the palatal surface of the first molar.

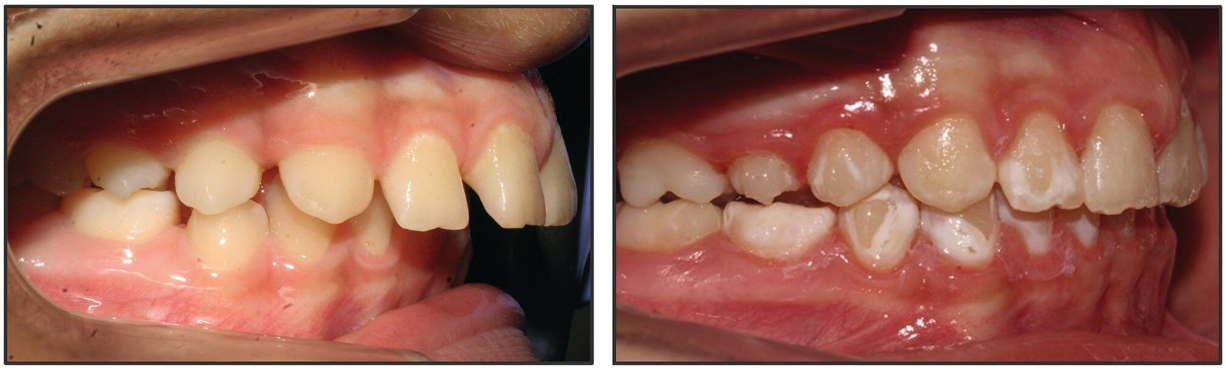


Figure 17.7 White spot lesions developed during orthodontic treatment.

Since the introduction of commercial aligners in 1998, treatment with orthodontic clear aligners is gaining more and more interest due to its esthetics and ease of use. Since it is a removable type of appliance, patients do not need to carry out extreme oral hygiene measures. However, when the aligners are worn the flow of saliva is limited, the self-cleansing activities of orofacial soft tissues is interrupted, and the development of plaque is frequently seen under the aligners. Moreover, if patients consume acidic beverages without removing these appliances, WSLs are likely to develop. Traditionally they have been used as retention appliances for years and bacterial

adhesion studies showed that the colonies of *S. mutans* and *Lactobacillus* spp. start to increase two months after the treatment (Türköz et al., 2012). In a prospective cohort study, Sifakakis et. al. (2018) investigated the salivary levels of cariogenic bacteria *S. mutans*, *Lactobacillus acidophilus*, and *S. sanguinis* among adolescents treated orthodontically with thermoplastic aligners (0.75 mm polyethylenterephthalat-glycol copolyester [PET-G] thermoplastic sheets) or self-ligating fixed appliances. Their results showed no differences in the salivary levels of *S. mutans* and *L. acidophilus* between adolescent patients treated for one month with thermoplastic aligners or self-ligating appliances; however, lower salivary levels of *S. sanguinis* were found in patients treated with thermoplastic aligners.

Azeem and Ul Hamid (2017) evaluated the incidence of WSLs in patients who had clear aligner treatment using the quantitative light-induced fluorescence (QLF) method. After a mean of 18 months of orthodontic treatment, the overall WSL incidence was found to be 2.85%, which is a remarkably reduced level compared to that seen after conventional fixed appliances. In addition to this, Albhaisi et. al. (2020) showed that the WSLs that were seen after clear aligner treatment were shallower but larger in area. Remineralization of shallow lesions is more responsive to WSL treatment. The literature needs more research to draw conclusions, but we can say that in patients with adequate oral hygiene habits, clear aligners are superior to fixed appliance techniques in terms of the number of cariogenic bacteria and WSL formation (Figure 17.7).

Evidence-based strategies against cariogenic activity during orthodontic treatment

The most important prophylactic measure against WSLs is implementation of a good dietary and oral hygiene regimen along with proper tooth brushing with a fluoridated dentifrice. The remineralization process is greatly enhanced by the low levels of fluoride in the saliva and plaque (Ten Cate and van Loveren, 1999). By controlling biofilm accumulation with a fluoride-containing dentifrice, the lesions can not only be arrested but also be partially repaired (Lima et al., 2008). Dentifrices typically contain sodium

fluoride, monofluorophosphate, stannous fluoride, amine fluoride, or a combination of these compounds, but the maximum concentration allowed in the European Union is 0.15%. Ogaard et al. (2004) demonstrated a dose–response effect and a fluoride concentration above 0.1% in dentifrices is recommended for orthodontic patients, because of their increased risk of WSLs. Considering the existing evidence related to caries and fluorosis risks, low-fluoride (500–550 ppm) dentifrices could be recommended for low caries–risk young children who are at risk of developing dental fluorosis in the permanent maxillary central incisors (less than 3 years of age), especially those living in fluoridated communities. In all other cases, dentifrices containing at least 1000 ppm fluoride should be used (Buzalaf, 2018).

Stannous fluoride, which interferes with the adsorption of plaque bacteria to the enamel surface, offers beneficial effects not only against caries but also against plaque-induced gingival diseases during orthodontic treatment (Ogaard et al., 1980; Boyd and Chun, 1994). Tin atoms in stannous products block the passage of sucrose into bacterial cells, inhibiting acid production. Ogaard et al. (2006) demonstrated an inhibiting effect of a combined stannous fluoride/amine fluoride toothpaste/mouthrinse against both decalcification and gingival bleeding in a prospective, randomized clinical study. Titanium tetrafluoride solutions, through formation of a retentive, titanium-rich, glaze-like surface coating on treated enamel surfaces, inhibit caries lesion development in patients wearing fixed appliances. At a low pH, titanium binds with an oxygen atom of a phosphate group to form Ti-O-Ti-O chains on the tooth surface and this covalently bound titanium covers the tooth surface by formation of a strong complex. This surface coating resists cariogenic challenges even under extreme alkaline and acidic conditions (Büyükyılmaz et al., 1994).

The effect of fluoride is limited when the pH level drops to lower than the solubility product of pure fluoroapatite (pH = 4.5). When this pH is exceeded, the liquid phase of the plaque will be undersaturated with hydroxyapatite and fluoroapatite, making remineralization no longer possible (Larsen, 1990). A dose response to fluoride may not be apparent in this stage and more fluoride may not produce a better clinical effect (Ogaard, 2001). Briefly, if the

patient is noncompliant with the implemented hygiene and dietary precautions, the use of a fluoridated dentifrice alone may not be effective in preventing the development of WSLs (O'Reilly and Featherstone, 1987). Supplemental professional sources of fluoride and other antimicrobial agents in the forms of varnishes, solutions, or gels are often recommended. Fluoridated mouthrinses containing 0.05% sodium fluoride used daily have been shown to significantly reduce lesion formation beneath bands. These mouthrinses may be combined with antimicrobial agents such as chlorhexidine (CHX), octenidine dihydrochloride, benzydamine, triclosan, or zinc to improve their cariostatic effect (Kocak et al., 2009). CHX varnishes for long-term use have been introduced (Ogaard et al., 2001), but are not recommended because of the metallic taste and frequent discoloration they cause to the teeth and tongue.

An in-office application of a high concentration of fluoride in the form of a varnish or sealant may be beneficial in noncompliant patients. This exposure to fluoride is limited to office-only application, because of the temporary discoloration of the teeth and the gingival tissues, and, at the same time, increasing expense to the patient and/or chairtime to the clinician (Bishara and Ostby, 2008). With topical fluoride application, a calcium-fluoride like material (CaF_2) builds up in plaque, on the tooth surface (enamel/dentin), or in incipient carious lesions, which acts as a reservoir for fluoride release when the pH is lowered (Ogaard, 1990). Vivaldi-Rodrigues et al. (2006) found that application of the fluoride varnish resulted in a 44.3% reduction in enamel demineralization in orthodontic patients. The Cochrane systematic reviews have not been able to reach a consensus on any topical preparation or schedule that would provide the greatest benefit for preventing enamel demineralization (Benson et al., 2004, 2019; Derks et al., 2004; Chadwick et al., 2005). In fact, Benson and coworkers recommended daily fluoride mouth rinsing (0.05% NaF) similar to Zachrisson more than 30 years ago (Benson et al., 2004). However, in a more recent Cochrane systematic review it was found that evidence is insufficient to recommend the use of fluoride-containing materials for attached braces to the teeth or intraoral fluoride-releasing devices (Benson et al. 2019).

Probiotic approach

The oral microbiome is an essential component of the human microbiome, and it refers to the microorganisms that live in the human oral cavity (Dewhirst et al., 2010). The oral cavity, containing over 700 species, is the second most complex microbiota in the human body, after the colon (Wade, 2013; Palmer, 2014). Bacteria, fungus, viruses, archaea, and protozoa are all part of the oral microbiome. According to the Human Oral Microbiome Database (www.homd.org), roughly 54% have been grown and named, 14% have been farmed but unidentified, and 32% are only known as uncultivated phylotypes. A growing number of studies have shown that the oral microbiota is important in the pathophysiology and development of numerous oral and systemic disorders (Dewhirst et al., 2010; Zhang et al., 2018).

Probiotic organisms are thought to act primarily through the following mechanisms: competition with potential pathogens for nutrients or adhesion sites; killing or inhibiting pathogen growth via the production of bacteriocins or other products; improvement of intestinal barrier integrity and upregulation of mucin production; modulation of cell proliferation and apoptosis; and stimulation and modulation of the mucosal immune system (Teughels et al., 2011). However, probiotics have unique properties in the oral cavity. Oral probiotics should be able to adhere to and colonize oral tissue, particularly hard, nonshedding surfaces, and eventually form a component of the biofilm (Meurman and Stamatova, 2007; Teughels et al., 2011). In addition, they should not digest carbohydrates; otherwise, pH will drop and caries will develop (Teughels et al., 2011).

Probiotic techniques have been examined to cure caries, mostly by interfering with cariogenic pathogen oral colonization. Näse et al. (2001) were the first to test *L. rhamnosus* GG for caries-inhibiting capacity *in vivo* and discovered that the test group had reduced dental cavities and lower *S. mutans* counts. Bifidobacterium (Çağlar et al., 2005), *L. reuteri* Bifidobacterium animalis (Cildir et al., 2009), *L. paracasei*, and *L. casei*, in addition to *L. rhamnosus*, have been shown to reduce the quantity of cariogenic bacteria and thereby prevent dental caries. Clinical research conducted in patients

undergoing orthodontic treatment showed that daily kefir consumption and use of probiotic toothpaste decreased salivary microbial colonization (Alp and Baka, 2018). In contrast, results of other studies showed that the probiotic bacteria had no significant impact on caries prevalence in tested groups (Taipale et al., 2012; Villavicencio et al., 2018). Nagarajappa et al. (2015) stated that the use of probiotics can reduce *S. Mutans* colony-forming unit (CFU) counts, which may have a preventive effect on the development of dental caries; however, the lack of long-term follow-up periods makes it impossible to suggest that the effect continues after stopping the bacteriotherapy, or its influence on the prevalence/ incidence of dental caries. This makes the clinician think about sustainability. In addition, it is known that even early administration (i.e. in the first year of life) of probiotics does not represent permanent colonization in the oral cavity (Taipale et al., 2012).

A meta-analysis of 50 randomized control studies found that present data are insufficient to recommend probiotics for dental caries management (Gruner et al., 2016). The same meta-analysis stated that probiotic treatment was found to have a favorable effect on gingival inflammatory markers, which is an important issue during orthodontic treatment. Additionally, a number of studies support probiotic therapy to prevent or treat gingivitis and periodontitis. Specifically, there are promising results with *L. reuteri* on gingivitis and periodontitis (Krasse et al., 2006; Iniesta et al., 2012) and with *L. brevis* on aggressive periodontitis (Shah et al., 2013). In contrast, a more recent systematic review concluded that probiotic administration does not seem to have an effect on gingival inflammation and enamel decalcification development in patients under treatment with fixed orthodontic appliances. That review pointed out that extrapolating data is very complex due to lack of standards among clinical studies. The authors underlined that more randomized control studies are needed, especially on finding the effective probiotic strains (no effect on inflammation and demineralization; Hadj-Hmou et al., 2020). In any case, it is crucial to note that dental oral diseases have a complex etiology, which means that lowering cariogenic bacterial levels might help, but does not guarantee disease control. Furthermore, identification of the

correct dose, treatment time, and optimal vehicles for a probiotic approach are still under research worldwide.

Other than probiotics, synbiotics have been under research for the last few years. The word “synbiotic” refers to products that contain both probiotics and prebiotics. Following medicine and the food industry, prebiotics are being coupled with probiotics in dentistry to boost the latter’s capacity to “outgrow” infections (Antoniadou and Varzakas, 2021). Only five combinations have been tried to date, and they are all in the preclinical stage (Tester and Al-Ghazzewi, 2011; Kojima et al., 2016).

Orthodontic treatment commonly alters the possibility of biofilm formation, thus every effort is worth it to change the bacterial community. On the other hand, dental disease is defined as a noncommunicable, bacteria-related lifestyle disease, so a good diet with less sugar is very valuable in fighting the disease (Pitts et al., 2021; Twetman, 2018).

Novel bracket adhesive protocols

Tooth-conserving and time-saving adhesive methods of retaining orthodontic attachments are replacing traditional methods and procedures. However, despite these advances, caries risk under and in the vicinity of multibonded appliances is of concern (Ogaard, 1989). GICs and resin-modified glass ionomer (RMGI) cements were introduced as orthodontic bonding adhesives to take advantage of some of their sustained fluoride-release capabilities (Swift, 1989; McCourt et al., 1990), but their bond strength was found to be equivocal while the concentration of fluoride released decreased with time (Miguel et al., 1995; Miller et al., 1996; Bishara et al., 2007). Nowadays, bioactive adhesive systems with antibacterial effects or intensive remineralization ability are considered to be beneficial.

Microleakage, an important postrestorative complication, is defined as the seeping and leaking of fluids and bacteria in the tooth–restoration interface (Gladwin and Bagby, 2004). The concept of microleakage has been underestimated by orthodontists. Formation of WSL at and under the adhesive–enamel interface is often due to microleakage that may be of clinical importance (Arhun et al.,

2006a; Arıkan et al., 2006). Expansion and contraction occur when the teeth are subjected to temperature changes by the ingestion of hot or cold foods. The linear thermal coefficients of expansion of enamel and ceramic or metal brackets and the adhesive systems do not match closely. Metal brackets repeatedly contract and expand more than ceramic brackets, enamel, or the adhesive system, producing microgaps between the bracket and the adhesive system, resulting in leakage of oral fluids and bacteria beneath the brackets. However, if microleakage cannot be prevented, inactivation of bacteria will be a direct strategy to prevent development of WSLs. Antimicrobial adhesive systems may be beneficial in such situations, ensuring antimicrobial effect at the site of therapeutic importance, which is the enamel surface under the bracket in this circumstance (Arhun et al., 2006a).

MDPB (12-methacryloyloxydodecyl-pyridinium bromide) is incorporated in various restorative materials since it allows immobilization of the antibacterial component by polymerization, halts the deterioration in the mechanical properties of cured resins, and improves inhibitory effects against bacterial growth on surfaces (Imazato, 2009). The use of argon laser for curing composite resins used for orthodontic attachments has been tried as it saves time and alters the enamel structure, rendering it less susceptible to demineralization. Combining laser irradiation with fluoride treatment can have a synergistic effect on acid resistance, thus preventing the formation of WSLs (Hicks et al., 1995).

When the brackets are bonded to the enamel using an adhesive resin, there is often an amount of flash around the enamel–bracket interface that needs to be cleaned before the resin is light cured. Even in the hands of a very careful clinician, the resultant enamel–bracket interface will expose some rough composite surface that may become a critical site for plaque accumulation (Sukontapatipar et al., 2001; Gwinnett and Ceen, 1979). The accumulation of dental plaque around brackets may cause enamel demineralization and possibly WSLs. Attempts have been made to minimize the amount of flash around the brackets to provide a smooth enamel–bracket interface, and one of the latest developments is the creation of a special type of adhesive system that eliminates the removal of flash. In 2015, the APC™ Flash-Free (FF) Adhesive Coated Appliance System (3M,

Maplewood, MN, USA) came onto the market that attempts to eliminate the need for flash removal around the brackets. The brackets incorporate an amount of prepasted adhesive with a nonwoven polypropylene matrix soaked with resin under the individually packed brackets. The nonwoven matrix acts like a sponge during bonding and the excess resin is soaked back into the base before the setting of the resin. Independent studies have investigated the manufacturer's claims regarding two main strengths of this adhesive system: adequate bond strength and smooth enamel–resin interface. Foersch et al. (2016) investigated the resin margin interface in brackets bonded with the APC FF system. The stereomicroscopic images revealed remarkably few excess composite remains around flash-free bonded brackets, with an average amount of visible resin between 0.16 and 0.08 mm measured in the bracket periphery. Furthermore, the filleted edge that is formed by the resin microscopically seemed to form a smooth and well-locking shape in this type of bracket bonding.

Short-term effects of FF brackets on bacterial plaque, microbial formation, and WSLs were evaluated in a comprehensive *in vivo* study that was conducted by Yetkiner et al. (2019). The main difference between the conventional bracket and the flash-free bracket was found to be the variety of bacterial content. The counts of *Aggregatibacter actinomycotemcomitans*, *Porphyromonas gingivalis*, and *Streptococcus oralis* were much lower in the FF group compared to the conventional APC bracket group. Therefore, even though the amount of plaque and number of WSLs were similar for the first three months of the treatment, fewer pathogenic bacteria were found around FF brackets. In another *in vivo* study, ElSherifa et al. (2020) evaluated enamel roughness and color after debonding APC FF brackets, APC Plus brackets without a flash-free system, and a conventional adhesive system. Atomic force microscope results revealed less roughness in the FF group and color evaluation with the spectrophotometer showed that the adhesive around FF brackets showed less discoloration compared to the other groups (ElSherifa et al., 2020). When the enamel–resin interface is smooth, less plaque accumulation will be seen and microleakage will also be less. Therefore, the clinician is advised to use advanced bonding materials to obtain a smooth marginal interface between enamel and resin.

Other than recently developed adhesive materials, GICs, especially RMGICs, are still an alternative for orthodontic bonding and banding procedures. In a recent review, Fricker (2022) mentioned the possible advantages of GICs in patients with a high caries risk. GICs have the trait of long-term fluoride release, which is characterized by an initial high peak that quickly declines to level off over a period of months (Ngo and Opsahl-Vital, 2014). As fluoride reserves run low, GICs can be recharged with fluoride using fluoride-containing oral care products such as topical fluoride gels, fluoride-containing toothpastes, and mouthrinses to keep the fluoride release going (Benington et al., 2001). The bond strengths of both chemically cured and resin-modified GICs improve over time; however, RMGICs reach maximum tensile strength faster than chemically cured materials (McCarthy and Hondrum, 1994). The mean shear bond strength of RMGIC is consistently lower than that of composite resin, according to *in vitro* investigations. However, higher adhesion is not necessarily desirable, as excessive bond strengths may cause iatrogenic injury during bracket debonding (Wiltshire and Noble, 2010). When debonding composite resin from hypomineralized enamel, such as WSLs, adhesive failure occurs more frequently at the enamel–resin contact than at the attachment–resin interface of mineralized enamel. When attachments are removed, the risk of injury to the hypomineralized enamel increases (Cochrane et al., 2017).

The clinician can choose the correct material for bonding by considering the properties of the enamel (i.e. AI, hypomineralization, etc.) and caries risk of the patient.

Pulpal reactions to orthodontic forces

The dental pulp is a specialized type of loose connective tissue, rich in cells such as odontoblasts, fibroblasts, and cells of the immune, nervous, and vascular systems (Leone et al., 2009). While performing complex functions such as having a nervous and vascular supply for vitality, carrying sensory impulses, and formation of protective secondary dentin, it is responsive to peripheral impacts, such as orthodontic forces. Morphological and structural changes occur in dental pulps subjected to such forces (Anstendig and

Kronman, 1972; Delivanis and Gauer, 1980; Popp et al., 1992; Kayhan et al., 2000). Although reports on these changes present conflicting data, most show degenerative changes that may have harmful effects on tooth vitality.

The pulpal reactions to the orthodontic force include pulp changes like cell damage, inflammation and wound healing, and changes that may lead to permanent damage to the pulp (von Böhl et al., 2012). Circulatory disturbances, vascular compression, and formation of secondary dentin after orthodontic force application have been reported (Stenvik and Mjör, 1970; Anstendig and Kronman, 1972). Radiorespirometric techniques, which measure the tissue respiration rate, indicated depression of the oxygen utilization system within the pulp cells after the application of orthodontic forces (Hamersky et al., 1980; Unsterseher et al., 1987). An average of 27% reduction in pulpal respiration has been seen after three days of orthodontic force application (Unsterseher et al., 1987) and this might compromise the long-term vitality of the tooth (Popp et al., 1992). Hypoxia in pulp cells due to reduced blood flow may negatively enhance mitochondrial function and proliferative activity (Amemiya et al., 2003). Significant elevation of aspartate aminotransferase (AST) activity, an enzyme that is released into the extracellular environment following cell death, has been demonstrated after one week of intrusive force application (Veberiene et al., 2009). Likewise, Perinetti et al. (2004b) observed elevated AST activity in orthodontically treated teeth and found these levels comparable to reversible pulpitis. It has been hypothesized that increased AST levels could be the result of circular disruption, reduction in oxygen levels, and pulp tissue apoptosis. Furthermore, an increased response to electrical pulp testing was seen, which is positively correlated to anatomical features such as pulpal weight and root surface area (Veberiene et al., 2009).

Several authors have detected the formation of calcified deposits in the dental pulps of teeth undergoing orthodontic treatment (Stenvik and Mjör, 1970; Delivanis and Gauer, 1980; Popp et al., 1992). However, Stenvik and Mjör (1970) concluded that these changes were not different from those in untreated teeth. Loss of tooth vitality during orthodontic treatment has also been reported, especially in previously traumatized teeth. Histologically, cell death

can be seen as either cellular necrosis and/or apoptosis. Even though previous studies called the changes in teeth undergoing orthodontic treatment necrosis, the term apoptosis is more suitable for nontraumatized teeth. Rana et al. (2001) investigated apoptotic changes with orthodontic mechanics in detail and could observe the maximum rate after three days of force application. In the long term, dental pulp damage due to orthodontic treatment varied from 2% to 17% for root canal obliteration and from 1% to 14% for pulpal necrosis in adolescents (von Böhl et al, 2012). In a systemic study by Weissheimer et al. (2021), there was shown to be low evidence in the current literature regarding the loss of pulp vitality during the application of orthodontic forces. However, a history of dental trauma may be considered a risk factor for the loss of pulp vitality during orthodontic treatment (Javed et al., 2015).

Several other factors are also involved in pulpal reactions to orthodontic force, the main one being the type of tooth movement. Intrusion, the movement that has the greatest impact on the root apex, is capable of occluding the pulpal blood supply (Vandevska-Radunovic et al., 1994; Sano et al., 2002). Moreover, Kvinnsland et al. (1989) and Nixon et al. (1993) reported a substantial increase in pulpal blood flow and in the number of capillaries after application of extrusive orthodontic forces. Mostafa et al. (1991) observed vacuolization and severe odontoblastic degeneration in dental pulps undergoing orthodontic extrusion for seven days. McDonald and Pitt Ford (1994) found decreased human blood flow after continuous light tipping forces, using laser Doppler flowmetry. Since orthodontic treatment involves complex three-dimensional (3D) tooth movements, it is not always possible to avoid movements that are relatively more detrimental.

Since the first rule of orthodontic mechanics is to avoid poorly controlled and jiggling forces (Krishnan and Davidovitch, 2009), the magnitude of the applied force is another important factor. Controlled intraoral orthodontic mechanics do not require heavy forces for tooth movement, but orthopedic treatment requiring forces over 500 g may have deleterious effects on the dental pulp. In a histological study, Küçükkeleş and Okar (1994) reported degeneration of vessel walls in teeth undergoing rapid palatal expansion (RPE) treatment. However, contrary to the results of

previous studies, a histomorphometric evaluation by Kayhan et al. (2000) has shown no pulpal differences between control teeth and teeth undergoing RPE. In a systematic review, the authors aimed to identify the optimal safe force levels for the pulp, but the literature showed inconclusive evidence regarding the force level that would cause the minimally detrimental pulp tissue reaction in humans (von Böhl et al., 2012).

The degree of pulpal reaction to orthodontic forces also depends on individual factors such as the age of the patient and the size of the apical foramen (Butcher and Taylor, 1951; Stenvik and Mjör, 1970). Hamersky et al. (1980) reported positive correlations between age and the rate of tissue respiratory depression. Therefore, the maturity of a tooth is an important aspect in preserving tooth vitality during orthodontic treatment, and clinicians should be cautious while moving teeth with closed apices.

As pulpal tissue is susceptible to thermal stress, temperature-generating orthodontic procedures such as stripping, thermal debonding, and residual adhesive removal after debonding require extra attention. The heat generated during rotary instrumentation may result in irreversible trauma to the pulp. Among the different modalities used for instrumentation, such as a handheld stripper, rotary disks, and an air-rotor stripping that utilizes diamond burs, the handheld stripper, which does not need any rotary instrument, has been found to be the safest method (Baysal et al., 2007). Thermal debonding using a carbon dioxide laser (Ma et al., 1997) is considered safest for debonding orthodontic brackets. Clean-up of residual resin using high-speed handpieces may cause vascular injuries and pulp necrosis. Zach and Cohen (1965) stated that a temperature rise of more than 5.5 °C will result in pulpal inflammation and an increase of 11 °C resulted in necrosis. Uysal et al. (2005) reported that clean-up of residual resin should be performed with adequate water cooling to avoid temperature changes exceeding the critical value. Eminkahyagil et al. (2006) concluded that tungsten carbide burs used at low speed may be the method of choice for adhesive clean-up.

Technological advancements in laser dentistry may be useful in the future for avoiding severe pulpal reactions. In a study performed on

rats, it has been shown that the use of low-level laser therapy (LLLT) during tooth movement results in an increase in vascularization and faster repair of pulpal tissue. LLLT has been shown to induce stem cell activity by increasing cell migration, proliferation, and viability, activating protein expression, and inducing the differentiation of progenitor cells (De Villiers et al., 2011). Low-level laser irradiation promotes the proliferation of mesenchymal and cardiac stem cells in culture (Zaccara et al., 2015). The therapeutic effects of LLLT, such as pain relief, acceleration of tissue healing, repair and neovascularization, increased fibroblast and collagen fiber proliferation, and decrease in the immune response, may provide an insight for optimization of orthodontic treatment (Abi-Ramia et al., 2010). The preferred dose of LLLT is 600–700 nm when a visible light spectrum is used (Tuby et al., 2007). According to the study by Zaccara et al. (2015), the parameters of LLLT (30 mW power, 660 nm wavelength, and 1.0 J/cm2 energy density) promoted cell proliferation. Laser therapy exerts a dose-dependent effect on biological responses and seems to have a cumulative effect at each new dose applied (Li et al., 2010).

Despite all these efforts to minimize adverse pulp reactions, it seems almost impossible to avoid hyperemia or reversible pulpitis during the early stages of orthodontic tooth movement. As shown by Popp et al. (1992), the signs of hyperemia diminish as blood flow returns to normal in 72 hours. These mild pulpitis reactions can be detected 2 hours after bonding/banding. Moderate pain caused by pulp hyperemia can last up to at least seven days (Polat and Karaman, 2005). Mild pain can be noted after each appointment due to the change in archwires, but pulp vitality is unaffected in most of these cases.

Differential diagnosis between symptoms of tooth movement and an inflamed tooth is very difficult, especially if there is a history of trauma. A patient with severe pain or pain that lasts for more than 10 days or who has darkening of the crown should consult a restorative specialist, preferably an endodontist. Radiographic evidence of an apical radiolucency may necessitate endodontic therapy (Hamilton and Gutmann, 1999), although orthodontic movement can be continued afterward.

During orthodontic treatment, the color of teeth may darken to gray or brown as a sign of discoloration, necrosis, or devitalization of the pulp. It is a rare phenomenon, but it does present an esthetic problem, especially when seen in an anterior area. It can also be seen during an orthognathic procedure in which an approach is made near the root apex, or direct resection is done, when pulp necrosis and discoloration and pulp diseases can develop (Kim, 2017; Figure 17.8).

Root resorption

Orthodontically induced external (apical) root resorption

Alveolar bone resorption is the basis of orthodontic tooth movement. Bone resorption occurs in a usual healthy periodontal environment, while the highly mineralized cementum is more resistant to the resorption process, because of its fluoride content and vascular nature. Moreover, the cemental surface is covered by a pre-cemental layer that is resistant to resorption (Reitan, 1974). The inflammatory process, incident and essential for tooth movement, is also a reason for orthodontically induced root resorption (OIRR). When orthodontic forces are applied over a sustained period of time, hyalinization of the compressed periodontal ligament (PDL) may develop rapidly. The defensive leukocytes that migrate out of PDL capillaries include osteoclast progenitors that promptly coalesce to form multinucleated cells, capable of resorbing mineralized tissues (Krishnan, 2017). External apical root resorption (EARR) is initiated when the protective layer of cementoblasts, interfacing with the hyalinized PDL, undergoes apoptosis and enables odontoclasts to resorb cementum and dentine. Initially, a protective layer of cementoid is removed that leaves a raw cemental surface open to odontoclastic attack (Brudvik and Rygh, 1993, 1994a, 1994b). It is usually seen in the apical region. There is a decrease in the hardness and elastic modulus of the cementum from the cervical to the apical region, making the apical areas prone to resorption (Chutimanutskul et al., 2006). When the forces are relieved, repair commences from the periphery, with fibroblast and cementoblast-like cells synthesizing collagenous fibrillar material and a new PDL. Most of the resorbed lacunae are repaired with secondary cementum (Reitan,

1985). Resorbed acellular cementum is always repaired with cellular cementum (Feller et al., 2016). According to Owman-Moll and Kurol (1998), 6–7 weeks after the termination of force, the amount of repair rises to 82%.

Root resorption caused by orthodontic therapy occurs in two locations: superficial surface resorption and in the apical third of the root (Figure 17.9). The increased incidence can be explained in two ways (Huang et al., 2005):

- First, the fulcrum of the tooth is more coronal to the apical third of the root and, due to the differences in the direction of the PDL fibers, forces are more traumatic to the apical region than to the coronal.
- Second, the middle and gingival thirds of the root are covered with acellular cementum, whereas the apical third is covered with cellular cementum, containing cells and blood vessels that have been damaged by heavy forces (Rygh, 1977).

Predisposing factors for root resorption can be divided into general factors and local factors (Krishnan, 2017). Among the general factors, the age at the start of orthodontic treatment, sex, ethnicity, systemic diseases and medications, and genetics can be mentioned. Among the local factors, tooth structure and root morphology are the main factors. Treatment and appliance type, amount of tooth displacement, type of tooth movement, duration, degree and amount of orthodontic force, anterior vertical intermaxillary elastics, and application of orthopedic forces were also assumed to be related to root resorption. Extraction treatment was found to be related to an increased rate of EARR, possibly because of the increased apical displacements and the close distance of the apex to the anterior cortical bone area (Sondeijeker et al., 2020; Yassir et al, 2021). However, a major factor for the occurrence of root resorption is individual susceptibility, which is not predictable (Rygh, 1977). The susceptibility to root resorption differs among individuals, as well as within the same individual at different periods of time. Hormones, body type, and the metabolic rate trigger signals that initiate fluctuations in osteoclastic and osteoblastic activities. In certain systemic diseases such as allergy and asthma, there is increased

susceptibility to resorption (Davidovitch, 1996; Davidovitch et al., 2000; McNab et al., 1999). The maxillary and mandibular incisors, maxillary first molars, maxillary first and second premolars, and maxillary canines are the teeth that are more prone to root resorption. One reason for the high prevalence of root resorption among incisors may be their thin root morphology, but it is more likely due to the excessive movement during orthodontic treatment – that is, round tripping – and contact with the cortical plates of alveolar bone, particularly during the use of intraslot torque, which generates very heavy forces (De Angelis and Davidovitch, 2009). If there was pretreatment root resorption, the rate might increase from 4% to 77% during treatment (Goldson and Henrikson, 1975). Previously traumatized teeth presented an important risk for OIRR (Linge and Linge, 1991), but Malmgren et al. (1982) concluded that resorption rates do not increase in the presence of trauma if a normal PDL environment is maintained (as a result of applying appropriate mechanics). Although Wickwire et al. (1974) found a greater incidence of resorption during orthodontic treatment in 53 endodontically treated teeth, Spurrier et al. (1990) and Remington et al. (1989) found lower resorption rates in such teeth due to their increased dentin hardness and density after the orthodontic treatment (Figure 17.10). Retreatments were not found to negatively influence the risk of EARR (Sondeijeker et al., 2020).

Figure 17.8 A maxillary incisor that showed discoloration two weeks after bimaxillary orthognathic surgery. Orthodontic force levels were reduced, hoping that regeneration might occur, but the brownish color did not change in eight months. Therefore, at the end of the orthodontic treatment nonvital bleaching was applied.

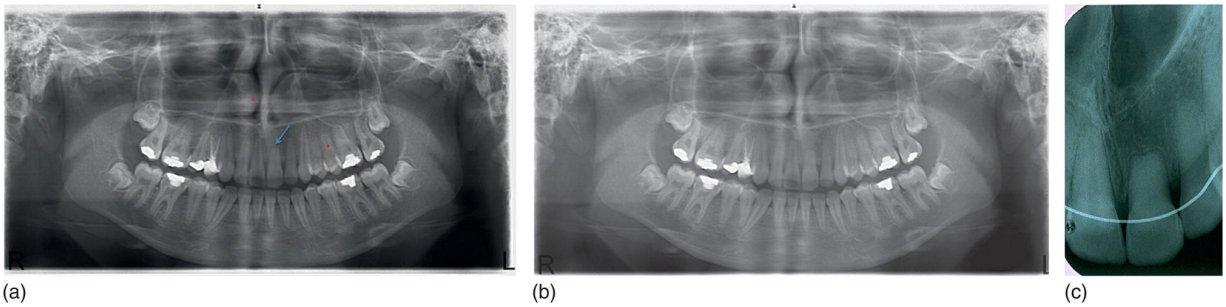


Figure 17.9 Orthodontically induced apical root resorption in the apical third of the root. (a) At the end of fixed appliance treatment. (b) At one-year follow-up. (c) Periapical radiograph at 14-month follow-up. Resorption has not progressed. The tooth has been splinted with a flexible wire retainer due to slight mobility.

Fixed appliances have more detrimental effects on teeth than

removable appliances (Linge and Linge, 1983). Specific movements like intrusion and torque are more associated with root resorption than the other types of movement. Resorption is also observed in teeth subjected to faulty mechanics in the early stages of treatment, such as in uncontrolled tipping of maxillary incisors in order to reduce excessive overjet (De Angelis and Davidovitch, 2009). According to a systematic review, orthodontic treatment with clear aligners might not avoid root resorption, but both the incidence and severity of resorption could be lower compared with results reported for treatment with fixed appliances (Fang et al., 2019). Pamukçu et al. (2020) found no differences in root resorption rates between nonextraction lingual treatment and labial treatment; however, currently there are no data regarding extraction treatment. The relationship between the length of treatment time and root resorption has been positively correlated by a majority of the studies (Brezniak and Wasserstein 2002; Sameshima and Asgarifar, 2001).

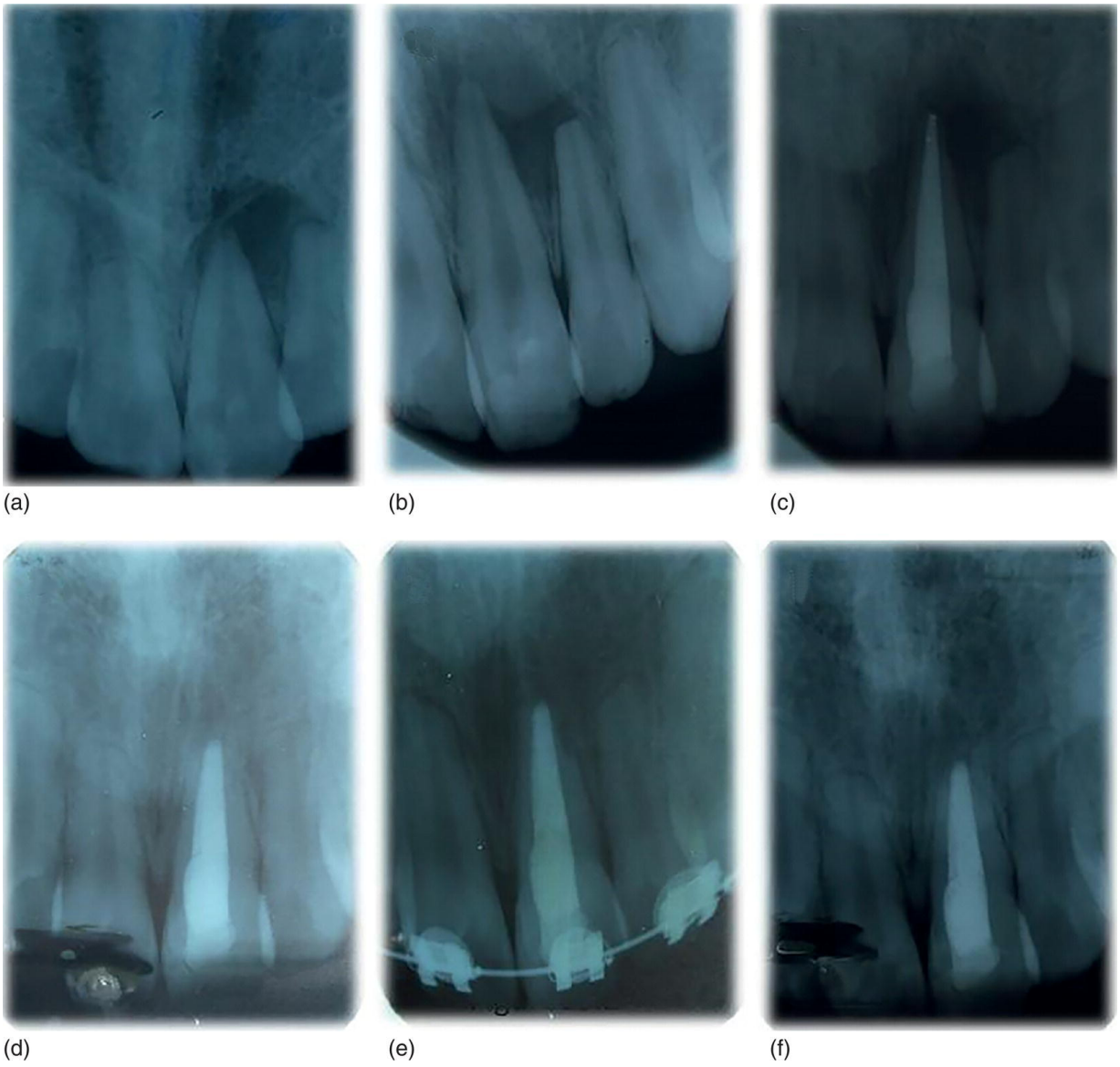


Figure 17.10 Root resorption due to orthodontic treatment. (a, b) The talon cusp of the left central incisor was ground down during orthodontic treatment. Note that only this tooth did not demonstrate apical resorption, as it was nonvital due to pulp/dentin exposure, which was not diagnosed during the grinding procedure. (c, d) Treatment of chronic apical periodontitis with root canal treatment and apical resection. (e) Patient was retreated orthodontically. (f) After the second orthodontic treatment, the left central incisor showed no resorption and was also asymptomatic without any mobility.

The presence of root resorption can be established using

conventional radiographic methods, subtraction radiography, cone beam computed tomography (CBCT), scanning electron microscopy, and histopathology (Nanekrungsan et al., 2012). The periapical method, especially with the paralleling technique, seems to be the best conventional method, with minimal distortion and superimposition of anatomical structures. The periapical and panoramic methods provide two-dimensional (2D) evaluation, but CBCT is the only method that provides 3D evaluation. Dental CBCT offers a lower radiation dose, fewer artefacts, and faster image projection than a conventional CT (Dudic et al., 2009), but is not recommended for this purpose because of the high radiation dose (Sondeijker et al, 2020). Histopathological examination and scanning electron microscopy are clearly not methods that are clinically applicable. Root resorption may also be diagnosed with the help of dentinal proteins such as dentin matrix protein 1 and dentin phosphophoryn, which are released into the gingival crevicular fluid during active root resorption (Mah and Prasad, 2004).

The clinician's role in minimizing root resorption

The strategies to minimize external root resorption should include identification of systemic and local risk factors at the stage of treatment planning, limitation of treatment duration, the use of light intermittent forces, and biannual radiographic monitoring in order to detect any possible root resorption at the earliest stage (Lim et al., 2011).

Treatment plans for patients with predisposing factors should ensure that teeth will not be moved unnecessarily and into contact with cortical plates of alveolar bone, in order to avoid any additional resorption. The timing of the first radiograph to detect the signs of EARR was proposed as 6–12 months after the initiation of fixed orthodontic treatment, especially in patients with premolar extractions (Sondeijeker et al., 2020). When a sign of EARR is detected, the clinician has to decide whether to continue or to stop orthodontic treatment. If the decision will be for the continuation of the treatment, then the treatment goals can be re-evaluated and modified, if needed. If any sign of resorption is seen in the radiographs, the application of orthodontic force can be interrupted for at least three months to allow for repair (Reitan, 1964; Levander

and Malmgren, 1988; Sondeijeker et al., 2020). After the rest period, caution is required and a follow-up radiograph after six months might be indicated, but, more importantly, the appliances should be adjusted to deliver the appropriate mechanical forces, and excluding the affected teeth from the appliances may also be an option. If the decision will be for termination of the treatment, especially in cases of generalized resorption, the clinician may be relieved to hear that iatrogenic root resorption usually does not progress once orthodontic force is discontinued.

A tooth with severe resorption and increased mobility can be splinted to the neighboring teeth. The retention appliances should be passive and regular retention check-ups should be made. The patient should be informed about the situation and advised to be careful in the use of these teeth. During the retention period, the clinician should prevent occlusal trauma to the resorbed teeth through modification in the retainers (Dougherty, 1968). Root canal treatment is usually not needed, but rarely when the pulpal nerve is affected the patient might experience some pain. In rare cases, resorption continues despite termination of orthodontic treatment and does not stop until splinting and endodontic therapy are performed (Gholston and Mattison, 1983). For severe, active lesions, endodontic treatment should be performed with a calcium hydroxide paste, but if the resorption has ceased, the canal can be filled with gutta-percha. A crown/root ratio of 1 : 1 is sufficient for maintaining the tooth. If the root length is shorter than this, the tooth is likely to be unable to bear the functional loads of mastication. The literature presents some case series and reports, but none of the resorbed teeth was lost during a follow-up period of 5–25 years (Sondeijeker et al., 2020). However, the patient should be informed that the affected teeth may be lost early due to periodontitis. Although vitality is rarely affected, endodontic treatment should be performed if the crown/root ratio is less than 1 : 1. A search for pharmacological agents capable of repairing root resorption revealed that bisphosphonates (Liu et al., 2004; Sedghizadeh et al., 2021), echistatin (Talic et al., 2006), and low doses of corticosteroids (1 mg/kg; Ashcraft et al., 1992; Demir and Arici, 2021) have positive effects, whereas high doses (15 mg/kg) have a reverse effect.

Invasive cervical root resorption

Invasive cervical resorption (ICR) is a relatively rare and aggressive form of external root resorption that begins with cemental damage just below the epithelial attachment, leading to progressive destruction of tooth structure (Gülşahı, 2014). It usually affects single teeth, but in rare cases multiple teeth are affected (Coyle et al., 2006). Cervical location is the characteristic feature, and resorption of coronal dentin and enamel creates a pinkish color as the vascular tissues become visible (Heithersay, 2004; Figure 17.11). The lesions are characterized by highly vascular fibrous tissue with osteoclasts arising from the PDL (Smidt et al., 2007). Since microorganisms are rarely found, microbial involvement in these lesions is doubtful (Heithersay, 1999; Trope, 2002). A study of 222 patients who displayed ICR showed that orthodontic treatment, trauma, intracoronal bleaching, and surgery involving the cementoenamel junction were the major predisposing factors. In that study, 21.2% of patients were reported to have a history of orthodontic treatment. Diabetes has also been suggested as a predisposing factor, as factors like inflammation and oxidative stress, the activation of clastic cells, and the promotion of angiogenesis are linked to the hypoxic cellular tissue environment (Galler et al., 2021). Regarding the relation to orthodontic treatment as a risk factor for cervical resorption, there are conflicting results in the current literature. In a recent systematic review (Khalaf et al., 2022), two randomized control trials (RCTs) and one cohort study were analyzed to investigate whether orthodontic treatment could be considered as a risk factor for cervical resorption. The RCTs (Dudic et al., 2017; Giannopoulou et al., 2016) showed that both a loss of cervical volume and an increase in the formation of cervical resorption were found in teeth that underwent orthodontic force application. However, in the cohort study by Thönen et al. (2013), 175 patients, who had completed their treatments about eight years before, were recalled for their final orthodontic check and cervical root resorption was found in only one patient after a CBCT evaluation. So orthodontic treatment has the potential to stimulate cervical root resorption, but the literature is still lacking high-quality studies to conclude a direct relation, instead of an idiopathic cause.

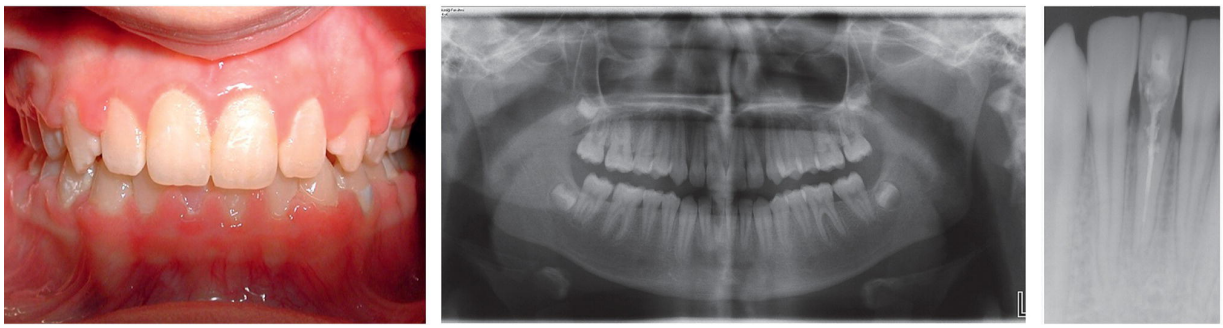


Figure 17.11 (a, b) Invasive cervical resorption after orthodontic treatment, demonstrating a pinkish color. (c) The patient was referred to an experienced endodontic specialist for treatment of invasive cervical resorption by elimination of the actively resorbing tissue and restoration of the defect with a suitable filling material (mineral trioxide aggregate). However, conventional root canal treatment was carried out by a general practitioner and the prognosis remained poor.

ICR is painless and rarely symptomatic. The resorption process starts below the gingival margin and extends apically and coronally along the root dentin (Smidt et al., 2007). The lesion is often separated from the pulp by the predentin layer, which is the last to resorb (Heithersay, 2004). A clinical feature is a pink coronal discoloration close to the gingival margin. It can go unnoticed for months to years and only become evident on routine radiography. Conventional radiographs taken from different angles can identify the involved surfaces, but a 3D visualization of the exact size and location of the lesion requires a small-field CBCT scan (Kim et al., 2003; Gulsahi et al., 2007; Gulsahi, 2014). CBCT is very useful in diagnosis and treatment planning of ICR. In addition, it is often used alongside conventional imaging to address the extent of the lesion and the prognosis of the affected tooth. Two important features of ICR differentiate it from internal root resorption. One is the absence of pulpal signs and the other is the radiographic appearance of the pulp canal size (Gulabivala and Searson, 1995; Smidt et al., 2007). In ICR the canal space is unchanged, and the radiolucency extends coronally and apically in the dentin (Figure 17.12).

ICR is quite aggressive; therefore, the orthodontist should refer the patient as soon as the lesion is diagnosed. The treatment should be

performed by experienced specialists to prevent tooth loss. The rationale for treatment of ICR is elimination of the actively resorbing tissue and restoration of the defect with a suitable filling material (Figure 17.13). Both nonsurgical and surgical treatment approaches can be used. Nonsurgical regimens involve topical application of a 90% aqueous solution of trichloroacetic acid for the induction of coagulation necrosis to the lesion area, curettage, endodontic treatment if pulpal perforation is present, and GIC restoration. The use of calcium hydroxide for neutralization of the lesion, elimination of microorganisms, and inactivation of toxic products is also recommended (Frank, 1981; Estrela and Holland, 2003). If the margin of the lesion is below the cervical line, orthodontic extrusion can be performed. Extrusive orthodontic forces can be applied for 4–6 weeks and during the extrusion crown shortening can be performed if premature contact occurs. Fiberotomy can be performed for maintenance of the extruded tooth (Smidt et al., 2007). The cases with cervical resorption do not usually show ankylosis, but if the healing occurred with replacement resorption with ankylosis, the orthodontic extrusion will be likely to fail (Luso and Luder, 2012; Figure 17.14).

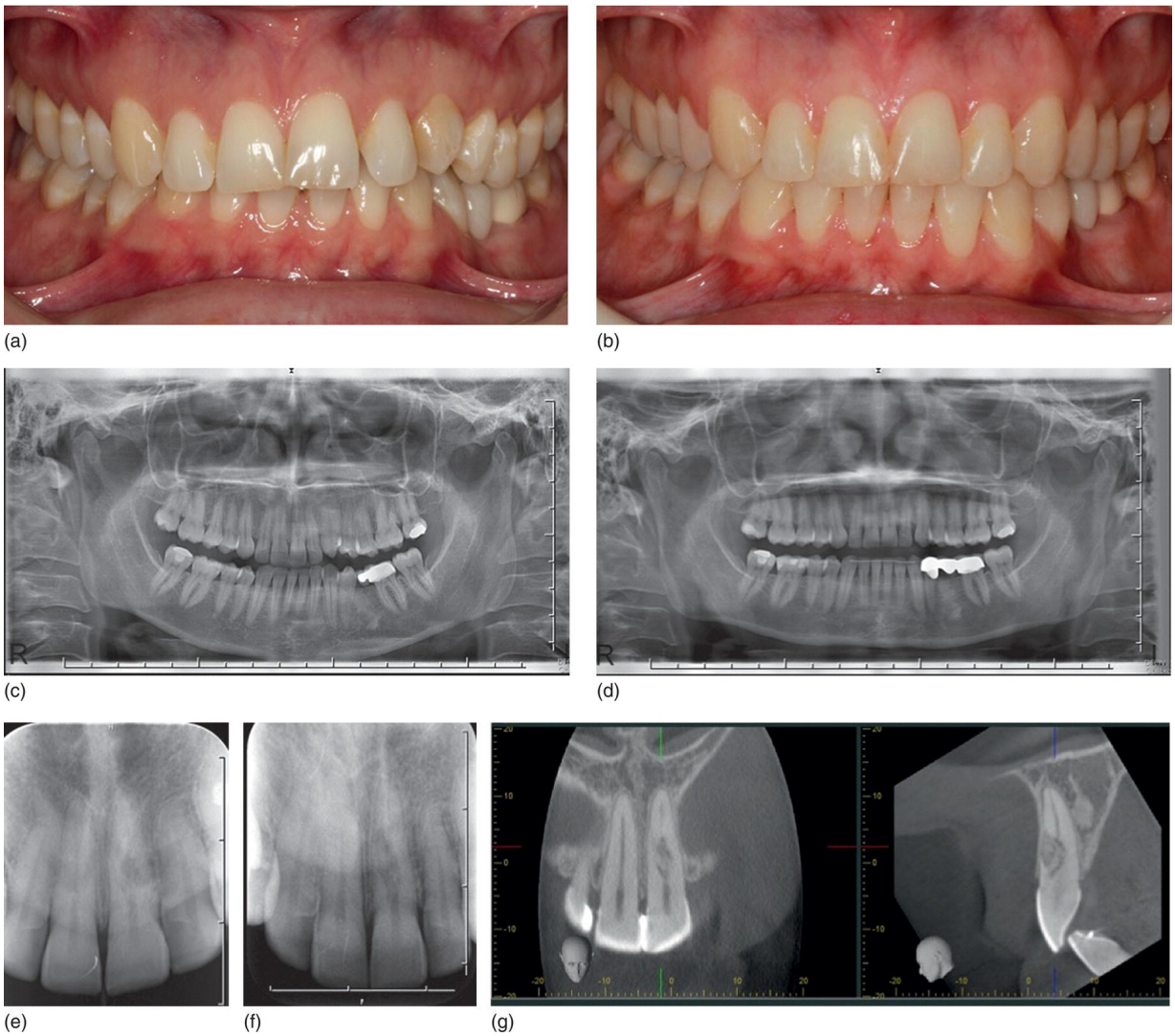


Figure 17.12 The 37-year-old patient's main complaint was rotation of her upper right canine and inadequate restoration space for # 35 (a, c). The internal resorption in # 21 was misdiagnosed at the beginning of the treatment (c). After one year of orthodontic treatment with fixed appliances, the rotations were corrected and adequate space for proper restoration of # 35 was obtained (b, d). At the end of the orthodontic treatment, the internal resorption of # 21 was diagnosed and it was decided to follow the patient to understand the prognosis. Follow-up periapical radiographs were taken after two years (e) and four years (f), and cone beam computed tomography scans were obtained six years after completion of the treatment (g).

Surgical treatment involves periodontal flap surgery, curettage, and restoration of the defect. Restorative materials that have been used

previously include amalgam, composite resin, and GIC (Lustmann and Ehrlich, 1974; Frank, 1981; Frank and Blakland, 1987). Currently, MTA is recommended to restore the resorptive cementum in cervical resorption cases (Frank and Torabinejad, 1998; White and Bryant, 2002; Yilmaz et al., 2010). Baek et al. (2005) have shown that the type of cementum coverage achieved using MTA had not been achieved with any other material. White and Bryant (2002) reported an increase in radiodense crestal bone when MTA was used with guided tissue regeneration to fill an external root resorption site with a bone defect. A platelet-enriched fibrin sealant (TISSEEL™, Baxter Healthcare, Deerfield, IL, USA) has been in use for a long time for sinus floor augmentation, treatment of peri-implantitis, intrabony periodontal defects, and alveolar ridge reconstruction. Ren et al. (2000) have demonstrated that TISSEEL enhances the healing of exposed pulp tissue in dogs. Though dentinal bridge formation was not present in most cases, the authors concluded that fibrin sealant was a promising material as a bioactive pulp capping agent.

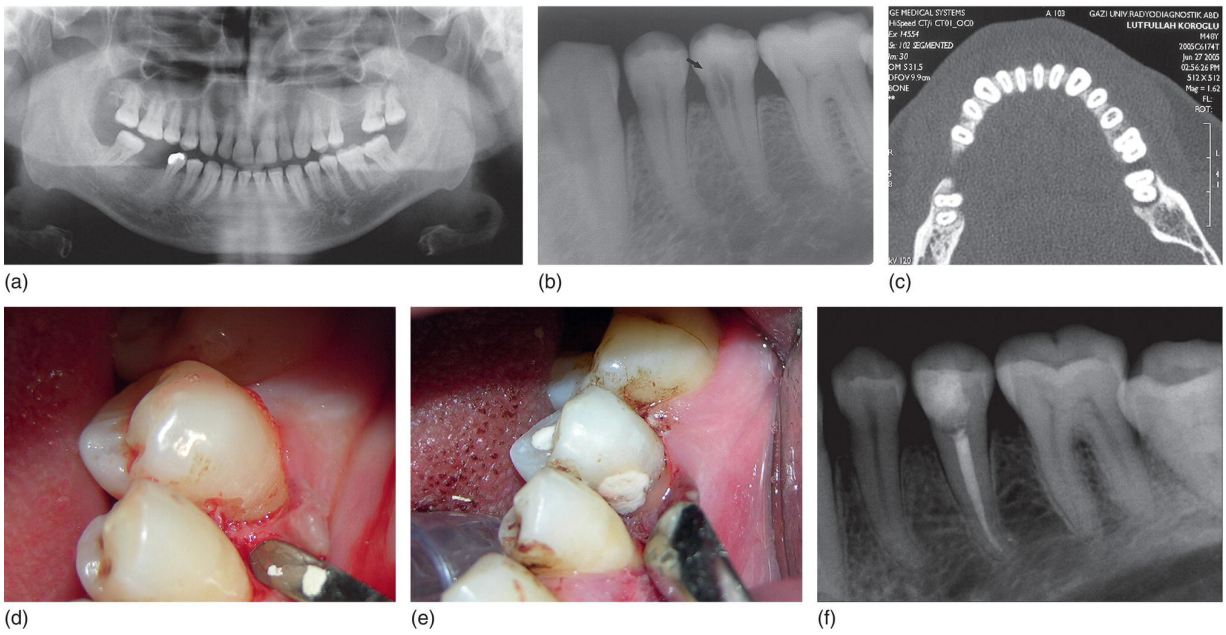


Figure 17.13 Diagnosis and treatment of invasive cervical resorption. (a) Note the extensive irregular radiolucency in the left mandibular second premolar in the panoramic radiograph. (b) The periapical radiograph of the left mandibular second premolar tooth shows an irregular radiolucent area in the tooth crown (arrow). (c) Axial computed tomography scans taken from coronal to apical and obtained with a bone window setting showing extensive resorption in the mesial cervical area of the left mandibular second premolar. (d) Intraoral appearance of the resorption area. (e) Intraoral appearance after the root canal treatment and restoration of the resorbed area. (f) Periapical radiograph at six-month follow-up.

Source: Gulsahi et al. (2007) / from Elsevier.

Figure 17.14 Ankylosis can occur in cases of invasive cervical resorption. (a, b) A patient referred to the orthodontic clinic for treatment of cervical resorption via orthodontic extrusion after periodontal curettage. (c) Orthodontic force was applied after occlusal grinding. (d) No movement occurred following three months of force application as the tooth was ankylosed. It was then extracted.

Emergency orthodontic treatment in trauma cases

There are instances where other dental disciplines may require orthodontic collaboration, such as in trauma patients referred from emergency clinics. Trauma to the orofacial region occurs frequently and comprises 5% of all injuries that require treatment (Glendor et al., 2007). Dental injuries, which are the most common among all

facial injuries, are experienced by more than 20% of children, mostly between the ages of 8 and 12 (Glendor et al., 2007; Moule and Moule, 2009). Boys sustain dental injuries about twice as often as girls do. Most dental injuries involving the maxillary incisors occur in cases of Class II Division 1 malocclusion, with increased overjet and inadequate lip closure (Forsberg and Tedestam, 1993; Burden, 1995). Emergency management of traumatized teeth is usually performed by a pediatric dentist or an endodontic/restorative dentistry specialist, but an interactive approach involving the orthodontist in the trauma management team is advised. Orthodontic treatment planning for patients with previously traumatized teeth often requires decisions regarding the long-term viability of the traumatized teeth and effects of trauma on the developing dentoalveolar complex.

Treatment of crown fractures

Treatment of an uncomplicated crown fracture can be accomplished quite successfully by either a build-up with acid-etch composite resin, or by reattaching the fractured segment, if available, using an adhesive bonding system (Figure 17.15). The expected outcome for either approach is excellent, with nearly 100% pulp survival regardless of root developmental status (Robertson et al., 2000). The appropriate time for evaluating the vitality of the tooth is eight weeks after the trauma.

A fracture involving dentin exposes dentinal tubules in direct communication with the pulp. Therefore, timely protection of the exposed dentin is advisable to prevent the pulp from undergoing infection-related necrosis. Complicated fractures of the primary teeth require decisions based on life expectancy of the primary tooth and vitality of the pulpal tissue (Flores, 2002; Shah, 2020). If the fracture occurs in an adult with fully formed roots, it will be more practical to perform root canal treatment prior to the prosthetic restoration and/or orthodontic treatment. On the other hand, it is very important to make every effort to preserve pulp vitality in young patients with developing permanent teeth, as continued pulp vitality facilitates root development (Fuks et al., 1987; Ojeda-Gutierrez et al., 2013). The exposed pulp will develop granulation tissue to protect

the exposed wound and bacteria will invade the pulp tissue gradually. However, it may take many days for bacteria to penetrate even a few millimeters, so the pulp can be preserved even if it has been exposed for more than 24–48 hours (Heide, 1991). Therefore, complicated fractures should not be viewed as hopeless situations for pulp survival in young patients. Cvek (1978) introduced a procedure known as the Cvek pulpotomy technique, which employs calcium hydroxide for pulp capping. This vital pulpotomy technique should be performed as soon as possible after the trauma. As long as the pulp is alive and is properly protected, continued root development can be expected.

If pulpal necrosis accompanies the fracture, the general treatment protocol involves root canal treatment followed by protective permanent restorations. The open and sometimes divergent apical morphology and weak root dentinal walls make endodontic procedures challenging and present restorative problems. More definitive treatment options such as implant-supported crowns or fixed prostheses may not be feasible until craniofacial growth is complete, which can be up to the age of 25 years (Op Heij et al., 2006).

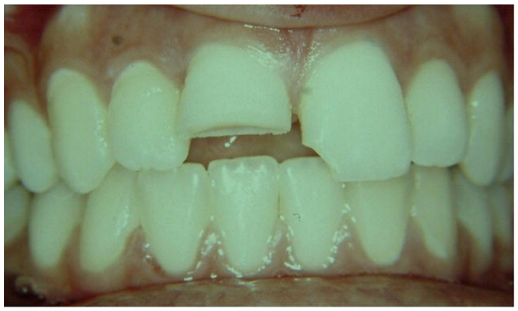
Apexification

Apexification is a method of inducing a calcified apical barrier in an incompletely formed root of a pulpless tooth, which has now become a routine endodontic procedure. The treatment involves the use of calcium hydroxide to fill a debrided, biomechanically prepared immature root canal. The calcium hydroxide leaches from the canal over time and needs to be replenished every 3–6 months. Apexification may take between 6 and 24 months to promote formation of a hard apical barrier to allow condensation of a gutta-percha root filling (Rafter, 2005). Recent studies suggest using MTA as an apical plug, as it reduces the duration of time required for the calcium hydroxide dressing and overall treatment (Felippe et al., 2006; Simon et al., 2007; Shaik et al., 2021; Figure 17.16).

Some patients requiring apexification might be under orthodontic treatment or are at an age when orthodontic treatment should be initiated. Delaying orthodontic treatment in these patients will

prevent the achievement of optimal treatment results, which are usually obtained in the growing stages. Steiner and West (1997) showed successful formation of the apical barrier in two incisors of an 11-year-old patient with apexification performed simultaneously with orthodontic treatment. Fully formed apical barriers were evident after two years of endodontic treatment and orthodontic treatment was completed six months later. Anthony (1986) also reported a successful apexification procedure during active orthodontic movement. These reports demonstrate that a calcified barrier develops even with ongoing resorption and apposition during orthodontic movement.

REPs are the method of choice for inducing vitality, apical growth, and thickening of dentinal walls in teeth with immature pulp. The radiographic image of root development of revascularized teeth has been demonstrated by many studies performed at different follow-up intervals. Saoud et al. (2014) reported in their study that earlier apical closure was observed at six months, and only 10 out of 20 REP cases showed complete apical closure one year later. Other studies have reported that an earlier change in root length was achieved at six months (Bose et al., 2009), and that root growth was observed to continue in 5–15% of cases after a one-year follow-up period (Jeeruphan et al., 2012; Bose et al., 2009). Similar to previous studies, Natera and Mukherjee (2018) also reported successful orthodontic treatment of REP-treated teeth similar to nonendodontically treated teeth.



(a)

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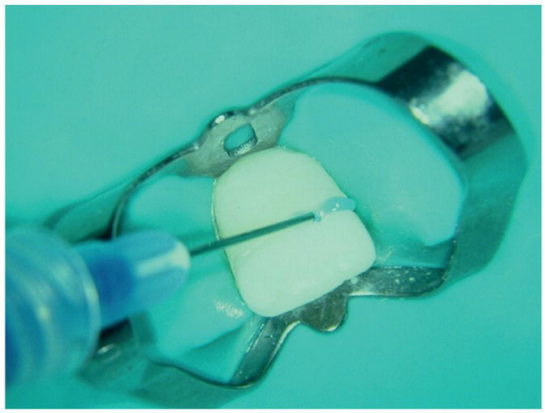

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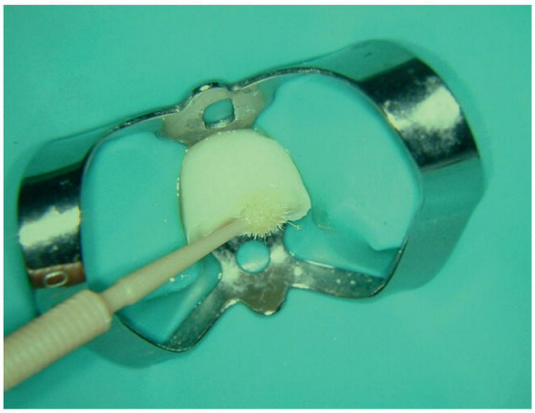

(g)

(h)

(i)

(j)

Figure 17.15 Step-by-step progression of reattachment of the fractured segment of a central incisor using an adhesive bonding system. (a–c) Intraoral and radiographic views before treatment. (d) Broken fragment of tooth. (e–g) Reattachment procedure. (h) After reattachment and polishing. (i, j) At one-year follow-up. The tooth was vital.

Source: Arhun and Ungor (2007) / courtesy of John Wiley and Sons.

Figure 17.16 Apexification treatment using mineral trioxide aggregate (MTA) as an apical plug. (a) Replantation of avulsed left central incisor one hour after trauma. (b, c) Three days after replantation. (d) Apexification treatment using MTA as an apical plug. (e, f) At the three-month follow-up. Courtesy of Dr. Sevi Burçak Çehreli.

Another common problem in teeth with open and divergent apical root areas is the high risk of cervical fracture during or after the root canal treatment. Most fractures are observed within three years of commencing long-term calcium hydroxide treatment. The frequency ranges from 77% in teeth with the least root development to 28% in

teeth with the fully developed roots (Cvek, 1992). The adverse effects of long-term calcium hydroxide administration on the physical properties of the root dentin were studied (Andreasen et al., 2002; Rosenberg et al., 2007). Andreasen et al. (2006) recommend placing calcium hydroxide for a maximum of four weeks followed by filling the canal with MTA. Other methods proposed to reduce the fracture risk include use of composite resin in the root canal and metallic posts embedded in MTA. Current evidence suggests that placement of composite resin materials deep into the coronal aspect of the root canal imparts superior fracture resistance (Desai and Chandler, 2009). Reducing the amount of coronal root canal filling and replacing it with composite resin should have the secondary benefit of reducing coronal leakage and contributing to endodontic success.

Even with the increased risk of fracture, these teeth should not be arbitrarily extracted because they help to maintain the developing alveolar ridge, act as a space maintainer, and preserve the natural appearance of the site. If the tooth eventually fractures after the completion of dentofacial growth, a permanent replacement can be more favorably placed. Root fractures, which comprise 0.5–7% of all trauma cases, are more likely to be observed in the maxillary anterior region of males in the 11–20-year age group (Andreasen et al., 2007). Radiographs may reveal one or more radiolucent lines separating the tooth fragments and multiple-angled radiographs can confirm these findings (American Academy of Pediatric Dentistry, 2004).

Treatment of root fractures

Main factors influencing the healing process of root fractures include the amount of displacement of the coronal segment, the stage of root development, and the severity of the trauma. Ideally root fractures are repaired with hard tissue, but sometimes there is also redundant healing with connective or granulation tissue (Skaare and Jacobsen, 2003). In permanent teeth, the location of the root fracture has not been shown to affect pulp survival after injury (Andreasen and Andreasen, 2000). Therefore, root fractures occurring in the tooth's cervical third or apical third can be treated successfully by stabilization of the repositioned fragment (Figure 17.17).

According to the guidelines of the International Association of Dental Traumatology, for treatment of root fractures the coronal segment should be repositioned as soon as possible and then stabilized in its anatomically correct position with a passive flexible splint for four weeks (Flores et al., 2007; Bourguignon et al., 2020). Avoidance of any occlusal contact is of prime importance (Hovland, 1992; Yates, 1992). Various types of splints have been introduced over the years for stabilization of fractured segments, including splinting via orthodontic brackets (Mackie and Warren, 1988; Cengiz et al., 2006). Orthodontic splints are often advantageous in multiple tooth injuries, as any tooth included in them can be removed from the splint or aligned into the desired position if needed.

Many authors have reported successful healing of crown/root or root fractures without any endodontic treatment (Poi et al., 2002; Erdemir et al., 2005; Polat-Ozsoy et al., 2008). The communication of the fracture line with the oral environment, which may promote bacterial contamination, determines the healing process (Hovland, 1992). If the apical root fragment is long enough to support a coronal restoration, the definitive treatment alternatives are to remove the coronal fragment and perform endodontic treatment, followed by a supragingival restoration or necessary gingivectomy, osteotomy, and surgical or orthodontic extrusion to prepare for restoration (Andreasen and Andreasen, 2000).

Figure 17.17 Treatment of horizontal root-fractured maxillary incisors. (a, b) Initial intraoral and radiographic views. (c) Orthodontic brackets and an 0.016 in. stainless steel archwire for splinting. First- and second-order bends were made in the archwire to retain forward positioning of the incisors during splinting in order to prevent the traumatized incisors from contacting the lower teeth. (d, e) Day 20: note the color change in the tooth. (f, g) Intraoral and periapical views after removal of brackets at week 14. (h, i) Clinical and radiographic appearance after nine-month follow-up.

Source: Polat-Ozsoy et al. (2008) / courtesy of John Wiley and Sons.

Orthodontic treatment of the teeth with repaired root fractures is possible, even if the fracture at the time of the accident is extensive, with marked fragment dislocation. In cases where the repair occurs without separation of the fragments, the apical fragment may remain

attached to the coronal portion throughout and following orthodontic treatment. On the other hand, separation of the segment may be enhanced by orthodontic tooth movement (Hamilton and Gutmann, 1999). It is recommended that teeth with these types of fractures be observed for at least two years before initiating orthodontic treatment. Hovland et al. (1983) presented a successful case followed up for eight years, in which a maxillary central incisor with a transverse fracture at the junction of the apical and middle thirds of the root was moved palatally and intruded during orthodontic treatment. Erdemir et al. (2005) also demonstrated satisfactory healing of a horizontal root fractured maxillary incisor without treatment, which was moved orthodontically a long time after the trauma (Figure 17.18).

Orthodontic extrusion of teeth, or so-called forced eruption, was first described by Ingber (1974) for treatment of one-wall and two-wall bony pockets that were difficult to manage with conventional therapy alone. The criteria to help determine whether the tooth should be forcibly erupted or extracted are root length, root form, level of the fracture, relative importance of the tooth, esthetics, and endo/perio prognosis (Kokich, 2002). Orthodontic extrusion can be achieved with various kinds of fixed or removable orthodontic appliances (Cengiz et al., 2005; Yüzügüllü et al., 2008). Bonding an attachment to the remaining root fragment might be difficult sometimes because of lack of available tooth tissue and difficulties in isolating the bonding interface from the gingival crevicular fluid and blood. Metal endodontic posts may be useful for extrusion of the root without buccal tipping (Arhun et al., 2006b; Figure 17.19). A more esthetic approach for bonding is building a composite core using a tooth-colored glass-fiber post (Yüzügüllü et al., 2008; Figure 17.20). It is possible to use a T-loop or a spring, as well as an elastic module, to apply vertical extrusive force. In order to achieve controlled root movement in the vertical and antero-posterior direction, first- and second-order bends on the main archwire can be used as well (Proffit, 2000: 615–673; Arhun et al., 2006b). A force of only 20–30 g is sufficient for extrusion. However, some clinicians prefer higher forces of 50–60 g for rapid extrusion of traumatized teeth (Malmgren et al., 1994). After adequate extrusion is achieved by forced eruption, a fiberotomy of the stretched periodontal fibers is

usually performed to prevent relapse (Heithersay and Moule, 1982; Malmgren et al., 1994).

Intrusive luxation

A special type of dental trauma for which an interactive strategy is required is intrusive luxation, common in the deciduous dentition. This might result in unexpectedly severe complications, such as pulp necrosis, inflammatory root resorption, ankylosis, replacement resorption, and loss of marginal bone support. Different approaches have been suggested for tooth repositioning, such as observation for spontaneous re-eruption, surgical crown exposure, orthodontic extrusion (with or without previous luxation of the intruded tooth), and surgical repositioning (Turley et al., 1987; Oulis et al., 1996). Immediate application of orthodontic force on traumatically intruded teeth facilitates extrusion, allowing early endodontic access. It can prevent ankylosis; however, it may increase the risk of external root resorption and marginal bone loss (Oulis et al., 1996; Chaushu et al., 2004b; de Alencar et al., 2007). The most appropriate time of initiating orthodontic extrusion after an injury is still controversial. It is customary to delay orthodontic tooth movement until the teeth have been symptomless for at least a few months. However, although the risk of root resorption is reduced, this observation period may result in the development of ankylosis and delay endodontic access (Turley et al., 1987). A high success rate (95.4%) was observed in orthodontically extruded teeth, both immediately (within 10 weeks post trauma) and later (after three months; Medeiros and Mucha, 2009; Figures 17.21 and 17.22). Using the adjacent teeth as anchorage for extrusion should be avoided, as they may also be affected by the trauma, and unwanted tipping or intrusion may result. In order to prevent side effects, adjacent teeth can be splinted, or palatal arches soldered to molar bands, and self-supporting labial arches can be used. Fixed retainers should be used for retention (Chaushu et al., 2004b).

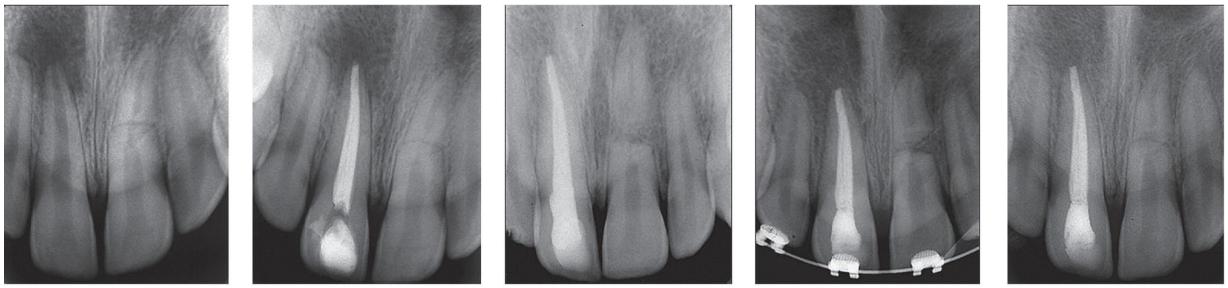

Figure 17.18 Orthodontic movement of a horizontally fractured tooth. (a) Periapical radiograph showing a radiolucency in the maxillary right central incisor and a horizontal root fracture in the left central incisor. (b) Postoperative radiograph. No treatment was performed in the maxillary right incisor as there was no evidence of pathology and pulp tests were positive. (c) Six months following endodontic treatment. The right central incisor has healed without treatment. (d) Radiograph one year after the endodontic treatment. Note the orthodontic brackets on the teeth. The orthodontic treatment was started three months previously. The coronal fragment of the right central incisor had moved relative to the apical. The orthodontic treatment was stopped as the orthodontic problem was mild. Pulp tests remained positive, but mobility increased slightly. (e) 12 years post trauma and 6 years after orthodontic treatment. The tooth was asymptomatic and showed a good appearance clinically and radiographically. Erdemir et al. (2005) / courtesy of John Wiley and Sons.

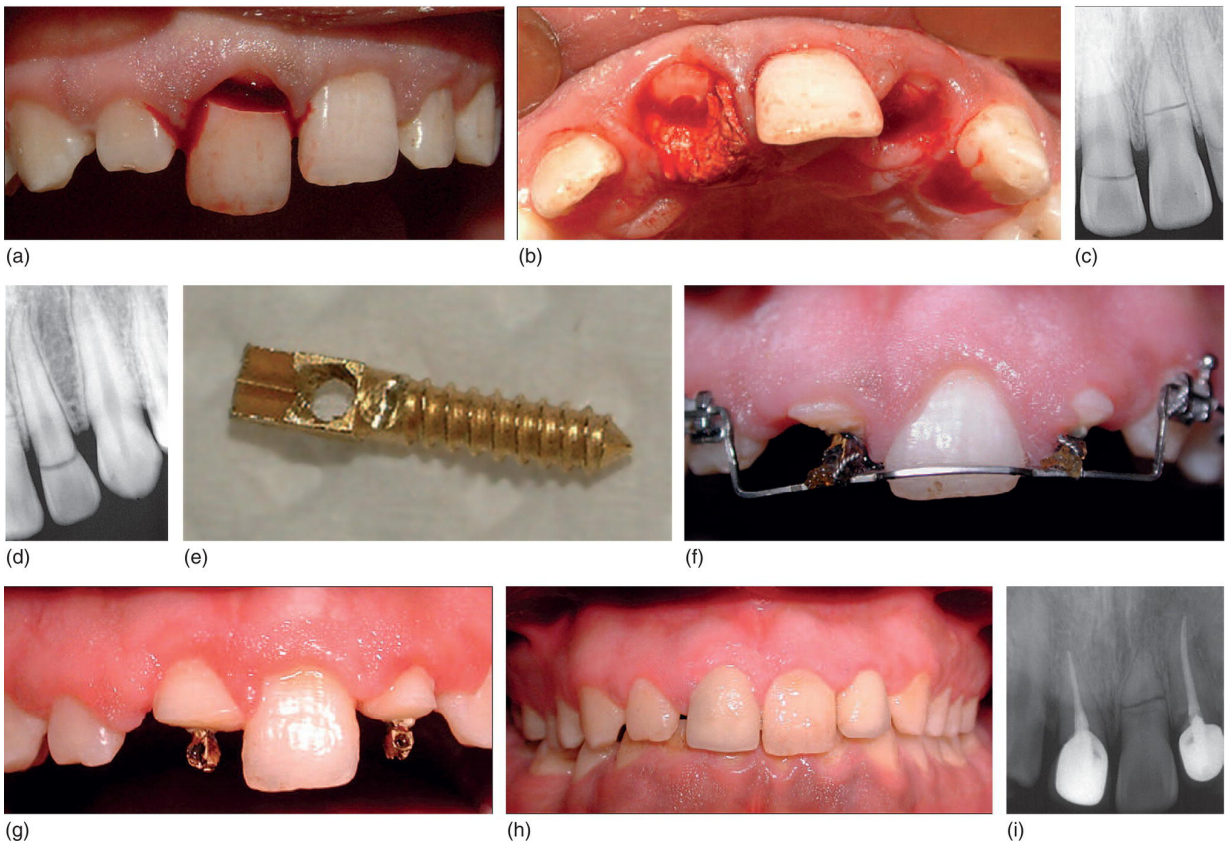

Figure 17.19 Orthodontic extrusion or forced eruption of roots via metal endodontic posts. (a–d) Fractured anterior teeth in a 19-year-old male patient as a result of a road traffic accident. The right central and lateral incisor was treated endodontically, while the left central incisor was untouched and observed. (e) Metal endodontic post with a drilled hole for orthodontic force application. (f) Orthodontic extrusion with posts. (g) The roots after extrusion. (h) Final restoration after gingival recontouring and fiberotomy. (i) At 19-month follow-up.

Source: Arhun et al. (2006a) / from Springer Nature.

Tooth avulsion

Tooth avulsion is defined as complete displacement of a tooth from its socket, severing the pulpal blood supply and exposing the cells of the PDL to the external environment (Andersson, 2007). In dentistry, an avulsed permanent tooth is considered to be one of the very few real emergency cases. Avulsion of permanent teeth is seen in 0.5–16% of all dental injury cases (Andreasen et al., 2019). The

most common age of occurrence is around 8–12 years, a time when the loosely structured PDL surrounding the erupting teeth provides only minimal resistance to an extrusive force (Andreasen and Andreasen, 2007). Treatment of avulsions is directed toward avoiding or minimizing the effects of the two main complications, attachment damage and pulpal infection (Fouad et al., 2020). While it is not possible for the original blood supply to be re-established after avulsion, under special circumstances it is possible for the replanted tooth to become revascularized. If the tooth is immature with an open apex, efforts should be made to promote revascularization of the pulp. In the tooth with a closed or open apex in which revascularization is unsuccessful, treatment efforts should be aimed at elimination of potential bacterial toxins from the root canal space (Lee et al., 2001). Replantation of teeth has been considered a temporary measure because many replanted teeth ultimately succumb to root resorption. However, many cases have been reported in which teeth have survived successfully for 20–40 years, with a normal PDL. The success rate of replanted teeth has been reported to be as low as 4% and as high as 50% (Andreasen et al., 1995a).

Figure 17.20 Orthodontic extrusion with a glass fiber post and composite core. (a, b) Before treatment. (c) After glass fiber post placement. (d) Composite resin crown for bracket attachment. (e) Initiation of orthodontic treatment, with horizontal lines showing the incisal edges before extrusion. (f) At the end of orthodontic treatment. (g) Final restoration with porcelain fused to metal crown.

Source: Yüzügüllü et al. (2008) / courtesy of John Wiley and Sons.

Figure 17.21 Traumatic intrusion of left central incisor (arrowed).

Guidelines published by the International Association of Dental Traumatology suggest that, for treatment of avulsed permanent teeth (Fouad et al., 2020), the choice of treatment should be based on the maturity level of the root – that is, open or closed apex – and on the condition of the PDL cells. The success of replantation is dependent on many factors, such as the time for which the tooth was out of the mouth (Kenny and Barrett, 2001), the type of splinting, and the duration of splinting (Kwan et al., 2012). The time out of the mouth determines the condition of the PDL cells (Kenny and Barrett, 2001) and the storage space that was utilized to keep the avulsed teeth (Barbizam et al., 2015). Depending on the length and level of maturation of the root, passive, flexible, and wire-composite splints are utilized to sustain the physiological stabilization of the replanted teeth for a period of two weeks. Successful periodontal healing after replantation seems not to be linked with the splinting duration (Hinckfuss and Messer, 2009a).

Figure 17.22 (a) Traumatic intrusion in a Class II Division 1 patient before orthodontic treatment. (b) After initial leveling with 2×4 mechanics prior to activator treatment. (c) At the end of functional treatment. Note the relapse in the vertical position of the traumatized tooth. (d) Intraoral view of the second stage of fixed appliance treatment.

Adhesive-bonded composite resin splints such as wire-composite splints and titanium trauma splints are recommended, because semi-rigid or flexible splinting allows physiological tooth movement, and such functional stimuli promote healing (Ram and Cohenca, 2004). In view of long-term splinting causing ankylosis, it is recommended that teeth should be splinted for up to two weeks rather than six weeks as previously practiced; splinting for one week may be adequate for periodontal healing (Andreasen et al., 1995a; Andreasen and Andreasen, 2007).

The timing of endodontic treatment of a replanted avulsed tooth depends on the maturity of the tooth and, if it is immature, the amount of time for which it was outside the mouth. Replanting

immature teeth in children is done to obtain pulp revitalization, which provides the teeth with further root development. Clinical guidelines recommend avoiding endodontic treatment of immature teeth, unless obvious signs of nonrevascularization are present or the period outside the mouth has been prolonged (Gregg and Boyd, 1998). In cases where spontaneous revitalization does not occur, apexification, pulp revitalization, or root canal treatment should be applied when pulp necrosis and infection are observed (Kahler et al., 2017). Extirpation may be delayed in immature teeth if there is a chance that the pulp is vital; root growth may then continue. The frequency of revascularization of a replanted immature incisor has been reported as 18% (Kling et al., 1986) and 34% (Andreasen et al., 1995b), being influenced by the extraoral time.

To prevent inflammatory root resorption in mature teeth, timing of pulpal extirpation is of greatest importance. Thus when endodontic treatment is indicated, the treatment should be applied within two weeks (Stewart et al., 2008; Hinckfuss and Messer, 2009b; Day et al., 2019). As the intracanal medicament, calcium hydroxide is generally suggested for up to one month following the root canal filling (Andreasen et al., 2002; Rosenberg et al., 2007). Corticosteroid or a corticosteroid/antibiotic mixture (if chosen to be used as an anti-inflammatory and anti-resorptive intracanal medicament) should be placed as soon as possible or right after replantation, and should be left *in situ* for at least six weeks if use of such a mixture is preferred (Bryson et al., 2002; Chen et al., 2008). Systemic antibiotic therapy (doxycycline or penicillin V) is recommended to prevent bacterial infection (Gregg and Boyd, 1998) and presented a positive effect on the repair process, contributing to a better pulpal and PDL repair (Melo et al., 2016).

In 7–8% of injuries, the avulsed tooth cannot be replanted, the replanted tooth develops progressive root resorption, or there are crown/root or root fractures, all of which lead to tooth loss (Borum and Andreasen, 2001). In such situations, the treatment modalities including no treatment, orthodontic space closure, conventional bridges, adhesive bridges, removable prosthetic appliances, single-tooth implants, and autotransplantation should also be considered (Andreasen et al., 2009; Figure 17.23). Apart from orthodontic space closure, autotransplantation of teeth appears to be the most

biologically oriented approach due to its bone-generating capacity and because it allows orthodontic treatment to be performed at an early age (10–12 years). Progressive root resorption, necrosis of the pulp, ankylosis, and infraocclusion are commonly reported problems related to autotransplantation (Schwartz et al., 1985). Successful autotransplantation depends on several factors, such as age at transplantation, the developmental stage of the tooth, donor type, the duration of extraoral exposure of the donor tooth during surgery, damage to the root cementum and the PDL, and the experience of the oral surgeon (Ahlberg et al., 1983; Schwartz et al., 1985). Zachrisson et al. (2004) stated that the optimal time for autotransplantation of premolars to the maxillary anterior region is when root development has reached two-thirds or two-fourths of the final length, enhancing the prognosis.

Various techniques have been described for stabilization of an autotransplanted tooth, including splinting with orthodontic brackets, ligatures, sutures, and composite resins. Long-term success rates vary between 74% and 100% (Lundberg and Isaksson, 1996; Gault and Warocquier-Clerout, 2002). More recently, Kvint et al. (2010) reported an 81% success rate in 215 consecutively transplanted teeth, with the highest success rate (100%) in transplantation of premolars to the maxillary incisor region. After 10 years, the survival rate of the transplanted teeth has been shown to be more than 90%, as established in systematic reviews and meta-analyses of autotransplantation (Almpani et al., 2015; Rohof et al., 2018). Furthermore, a systematic review by Machado et al. (2016) into the long-term prognosis emphasizes studies that had a follow-up period of more than six years. The long-term prognosis of autotransplantation was found to be very successful, with an 81% survival rate. Autotransplantation of teeth with incomplete root formation is among the treatment options (Machado et al., 2016).

Autotransplantation of cryopreserved teeth has also been reported (Schwartz and Rank, 1986; Temmerman et al., 2006). This procedure requires a special facility and expertise to avoid damage to the PDL and dental pulp. The main advantage is that the transplanted teeth can be moved orthodontically (Fujita et al., 2008; Andreasen et al., 2009).

Special attention should be given to the pulpal response of orthodontically moved autotransplanted teeth, as transplantation of teeth leads to interruption of the pulpal vascular and neural supply. As Skoglund et al. (1981) stated, pulpal necrosis occurs in most transplanted teeth. Repair includes revascularization, but pulpal obliteration mostly cannot be avoided. Although revascularization can be observed at the end of the first month (Skoglund et al., 1978), pulpal reinnervation may not be apparent even after three months (Robinson, 1983). Since sensory pulpal nerves are essential for regulating blood flow via release of vasoactive neuropeptides, reduced pulpal innervations may compromise vasodilatation and angiogenesis and, as a result, pulp survival (Kerezoudis et al., 1995; Berggreen and Heyeraas, 1999). Paulsen et al. (1995) reported occurrence of late pulpal necrosis five years after orthodontic derotation of premolars. Bauss et al. (2004) evaluated the influence of derotation and extrusion on pulps of autotransplanted third molars, and found that these movements were not associated with any additional risks to the long-term survival of transplanted single-rooted third molars. However, the authors concluded that special care should be taken while derotating autotransplanted multirooted molars.

Root resorption occurs when a donor tooth with partial or total lack of vital PDL is transplanted. It is categorized as replacement resorption, inflammatory resorption, or surface resorption (Andreasen, 1992; Figure 17.24). Metabolic byproducts produced by bacteria present in necrotic pulp initiate periodontal inflammation, leading to inflammatory resorption of the transplanted tooth. Therefore, root canal treatment is often necessary for satisfactory clinical results in transplanted or replanted teeth with complete root formation (Schwartz et al., 1985; Eliasson et al., 1988). Unlike replacement resorption, inflammatory resorption can be arrested by root canal therapy if it is performed early. According to Andreasen and Hjorting-Hansen (1966), endodontic treatment should be started only when a tooth becomes symptomatic or when bone lesions develop. Inflammatory resorption usually occurs 3–4 weeks after transplantation, whereas replacement resorption (ankylosis) takes 3–4 months to 1 year to become evident (Thomas et al., 1998). Most authors recommend endodontic treatment 7–14 days after

transplantation, as this time period is considered sufficient for the start of possible pulp necrosis and inflammatory resorption (Andreasen, 1992; Thong et al., 2001; Pohl et al., 2005).

Autotransplantation of teeth offers an effective treatment option, particularly when combined with an appropriate orthodontic treatment plan. Subsequent to autotransplantation, a delay of at least 1 month (Jonsson and Sigurdsson 2004), 1–2 months (Kokai et al. 2015), 2–3 months (Frenken et al. 1998), 3–6 months (Bauss et al. 2003, 2004), or 5–6 months (Lagerström and Kristerson, 1986; Watanabe et al. 2010) has been recommended before applying active orthodontic forces. On the other hand, Fujita et al. (2008) have recommended using stable light orthodontic forces (using superelastic nickel–titanium alloy archwires) after just a short period of splinting (4 weeks) in order to avoid ankylosis and inflammatory root resorption. Berglund et al. (1996) reported that the use of orthodontic force (jiggling force) on the tooth to be transplanted prior to autotransplantation decreased the risk of damage to the PDL. Nishimura et al. (2009) reported on successful 10-year follow-up of an orthodontic case with an autotransplanted mature tooth with prior application of jiggling forces. Fukui et al. (2009) recommended monitoring of transplanted teeth during and after orthodontic treatment because of their susceptibility to inflammatory root resorption. In a recent systematic review on autotransplantation including controlled clinical trials, a total of 934 autotransplanted teeth of 715 patients was evaluated in the long term, and it was concluded that there was an increase in root resorption influenced by orthodontics, but without affecting the general clinical result in the long term. The authors also reported that even though it has not been sufficiently addressed, the bone and periodontal tissue did not appear to be significantly affected by orthodontics (Lacerda-Santos et al., 2020).

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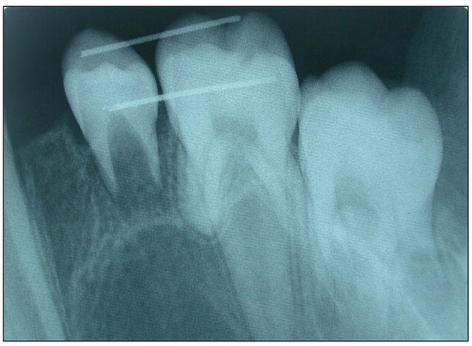

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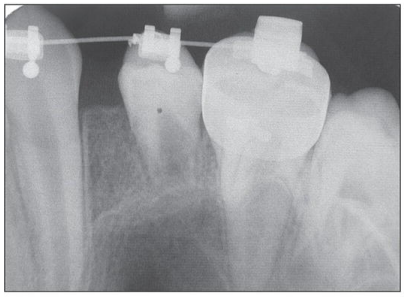

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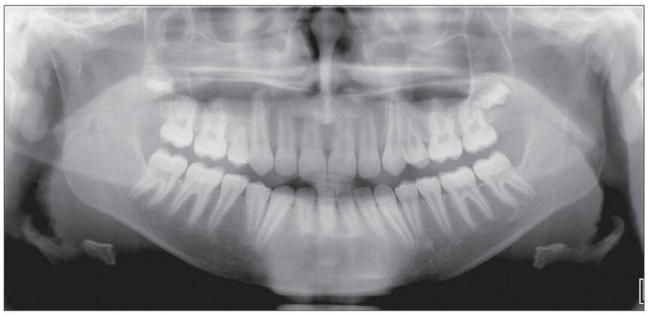
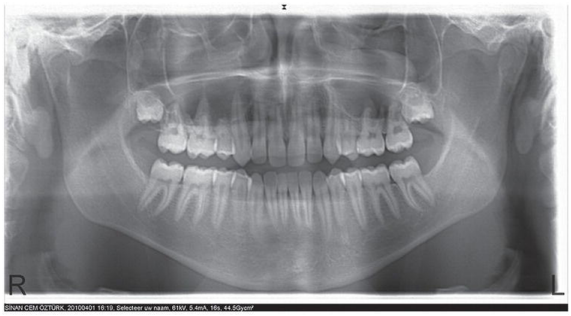


(i)



(j)

Figure 17.23 Autotransplantation. A boy, aged 11.3 years, presented with a congenitally missing maxillary right second premolar. The right first premolar was also missing due to intentional extraction in order to correct the position of the buccally positioned canine. The treatment plan was to transplant the left second premolar germ in the place of the missing premolars on the right side. (a) Pretreatment panoramic radiograph. (b–e) The donor tooth after splinting (b), after placement of brackets (c), after orthodontic treatment (d), and after seven years' follow-up (e). (f–h) Intraoral right views at the beginning, at the end of treatment, and at the seven-year follow-up. (i) Panoramic radiograph at the end of the fixed appliance treatment. (j) Panoramic radiograph seven years after finishing of active treatment.

(a) (b)

Figure 17.24 (a, b) The maxillary left central incisor was replanted two years ago, but no endodontic treatment was carried out. Both inflammatory and replacement resorption is evident radiographically. Courtesy of Dr. Sevi Burçak Çehreli.

Tooth ankylosis

Ankylosis of teeth can lead to serious clinical problems such as tilting or migration of adjacent teeth, supraeruption of the opposing teeth, impaction of the succeeding permanent teeth or eruption delay, midline deviation, alveolar bone loss, and lack of alveolar bone development of the involved area (Becker and Karnei-R'em, 1992a,

1992b; Becker et al., 1992; Kurol, 2002, 2006). Early clinical diagnosis of ankylosis is based on the typical metallic sound heard on percussion of the tooth, marked decrease in the normal physiological facial-lingual excursion, and lack of tooth mobility. Ankylosis can be evidenced on a periapical radiograph as an interruption of the PDL in a small area. However, early detection of ankylosis on dental radiographs is often difficult because the areas of ankylosis are very small, typically located on the labial or lingual surface of the root, and not visible on the 2D radiograph (Isaacson et al., 2001). A more acceptable and reliable sign of ankylosis is infraocclusion, as only a third of ankylosed teeth will have a metallic sound on percussion or show loss of PDL space in radiographs (Raghoebar et al., 1989). The diagnosis of ankylosis can be confirmed when the affected tooth does not move when subjected to orthodontic forces.

Ankylosis in deciduous teeth is about 10 times more likely than in the permanent dentition (Mullally et al., 1995) and twice as likely in the mandibular than in the maxillary arch, with higher incidence in the molar region. With a permanent successor in a normal position, a six-month delay in shedding time can be expected for ankylosed deciduous molars compared with normal teeth. Thus, early extraction of the ankylosed deciduous molar is unnecessary (Kurol and Koch, 1985). If the permanent successor is missing, spontaneous exfoliation is not likely. However, root resorption might continue, and an impaired vertical position might occur due to ankylosis (Kurol and Thilander, 1984). If the loss of height is mild or moderate, this situation can be accepted, or the occlusal height can be restored. In severe infraocclusion, extraction is recommended as early as possible to promote spontaneous mesial migration of the permanent molars (Nishimura et al., 2009; Figure 17.25).

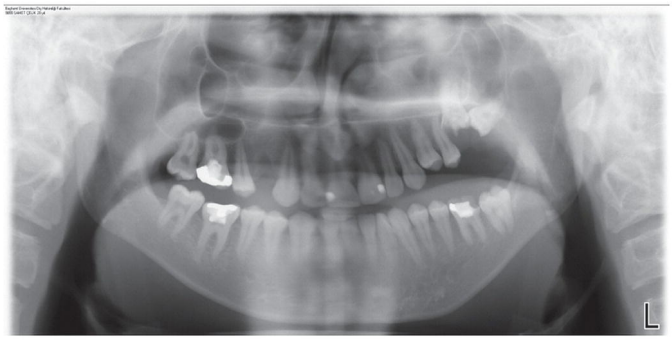
Retention of a permanent ankylosed tooth in a young patient is complicated by the arrested development of the alveolar ridge, coupled with the continuing facial growth of the child. It has been proposed to remove the ankylosed tooth at the start of the rapid phase of adolescent growth (Steiner and West, 1997). Ankylosed teeth are excellent sources of rigid anchorage for orthodontic or orthopedic movement (Roberts, 2000).

Extraction is not the only treatment approach for an ankylosed tooth. Prosthetic build-up is also possible in mild cases, if the infraocclusion is less than 5 mm (Mullally et al., 1995; Chaushu et al., 2004a). If the ankylosed tooth is extracted and replaced with a prosthetic restoration, the results may not be esthetically acceptable due to the presence of an alveolar defect. Additional surgical procedures may be required, such as ridge augmentation or onlay bone grafts (Isaacson et al., 2001). Malmgren et al. (1984) described a method in which only the crown is removed and the ankylosed root is left in place. As the root is resorbed and replaced by bone (replacement resorption), the height and width of the ridge are maintained, allowing for placement of a more natural-looking restoration. Lee et al. (2009) suggested using miniscrew implants and cantilever uprighting springs to achieve root movement of the adjacent tooth into the extraction space of an ankylosed molar in order to restore the alveolar bone defect.

(a)

(b)

(c)



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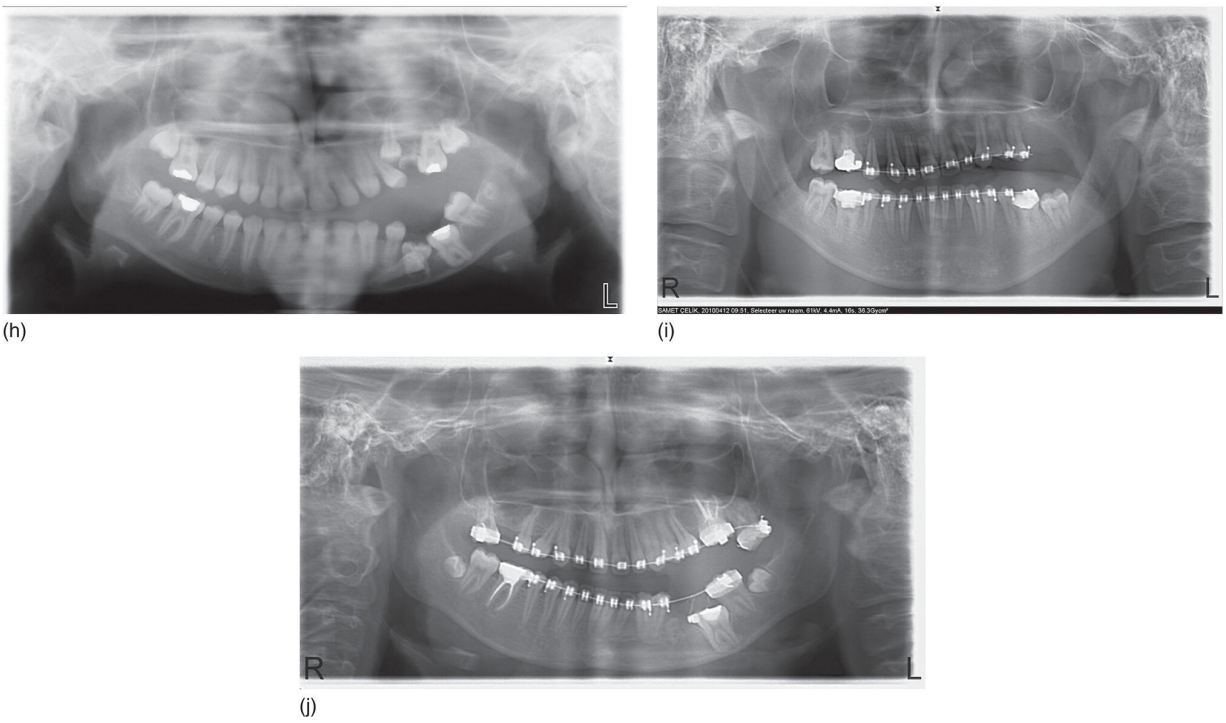


Figure 17.25 Primary failure of eruption (PFE) and ankylosis of teeth in the left posterior region of two siblings. Pretreatment intraoral views and panoramic radiographs of (a–d) the brother and (e–h) the sister. (i, j) In PFE, the affected teeth cannot be moved with conventional orthodontic mechanics.

Orthodontic treatment combined with surgical luxation might be an acceptable approach in some cases, although there are associated risks, including fracture, recurrence of ankylosis, need for endodontic treatment, and intrusion of adjacent teeth (Razdolsky et al., 2004; Kofod et al., 2005; Lim et al., 2008). The ankylosed tooth can be extracted and reimplanted into the socket thus created, but this may result in external root resorption (Proffit, 1986: 191–192, 408–411). Another treatment alternative is mobilization of the ankylosed tooth along with surrounding bone by interdental osteotomy and repositioning of the tooth–bone segment in its proper position, followed by fixation with an archwire or acrylic splints (Medeiros and Bezerra, 1997). Surgical repositioning is one of the best treatment alternatives, but total mobilization of the segment and separation of the palatal mucosa may compromise the blood supply of the segment, and the gingival tissues may not follow the movement of the tooth–bone segment, resulting in areas of gingival

recession and differences in the gingival margin level (Alcan, 2006). Distraction osteogenesis is a promising technique for moving ankylosed teeth, as it induces expansion and regeneration of soft tissues along with that of the bone. The most important advantage of distraction osteogenesis is bringing the clinical crown, incisal edge, and gingival margin into their appropriate position relative to the neighboring teeth (Razdolsky et al., 2004; Susami et al., 2006). Management of ankylosed teeth with distraction osteogenesis can be performed with orthodontic tooth-borne distractors or internal bone-supported screw distracters, followed by leveling with archwires (Isaacson et al., 2001; Kinzinger et al., 2003; Razdolsky et al., 2004; Kofod et al., 2005; Alcan, 2006; Figure 17.26). Because of the bulky nature and cost factors along with the difficulty in placement of distraction devices, Dolanmaz et al. (2010) proposed conventional orthodontic treatment mechanics instead of additional devices.

Ramaglia et al. (2019) proposed a piezoelectric-assisted distraction osteogenesis procedure for the treatment of ankylosed permanent front teeth and reported promising results on five cases.

(a)

(b)

Figure 17.26 Treatment of ankylosis with osteotomy and orthodontic mechanics. (a) Before treatment (ankylosed maxillary central incisor four years after reimplantation). (b) Alignment following osteotomy and orthodontic mechanics over a period of four weeks.

Immediate postorthodontic period

After the completion of orthodontic treatment, the orthodontist should evaluate in detail the oral hard and soft tissues for any iatrogenically induced pathologies. After debonding, it is advisable to test the vitality of the teeth. Only a few studies have evaluated the long-term vitality of orthodontically treated teeth. Although pulpal changes such as root canal obliteration and loss of tooth vitality have been observed in some patients, Popp et al. (1992) found no differences in pulpal changes in patients five years out of retention and in untreated controls. If any finding justifies seeking advice from medical or dental specialists, a prompt referral should be made.

The caries risk is not zero after debonding. Precautions, including proper diet and oral hygiene maintenance, should continue, because bonded retainers might also provoke a cariogenic challenge. Debonding reduces the cariogenic potential and increases the accessibility of mechanical cleaning. However, resin remnants may present a potential risk for plaque accumulation on the posterior and mandibular teeth where brackets are bonded close to the gingival margin (Fjeld and Ogaard, 2006). Any WSLs that have developed might reduce to some extent, depending on the severity of the lesions, due to the continuous wear caused by tooth brushing rather than due to remineralization after debonding (Artun and Thylstrup, 1986). Willmot (2004) reported a rapid reduction in size in most cases during the first 12 weeks after appliance removal, with little reduction observed after 26 weeks. A “remineralizing therapy” should follow two fundamental principles:

- The presence of the dental biofilm should be removed with tooth brushing.
- Fluoride should be prescribed either to arrest existing lesions or to reduce the progression of new lesions (Kudiyirickal and Ivancaková, 2008).

Natural remineralization produces greater resistance to further dissolution as the mineral components are replaced with a less soluble substance that may have a larger crystal size (Silverstone, 1983). Applying high concentrations of fluoride to WSLs may seem

to be the best method for remineralization; however, a high fluoride concentration may immediately remineralize the most superficial layer of enamel, leaving the deeper enamel crystals relatively unaffected (Bishara and Ostby, 2008). To avoid this problem, low-dose fluoride applications have been recommended to enhance subsurface remineralization. A 50 ppm fluoride mouthrinse was shown to be more efficacious with regard to remineralization than a control solution or a regular mouthrinse containing 250 ppm fluoride (Linton, 1996). These arrested lesions may persist life-long, keeping their white color, or they may take up exogenous stains from foods, with a change in color to yellowish to dark brown. Acid etching of fluoride-treated lesions increases the surface porosity and facilitates remineralization of the lesion by oral fluids (Hicks et al., 1984).

Casein phosphopeptide–amorphous calcium phosphate (CPP-ACP) – a product derived from milk casein – is capable of being absorbed through the enamel surface (Reynolds, 1987). CPP-ACP is a delivery system that allows freely available calcium and phosphate ions to attach to enamel and reform into calcium phosphate crystals. The free calcium and phosphate ions move out from CPP-ACP and into the enamel rods and free themselves to form apatite crystals (Reynolds, 1997). A number of different media have been developed to deliver CPP-ACP, including a water-based mousse, a topical cream, chewing gum, mouthrinses, and sugar-free lozenges. Studies of the effects of CPP-ACP have shown promising dose-related increases in enamel remineralization in demineralized lesions (Reynolds et al., 2003; Sudjalim et al., 2006). The addition of fluoride to this paste should further enhance the precipitation of this mineral into subsurface incipient lesions (Donly and Sasa, 2008). The use of sugar-free gums, such as xylitol, for their salivary stimulation effects has been recommended after the removal of fixed orthodontic appliances, although as yet there is a lack of quantitative data to help evaluate whether the effect is clinically beneficial (Willmot, 2008). Recently, CPP-ACP was added to yogurt. Shen et al. (2020) tested the yogurt with added CPP-ACP on subsurface enamel lesions. According to the findings of this study, several processed yogurts with added sugar may cause enamel demineralization when eaten on a regular basis by people who have poor dental hygiene.

CPP-ACP added to these yogurts may help prevent demineralization and enhance enamel subsurface lesion remineralization, making them safer for teeth.

Toothpastes containing nano-hydroxyapatite (n-Hap) and its precursors have been shown to supply calcium and phosphate ions to tooth hard tissues, decreasing demineralization and encouraging remineralization. n-Hap may also produce a protective layer over tooth hard tissues, with chemical properties similar to natural tissues and biomimetic features (Cochrane et al., 2010; Nongonierma and Fitzgerald, 2012; Amaechi et al., 2021; Mielczarek and Michalik 2014).

Resin enamel infiltration is an alternative, and promising, therapeutic approach for preventing further progression of enamel lesions that are not expected to remineralize or arrest with noninvasive measures. This treatment aims to occlude the microporosities within the lesion by infiltration with low-viscosity light-curing resins that have been optimized for rapid penetration into the porous enamel (infiltrants). In contrast to fissure sealing, where the diffusion barrier is placed on the lesion surface, the infiltration technique aims to create the diffusion barrier within the lesion, by replacing lost mineral with resin (Paris et al., 2007). After surface conditioning using hydrochloric acid (HCl) gel, a resin infiltrant is applied on top of the lesion (Meyer-Lueckel et al., 2007). The resin penetrates the lesion body, driven by the capillary forces, and excess material is removed from the surface before the resin is light cured (Meyer-Lueckel and Paris, 2008). A positive side effect of resin infiltration is that the WSLs lose their whitish appearance when their microporosities are filled with the resin and look similar to sound enamel. Thus, this treatment may be used not only to arrest enamel lesions, but also to improve the esthetic appearance of buccal white spots (Paris and Meyer-Lueckel, 2009). In orthodontic patients with WSLs, the best results are achieved if the infiltration treatment is started shortly after debonding, targeting the relatively active lesions. With regard to possible side effects, a short contact time with HCl does not cause any considerable alterations in the gingiva, although exposures of 30 seconds or more might evoke ulceration (Croll et al., 1990). It has been argued that irrespective of the seal, bacteria trapped in the apical end of the lesion could trigger

the caries process. However, there is good evidence that entrapped bacteria are not harmful if the lesion has been properly sealed (Kidd, 2004; Figure 17.27).

Recently, two systematic reviews and meta-analyses were published about resin infiltration. Zakizade et al. (2020) reported that the resin infiltration technique has a significant advantage for enhancing the surface hardness of WSLs; however, re-establishing the surface hardness of resin-infiltrated WSLs similar to sound enamel is doubtful. Besides, resin infiltration is found to be more effective for enhancing the surface hardness than fluoride application, enamel pro-varnish, and colloidal silica infiltration. Bourouni et al. (2021) reported that the resin infiltration technique was a viable option to mask the WSLs and mild to medium fluorosis, but the conclusion was based on only few well-conducted RCTs with moderate to high risk of bias.

Figure 17.27 (a, b) Masking of the white spot lesion on the labial surface of the canine by resin infiltration.

Microabrasion, whose use has been advocated for the removal of postorthodontic demineralized white lesions, is merely the application of an acidic and abrasive compound on the surface of the enamel for the removal of superficial, noncarious enamel defects (Croll and Bullock, 1994; Croll and Helpin, 2000). Research indicates that a one-minute application of a commercially available microabrasion compound will remove 12 μm on the first application and 26 μm on subsequent applications, leaving a highly polished enamel surface (Waggoner et al., 1989). This phenomenon of less removal of enamel on the first application than on subsequent

applications is due to the fluoride-rich surface enamel. Following microabrasion, a four-minute, 2% sodium fluoride treatment is recommended. Only a few quantitative studies have assessed the success of the microabrasion technique in improving the cosmetic appearance of postorthodontic, demineralized enamel lesions. If the outcome is found to be unsatisfactory, vital tooth bleaching can be considered as the next step, which is a treatment that camouflages mild and moderate fluorosis or WSLs by whitening the surrounding enamel surfaces.

Esthetic improvements

Meeting the esthetic objectives of the patient and the clinician may involve the placement of composite restorations or ceramic veneers. The latter treatment requires the removal of sound tooth structure and is typically costlier. The patient and the family should be informed about the damages versus the benefits and the duration of the operative interventions, with an emphasis on the sacrifice of sound tooth structure. However, this option might be the most successful in addressing the esthetic concerns of the patient in severely compromised situations (Bishara and Ostby, 2008).

Interincisal diastemas

Interincisal diastemas, especially a maxillary midline diastema, frequently depress anterior smile esthetics (Bernabe and Flores-Mir, 2007). They can compromise dentofacial harmony (Witt and Flores-Mir, 2011) and cause functional (Farronato et al., 2012) and psychological distress for patients during daily life while talking or eating, leading to a detrimental effect on self-esteem (Gkantidis et al., 2008).

Maxillary midline diastemas greater than 0.5 mm are considered malocclusions (Kabbach et al., 2018; Sen and Iselr, 2019). Although laypeople tolerate diastemas around 1.00 mm (Del Monte et al., 2017), maxillary midline diastema is one of the most common complaints of patients who seek orthodontic treatment (Chu et al., 2011). Location of the insertion of the labial frenum, supernumerary teeth, lateral incisor agenesis, peg-shaped laterals, small tooth size

relative to jaw size, pathological tooth migration, deep overbite with steep incisal guidance, anterior tongue posture, excessive arch width, microdontia, cysts in the midline region, habits such as finger sucking, hereditary or ethnic characteristics, and relapse after orthodontics are considered as the etiological factors (Sękowska et al., 2018). Moreover, chronic inflammatory periodontal diseases may also contribute to the existing clinical situation or arise alone (Abraham and Kamath, 2014). Frequently, a peg-shaped lateral incisor may accompany diastemas. Its prevalence in African Americans is twice that among white, Asian, or Hispanic people (Gass et al., 2003).

The maxillary frenum attaches the tubercle of the upper lip to the palatine papilla and originates from the tectolabial band. The presence of a distinct maxillary labial frenum is a normal finding in infants, and a maxillary midline diastema is frequently seen in the mixed dentition. Although it is expected to vanish as the permanent canine teeth erupt (Huang and Creath, 1995), it may remain in approximately 7% of adolescents. A midline diastema larger than 2 mm may not close naturally (Delli et al. 2013). However, the incidence of the participation of the labial frenum as the cause of maxillary midline diastema is controversial (Wheeler et al., 2018).

The American Academy of Orthodontists, the American College of Oral and Maxillofacial Surgeons, the American Association of Oral and Maxillofacial Surgeons, and the American Association of Orthodontists have no guidelines or position statement regarding this situation. However, the American Academy of Pediatric Dentistry *Guideline on Pediatric Oral Surgery* (2014) states: “Treatment is suggested when the attachment exerts a traumatic force on the gingiva causing the papilla to blanch (whitening of the tissue between the incisors when the upper lip is everted) when the upper lip is pulled or if it causes the diastema to remain after eruption of the permanent canines.” It also recommends that treatment be delayed until the permanent incisors and canines have erupted and the diastema has had a chance to close naturally. If orthodontic treatment is to be performed, frenectomy should be postponed until the diastema is closed.

A systematic review of the literature has reported that orthodontists prefer posttreatment frenectomy, suggesting that orthodontic forces may lead the frenum to remodel (Suter et al., 2014). When that is the case, it is believed to increase the turnover of the transseptal periodontal ligament fibers, with the newly developed fibers increasing incisor stability. However, this theory is not supported by controlled clinical research (Wheeler et al., 2018).

Once the etiology is defined, an appropriate treatment plan can be performed that may involve several dental specialties (Romero et al., 2018; Kabbach et al., 2018; Sen and Iselr 2019). Nowadays, esthetic restorative treatments are frequently demanded treatment modalities. It should always be kept in mind that the concept of beauty is subjective and what is considered beautiful by the dental specialist may not match the perception of the patient. Data from a systematic review by Parrini et al. (2016) and the work of Kokich et al. (1999) show that laypeople and dental specialists have a different threshold of esthetic perception, and therefore dentists should be careful not to impose their norm of beauty on patients and create a personalized smile that reflects physical and dentofacial harmony (Pontons-Melo et al., 2019).

Interincisal diastemas may remain even after the orthodontic treatment because of discrepancies of teeth and jaw sizes or relapse. Following the concept of the contemporary minimally invasive approach, additive direct or indirect restorations without preparing sound tissues favor promising clinical results (Frese et al., 2013). The structural improvements in adhesive technology and resin composite materials in the last two decades have endorsed minimally invasive dentistry. Thus, bioadditive treatments with resin composites under the “golden proportion” concept for the closure of diastemas and peg-shaped tooth re-anatomization enable esthetic, conservative, repairable, and reversible outcomes using a minimally invasive restorative technique (Pontons-Melo et al., 2021).

It is well known that acceptable adhesion to enamel and dentin is accomplished by etch-and-rinse and two-step self-etch adhesives (Gresnigt et al., 2012). However, on sound and uncut enamel, the etch-and-rinse technique is certainly the most efficient approach to reach stable and high-quality adhesion (Peumans et al., 2005; Van

Meerbeek et al., 2003). Adhesion to enamel by micromechanical interlocking of resin tags is still considered to be the gold standard where up to 40 Mpa is achieved in *in vitro* studies, sometimes even exceeding the cohesive strength of the enamel itself (Van Meerbeek et al. 2010; Figures 17.28–17.31).

Although ceramics are highly esthetic materials with respect to resin composites, indirect treatment modalities are to be performed in multiple sessions involving laboratory stages with high costs and sacrifice of intact enamel (Calamia and Pantzis, 2015). Direct resin composite restorations are reported to have promising results, with claims that they are strong, stay in place for many years, and have excellent esthetic potential, which enables them to accurately simulate the appearance of normal tooth structure (Manhart et al., 2004). They also cost much less than equivalent indirect restorations (Wolff et al., 2010).

However, the pitfall of resin composite is its limited color stability over time and resin chipping. If the existing restoration is still clinically satisfactory, chipping can be repaired using state-of-the-art adhesive repair techniques by adding new composite layers. Color changes sometimes may be improved by polishing or refurbishment (Lempel et al., 2017). In this way, shorter chairtime, reduced economic burden, and better prognosis of the teeth that keeps the patient out of a repeated restoration cycle are the benefits of direct resin composites (Ruschel et al., 2017).

Today, there is a wide range of different resin composite materials on the market and as a material of choice nanofilled resins were developed to attain comparable wear resistance and mechanical strength, but with improved esthetics due to their excellent ability to be polished, polish retention, and lustrous appearance with respect to microfilled ones (Endo et al., 2010). Concerning mechanical properties, nanoclusters seem to have higher damage tolerance combined with improved clinical performance (Curtis et al., 2009). In addition, the composite material can match the color of neighboring tooth tissues by scattering visible light through a larger number of smaller particles in the resin composite. This “chameleon” effect (Pereira Sanchez et al., 2019) is achieved by shifting the composite color toward the color of the surrounding environment

(Paravina et al., 2006). So with this technology, clinicians can perform simple, monochromatic esthetic restorations. Manufacturers are also launching innovative esthetic composite kits that include fewer shades, corresponding to all shades in the Vita Classic Shade Guide. Although the chameleon effect has been confirmed recently, the shade of the underlying dentin and the thickness of the enamel layer are the restrictions of their usage (Bakti et al., 2018). The rate of blending is dependent on the restoration type and increases in smaller restorations compared to larger ones (Bakti et al., 2018).

Figure 17.28 A patient presenting midline diastema and peg-shaped left lateral incisor (a, e). After orthodontic treatment the spaces were reduced and prepared for restorations (b). Composite resin restorations were completed after gingivectomy and frenectomy procedures (c, d, f).

In the literature there are numerous middle- and long-term studies demonstrating the clinical performance of diastema closure and reshaping with direct resin composites. Lempel et al. (2017) showed that microhybrid and nanofilled direct composite restorations had an acceptable clinical durability, with repairable failures in anterior additive restorations having a 1.43% annual failure rate after seven years of clinical function. Comba et al. (2021) investigated

orthodontically treated patients and reported that the use of direct nanohybrid composite restorations showed good clinical performance after five-year follow-up. The same study also showed better performance of the restoration when the composite was used for tooth recontouring than for diastema closure. Similar results were found by Wolff et al. (2010), who classified more than 90% of diastema closure restorations as “clinically excellent” or “clinically good,” with a mean follow-up interval of 55.1 months. Another clinical study conducted by Prabhu et al. (2015) evaluated the performance of composite resin used to restore midline diastema between the maxillary and mandibular central incisors for 60 months and reported a 91% overall retention rate. Four-year clinical evaluation of direct composite build-ups for space closure after orthodontic treatment by Demirci et al. (2015) showed favorable survival rates.

Figure 17.29 Orthodontic and restorative treatment of a Class II patient with impacted upper right canine, peg-shaped upper lateral incisor. and missing lower left second premolar (a–f). Composite restorations of incisors (b, d) were made after completion of the fixed appliance therapy of 34 months. The space for the lower left second premolar will be restored with an implant restoration when the patient is 18 years old (f).

Figure 17.30 (a) The patient presented with a missing central incisor due to previous trauma. Fixed orthodontic treatment was applied to provide space to restore the right lateral incisor as a central incisor. (b) After the orthodontic treatment, gingivectomy to # 14, 13, and 12 was performed and (c) composite resin restorations were made.

Figure 17.31 Orthodontic and restorative treatment of an adult patient presenting a missing upper left canine, second premolar, and impacted upper right second premolar (a, b, d, g, i). The impacted right premolar was extracted, the left first premolar was repositioned and reshaped as the canine, and an implant restoration was made to replace the first premolar (c, e, f, h, j).

Korkut and Türkmen (2021) reported mean survival of the diastema closure and recontouring restorations to be 46.2 months, with an annual failure rate ranging from 0.9% to 3.4%. In another study, Coelho-de-Souza et al. (2015) retrospectively evaluated the clinical

performance of direct anterior composite build-ups in vital and nonvital teeth and reported a 95.1% survival rate for vital teeth at the end of 3.5 years. Frese et al. (2013) investigated 284 direct composite build-ups and reached a five-year survival rate of 79.2%.

The use of a computer-aided design and computer-aided manufacturing (CAD/CAM) composite resin is an excellent option, offering advantages when compared to direct resin restorations and even in partial ceramic veneers (Lebon et al., 2015; Mainjot, 2020). While dental ceramics can be easily etched, predictably bonded, color stable, and wear resistant (Signore et al., 2013), the properties of the CAD/CAM composite resins enable thin designs, with less possibility of chipping of the margins and less milling time than ceramics (Schlichting and Magne, 2020). In addition, they can be repaired and characterized easily (Schlichting and Magne, 2020). Among several possible treatments available, laminates may be one of the preferred options for esthetic treatment of a diastema owing to improved esthetics, color stability, and mechanical properties, which may be indicated when there is appropriate remaining sound dental structure (Viswambaran et al., 2015; da Cunha et al., 2014).

An absence of interdental papilla inevitably accompanies diastema. For better esthetic results papillary reconstructions may sometimes be indicated to fill the black spaces between interproximal surfaces; however, the prognosis of these reconstructions is uncertain (Jeong et al., 2016). When a diastema is orthodontically closed, the interdental gingiva is squeezed and physically displaced coronally into the black triangular area, creating the interdental papilla (Pizzo Reis et al., 2020). A previous study concluded that when the distance between the contact point to the crest of bone is 5 mm or less, the papilla is present almost in 100% of cases; however, when this distance increases, the chances of the presence of papilla decrease (Tarnow et al., 1992).

In more complex cases, the team should include other dental and/or medical professionals to perform esthetic touch-ups like gingivoplasty, lip lengthening, genioplasty, or Botox applications (Figures 17.32 and 17.33).

Figure 17.32 An adult patient presenting severe skeletal Class II and open bite malocclusion (a, d, g, i), treated orthodontically with upper premolar extractions (b, e, h) prior to genioplasty and lip-lengthening operation and botox application for correction of profile and smile esthetics (b, c, e, f, h, j).

Figure 17.33 (a–e) Nonsurgical orthodontic treatment of a patient presenting open bite and gummy smile. The open bite was corrected with fixed orthodontic treatment using skeletal anchorage (zygomatic miniplates and palatal mini-implants) for posterior intrusion (b, d). A lip-lengthening procedure was performed in order to correct the gummy smile (e).

Clinical management of missing lateral incisors

Clinical management of missing lateral incisors has been mainly accomplished with either orthodontic space closure or space opening. There are at least six possible options for treating congenital agenesis of the maxillary lateral incisors:

- A conservative approach with esthetic remodeling of the deciduous maxillary lateral incisor employing a composite resin.
- Orthodontic space closure with mesial repositioning of the canine, followed by tooth recontouring.
- Orthodontic treatment to open a space with placement of fixed dental prostheses.

- Orthodontic treatment to open a space with placement of implant-supported fixed prosthetic restorations.
- Orthodontic treatment to open the space that may be restored by autotransplantation of premolars.
- Orthodontic treatment to close the gap and redistribute the spaces to the posterior regions for implant placement.

Orthodontic space closure is an evidence-based, effective treatment option that aims to achieve optimum esthetic and functional results with a minimally invasive restorative option. During planning treatment priority should be given to this option in adolescents, as there will be no need to wait until the end of the growth period to perform implant surgery or indirect prosthetic alternatives (Botelho et al., 2016; Jamilian et al., 2015). This treatment modality allows the dentition to adapt to the continuous facial changes over the patient's life without having an artificial prosthesis, and avoids the patient being a regular customer of the dentist in the future (Figure 17.34).

According to the Angle Society of Europe, space closure should be considered especially in patients with increased maxillary tooth display, such as those with vertical maxillary excess (Johal et al., 2013). A bi-protruded or convex profile with protrusion of the upper incisors, and a balanced profile with normo-inclined anterior teeth, a tendency toward crowding, and a minimum or absent space in the arch are indications for the closure of the agenesis space. From the occlusion point of view, Class II malocclusion with discrepancy or without arch length discrepancy treated with extractions from the lower arch, or Class I malocclusion with lower crowding, increased overjet, and open bite, may require closure of the space. Esthetic analysis of the canine is also necessary: if the canine is mesialized, small with an acceptable color, and compatible with the adjacent teeth, closing the space is indicated.

Traditionally, the space closure alternative is indicated in Class II malocclusions, and in cases of mandibular crowding and incisor protrusion, while the main esthetic procedure is to grind the canine so that it resembles a lateral incisor. On the other hand, space closure would not be suggested in Class III malocclusions, in patients with a short face/concave profile, and in those with large canines

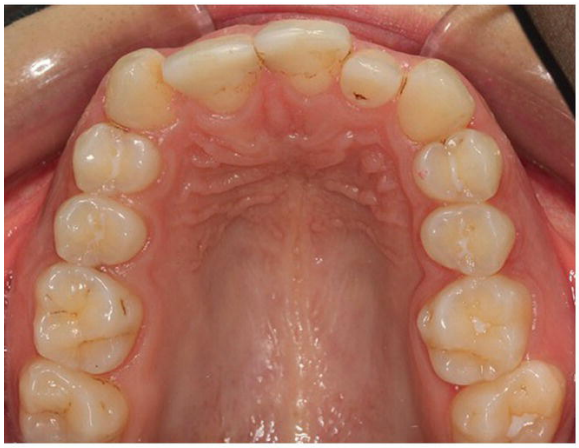
(Rosa, 2020). Treatment by mesial movement of canines to close the space and reshaping them into lateral incisors is preferred in patients with Class I and Class II malocclusion without severe crowding in the lower arch (Negi and Amita, 2020). Nowadays space closure is possible in all malocclusions (Rosa, 2020). It should once more be emphasized that the only indication for opening the space may be in patients who have a low smile line and do not show any gingiva on smiling.

(a)

(b)

(c)

(d)



(e)

(f)

(g)

(h)

Figure 17.34 A 22-year-old patient with missing upper right lateral incisor (a, e, g). The patient was treated with extraction of the left lateral incisor to achieve a more symmetrical appearance. A temporary pontic was used during space closure with fixed appliances (b). During fixed orthodontic treatment, canines were ground from the distal and incisal, extruded and tipped mesially to mimic lateral incisors, and the palatinal cusps of the first premolars were ground as well (c, f). After 23 months of orthodontic treatment, the canines were restored with composite resin to look like lateral incisors (d, h).

Canine substitution can be readily accomplished with a satisfactory esthetic outcome and excellent long-term treatment results by performing optimal torque control, differential intrusion of the first premolars and extrusion of the canines, gradual grinding of the canine cusps and buccal curvature, bleaching, a minor surgical procedure for crown lengthening, and additive reshaping of the six anterior teeth using either ceramic veneers or composite (Qadri et al., 2016; Zachrisson et al., 2011). Thanks to advances in esthetic and restorative dentistry, this approach can produce positive outcomes. Besides, central incisors often need to be built up because patients with congenitally missing teeth have an undersized dentition (Wright et al., 2016; Al Rushaid et al., 2016). The central incisors need to be enlarged, in both width and length, to obtain a correct thickness and smile arc (Rosa, 2020).

During the bioadditive restorative treatment, teeth can be made to appear narrower or wider using a variety of illusion techniques. If the distal aspect of the tooth is lingualized, the tooth will appear narrower when viewed from the facial. Mesio-incisal and disto-incisal angles define the negative dark space behind the teeth that is present when patients open their mouth. These angles may be manipulated to create desired illusions of tooth width. Rounding the incisal corners opens the interincisal embrasure, thereby creating more negative dark space and giving the tooth a narrower appearance. Closing the incisal embrasure produces the illusion of a wider tooth when viewed from the front, with the mouth opened as when the patient is laughing (Bassett, 2020).

A systematic review of the literature has shown that space closure followed by canine recontouring is superior in terms of esthetic and periodontal aspects with respect to prosthetic treatment (Silveira et al., 2016). This treatment plan is widely adopted by dental specialists depending on advancements in adhesive and resin composite technologies (Rosa and Zachrisson, 2010). Furthermore, the healthy gingival tissues and intact interdental gingival papilla will change in synchrony with the patient's own teeth over a lifetime (Rosa and Zachrisson, 2007).

The timing of the restorations is crucial for the success of interdisciplinary treatment. Direct resin composite restorations should be done immediately after removal of the orthodontic appliances (Rosa and Zachrisson, 2014). A systematic review showed that no differences in occlusal function, prevalence of cervical abfraction, or signs of temporomandibular disorder (TMD) were present in patients treated with space closure and recontouring of the canines (Silveira et al., 2016). The study also revealed that neither canine nor group disocclusion was found to be related to TMD (Silveira et al., 2016). Clinical research also showed that patients treated with canine substitution have improved periodontal health and reported higher levels of satisfaction and self-esteem with their appearance compared to those with dental prostheses (Pithon et al., 2021; Abu-Hussein et al., 2015).

In unilateral cases, a space-opening alternative may be preferred to maintain facial symmetry. However, both treatment modalities can be recommended for bilateral cases depending on the aforementioned patient-related factors (Rosa and Zachrisson, 2010). The space-opening solution requires a prosthetic replacement of two possible categories: a single tooth implant or a fixed dental prosthesis (Kokich et al., 2011). In the presence of a concave or flat profile, Class III or Class I with tendency to Class III, or of lower diastemas, diminished overjet, deep bite, or well-localized and dark-colored canines, it is recommended to open spaces and to plan rehabilitation with implants (Silveira et al., 2016; Torres et al., 2018). To obtain correct implant rehabilitation from both esthetic and functional points of view, adequate bone thickness and adequate space are necessary. Before implant placement, teeth adjacent to the missing lateral incisor should have parallel roots and adequate space

must be created coronally and apically. Appropriate space is determined by occlusion, by esthetics, and by the distances between the implant and the adjacent teeth, which should ideally correspond to about 1.4 mm (Kokich, 2004). Standard-diameter implants require sufficient width of the alveolar ridge (>5.5 mm) and the critical condition for good osseointegration is to have at least 2 mm of healthy bone around the implant (Branemark et al., 1977; Figure 17.35). These conditions are not always available in the presence of agenesis of the lateral incisors. Besides, several studies show that the orthodontic opening for the insertion of an endosseous implant generates a reduction in the height and width of the bone crest. Several methods have been offered to solve the problem of scant bone thickness in those cases requiring an implant–prosthetic rehabilitation: techniques to change the axis of insertion of the implants, exposing the prosthetic restoration to the concrete risk of failure, techniques of ridge augmentation (guided bone regeneration) with re-absorbable membrane, bone grafting, ridge expansion using split-crest, edentulous ridge expansion, and ridge expansion osteotomy. However, these bone-augmentation procedures increase the risk of possible side effects, costs, and treatment duration (Bidra and Almas, 2013).

The main advantage of implant placement is that adjacent teeth stay intact, keeping the normal position, and allow a canine-protected occlusion. However, the timing of placement of the implants is a major issue to consider. The timing for implant placement after the end of growth is generally about 20–21 years of age for men and 16–17 years of age for women (Paduano et al., 2014; Figure 17.36). Infraocclusion of the implant-supported restoration (Zitzmann et al., 2015) is quite common, and several individual factors related to facial growth, occlusion, dental continuous eruption, and wear should be evaluated. The infraocclusion of the single-tooth implant cannot always be solved by elongating the incisal margin or placing a new crown, causing severe esthetic and functional problems. This progressive infraocclusion suggests that implant placement in a young patient should be delayed as long as possible, especially in patients with a high smile line (Cocconi, 2020).

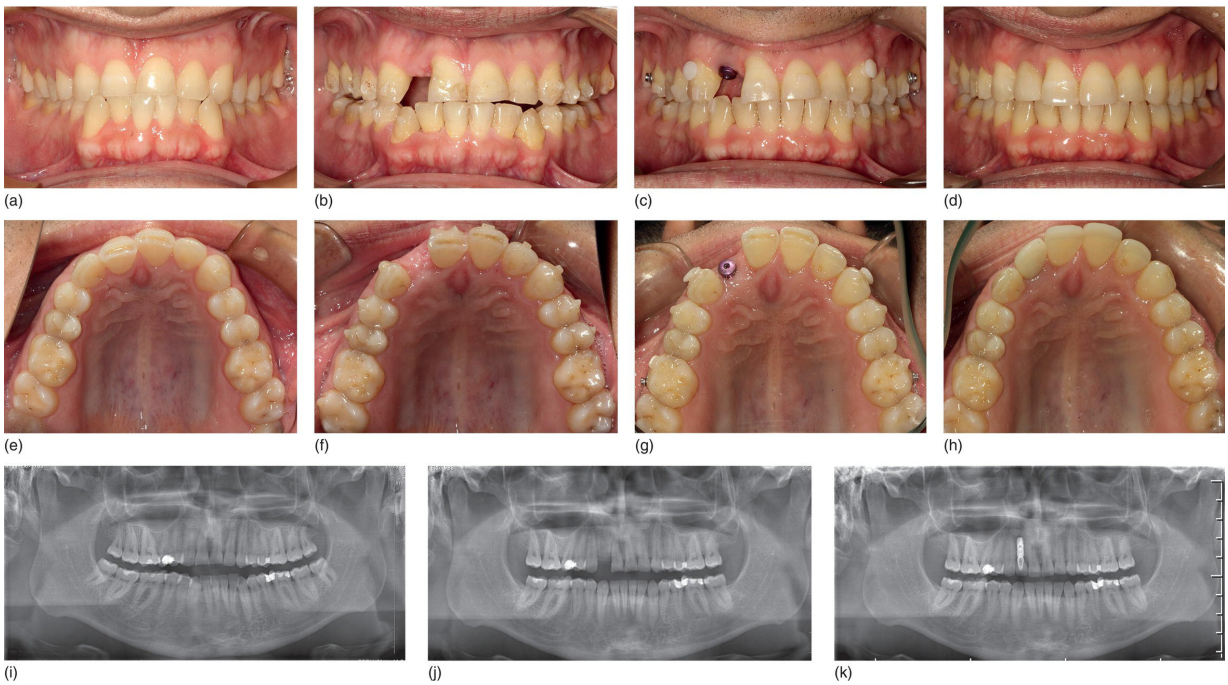


Figure 17.35 A patient with Class III malocclusion and a missing upper right lateral incisor (a, e, i). The treatment plan comprised opening of the lateral incisor space for an implant restoration and correcting the anterior crossbite. The orthodontic treatment was initiated with fixed appliances for six months to be able to open sufficient space between the roots of # 11 and 13 for implant placement and followed by clear aligners (b, f). Aligners were used prior to implant placement and the total treatment duration with aligners was 21 months (c, g, j). The central incisors and the left lateral incisor were also restored via composite resin restorations at the end of the treatment (d, h, k).

Figure 17.36 A young adult patient with Class II malocclusion, increased overjet and overbite, and missing upper laterals and right first molar (a, d, g). Canines were distalized to open spaces to replace the lateral incisors, the molar space was closed, and the incisor relationship was corrected (b, e, h). Implant restorations were made to achieve an esthetic outcome (c, f, i).

Thus, osseointegrated dental implants are contraindicated in growing patients due to the risk of implant submergence after the eruption of surrounding teeth (Cope and McFadden, 2014). There is a need for provisional restorations to keep the space until growth is complete (Ciarlantini and Melsen, 2017). Various temporization options are available, including removable or fixed retainers with a pontic and bonded bridges such as the Maryland or fiber-reinforced resin composite bridge (Ciarlantini and Melsen, 2017; Thoma et al., 2017). In the meantime, the alveolar bone may be preserved by retaining the primary tooth (Sheerah et al., 2019). Removable appliances with pontics are poorly tolerated due to compromised

esthetics, as the edentulous space is exposed to others when removing the appliance while eating (Kalia, 2015). Likewise, bonded bridges may cause technical complications such as chipping and debonding (Thoma et al., 2017).

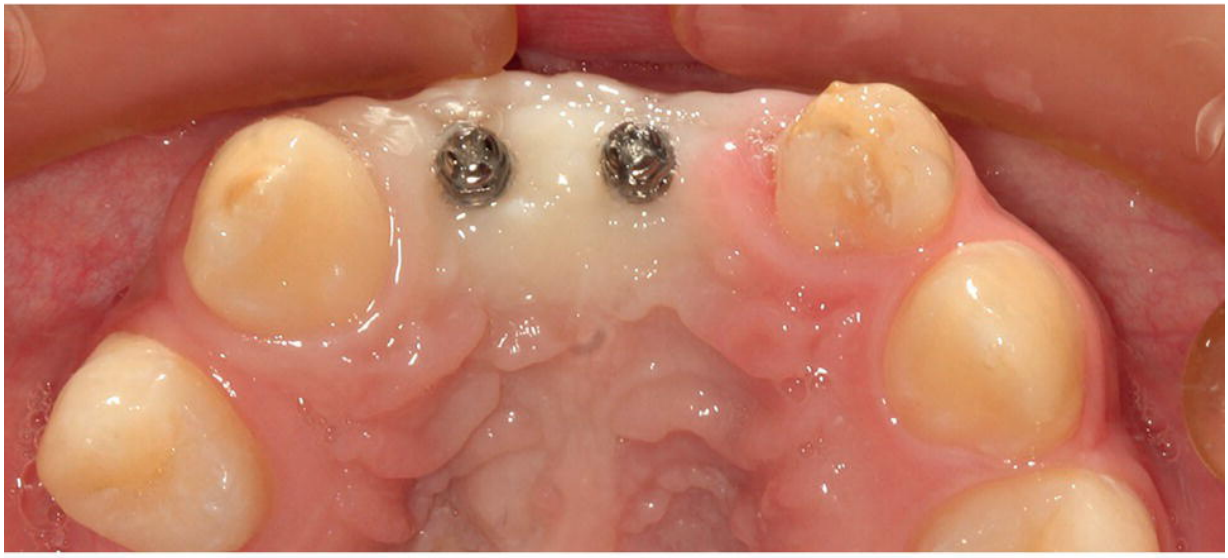
Fiber-reinforced composite-supported fixed partial dentures may offer a viable alternative treatment modality for temporization until growth is complete, or sometimes for definitive restorations where possible (Ahmed et al., 2017). Fiber-reinforced partial dentures have enhanced esthetics, low cost, better bond strength, and can be fabricated by both direct and indirect methods with minimal tooth preparation (Ahmed et al., 2017). The long-term esthetic impact of prostheses has been demonstrated to be less favorable to both patients and clinicians (Armbruster et al., 2005a, 2005b). In addition, the financial cost and potential biological impact of the prosthesis and potential for failure may have influenced the clinician's decision to close spaces (Krassnig and Fickl, 2011; Kokich et al., 2011; Grossmann et al., 2009). Furthermore, these treatment options have been associated with atrophy of the alveolar bone due to lack of alveolar loading, which might necessitate future soft and hard tissue grafting procedures prior to implant placement (Uribe et al., 2013; Tuncer et al., 2015; Figure 17.37).

Miniscrew implant-supported pontics are other temporization options. However, the literature about this concept is limited to case reports or case series, not RCTs (Cope and McFadden, 2014; Ciarlantini and Melsen, 2017; Kalia, 2015; Wilmes et al., 2014). The results showed that miniscrew-supported pontics can remain functionally stable for prolonged durations (up to approximately eight years) with minimal risk of complications such as failure, infraocclusion, and peri-implant angular bony defect formation (Figure 17.38).

The potential benefits include stimulation of bone remodeling, preservation of alveolar bone volume, space maintenance, and ease of placement and removal, since their surfaces are not surface-treated and osteointegrate as dental implants do (Cope and McFadden, 2014; Kalia, 2015; Graham, 2007). Thus a dental implant can be placed immediately after its removal on growth completion (Paquette, 2010).

Figure 17.37 Treatment plan of the patient with missing upper lateral incisors (a, c) was to open spaces for implant restorations. As the patient was still 14 years old at the end of orthodontic treatment, long-term retention until the final implant restorations could be placed was achieved via fiber-reinforced bonded composite resin bridges (b, d).

(a)



(b)

Figure 17.38 As the implant restorations for missing teeth are preferably made after vertical facial growth has ceased, long-term retention of the lateral implant space is required in younger patients. The height and width of the dento-alveolar bone could be maintained by placing a temporary mini-implant. (a) A mini-implant placed bucco-palatinally in a patient with a missing lateral incisor, and (b) two mini-implants placed vertically to maintain the bone for missing incisors.

Conventional fixed partial dentures are not preferred today as they

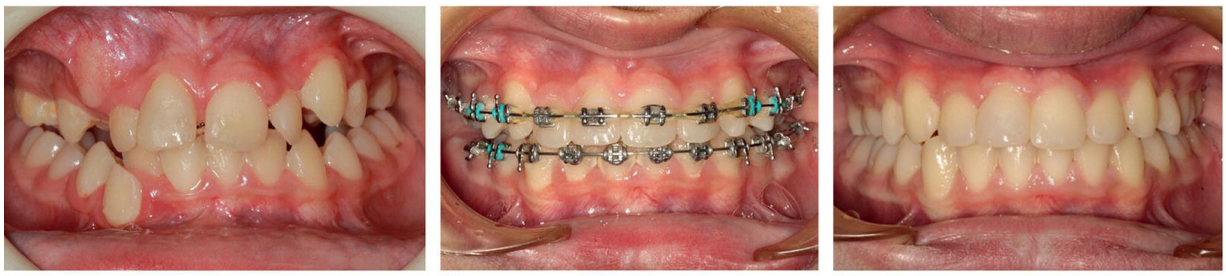
are the most invasive treatment option that involves the circumferential and occlusal reduction of adjacent teeth (Khetarpal et al., 2013). Resin-bonded fixed partial dentures have been used to restore single teeth anteriorly (Lally, 2012). Recently, with the increased focus on esthetic enhancement and rapid development in adhesive technology, labial veneer–retained fixed dental prostheses have emerged through clinical reports as a possible treatment option, allowing preservation of tooth structure with mid-term and long-term survival rates (Naguib et al., 2021).

Autotransplantation is an advantageous option with the benefits of bone induction, promotion of a normal alveolar process and PDL development, and the capability of orthodontic movement. Even if the autotransplant is lost, there will still be a chance of implant placement since growth is completed (Park et al., 2010). However, success depends on the stage of the donor tooth's root development. Some authors recommend an ideal root of the premolar tooth from three-fourths to four-fifths (Andreasen et al., 1990) or one-half to three-fourths of the final root length (Rohof et al., 2018). If the root has developed by less than half, the treatment may be too traumatic and interfere with further root development. In contrast, if a tooth with complete root formation is transplanted, it will require root canal therapy (Nimčenko et al., 2013). In open apex teeth, the pulp can revascularize through capillary vessel growth at the apex (Tsukiboshi, 2002). Long-term studies have shown the positive effects of autotransplantation (Amos et al., 2009; Andersson et al., 2012), with survival rates at over 90% and success rates of 79% (Vilhjálmsson et al., 2011; Figure 17.39).

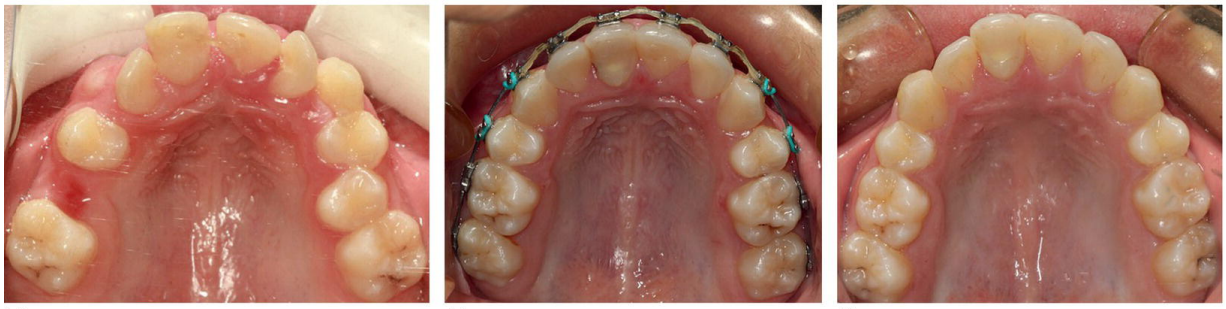
Conclusion

In a beauty-addicted society, where a pleasing smile serves as a powerful weapon, the demand for orthodontic treatment is increasing. Treating uncomplicated, caries-free adolescent patients with good oral hygiene is every clinician's dream, but this is not always the case for several reasons, such as a requirement for complex restorative procedures, trauma that occurred before the onset of orthodontic treatment, or complications evolving during or at the end of mechanotherapy. The management of these problems

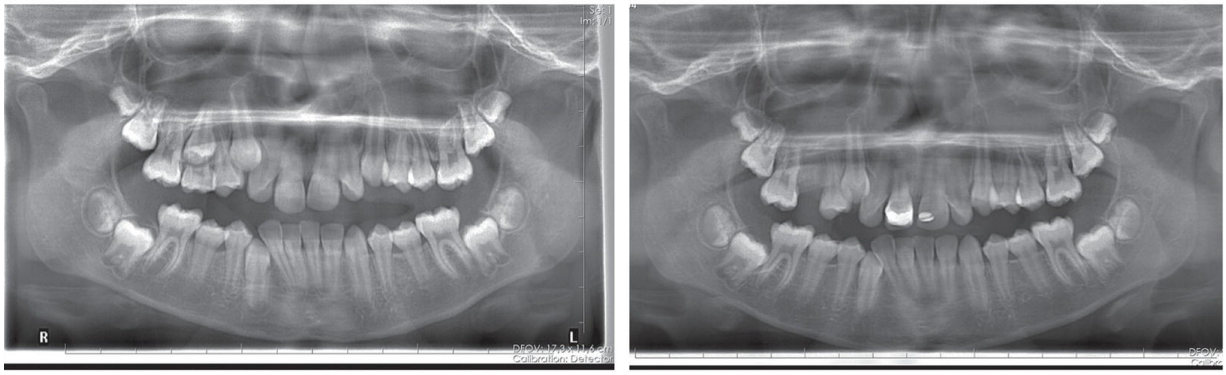
often requires interactive collaboration between orthodontic, endodontic, pediatric, and restorative dentistry specialists. In this situation, the orthodontist should assume the leading role as coordinator of the various treatment phases, thus optimizing the outcome by minimizing the risks. By forming close cooperative links between the different disciplines, the ultimate goal of a healthy, esthetic, and functional oral rehabilitation can be attained. Each of these specialties is constantly advancing and improving due to ongoing research in the biological and physical sciences. Therefore, having thorough knowledge about contemporary restorative and endodontic treatment approaches (the main thrust of this chapter) is a must for an orthodontist. By becoming familiar with these developments, and interacting with other experts, orthodontists can enhance the quality of orthodontic care, and preserve the favorable outcome of the interactive effort for a long time.



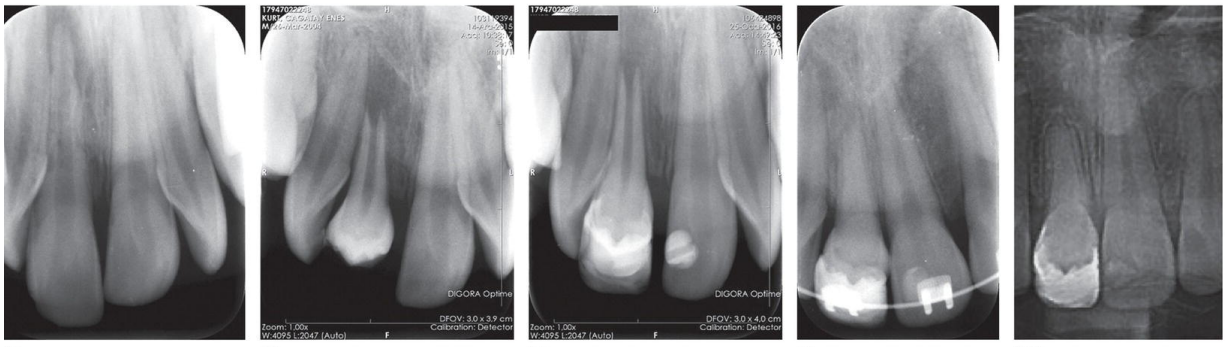
(a) (b) (c)



(d) (e) (f)



(g) (h)



(i) (j) (k) (l) (m)

Figure 17.39 (a, d) Intraoral view of the patient three weeks after autotransplantation. (b, e) Intraoral view during orthodontic treatment. (c, f) Intraoral view at the end of orthodontic treatment. (g, i) Initial othopantomograph and periapical radiograph. Note the untreatable root resorption on tooth # 11 due to trauma. (h) Orthopantomograph after six weeks following autotransplantation. (j) Periapical radiograph on the day of autotransplantation. (k) Periapical radiograph just before orthodontic treatment. (l, m) Periapical radiograph during treatment and at the four-year follow-up.

References

Abbasoglu, Z., and Kuvvetli, S.S. (2021). Influence of maternal attitudes and parenting style on children's dental caries experience. *Journal of the Pakistan Medical Association* 71: 2325–2329.

Abi-Ramia, L.B.P., Stuani, A.S., Stuani, A.S. et al. (2010). Effects of low-level laser therapy and orthodontic tooth movement on dental pulps in rats. *Angle Orthodontist* 80: 116–122.

Abraham, R., and Kamath, G. (2014). Midline diastema and its aetiology—a review. *Dental Update* 41: 457–464.

Abu-Hussein, M., Watted, N., Hegedűs, V. et al. (2015). Congenitally missing upper laterals. Clinical considerations: Orthodontic space closure. *Journal of Dental and Oral Health* 1: 82–89.

Ahlberg, K., Bystedt, H., Eliasson, S. et al. (1983). Long-term evaluation of autotransplanted maxillary canines with completed root formation. *Acta Odontologica Scandinavia* 41: 23–31.

Ahmed, K.E., Li, K.Y., and Murray, C.A. (2017). Longevity of fiber-reinforced composite fixed partial dentures (FRC FPD)—systematic review. *Journal of Dentistry* 61: 1–11.

Ahn, S.J., Lim, B.S., and Lee, S.J. (2007). Prevalence of cariogenic streptococci on incisor brackets detected by polymerase chain

reaction. *American Journal of Orthodontics and Dentofacial Orthopedics* 131: 736–741.

Al-Ani, A.H., Antoun, J.S., Thomson, W.M. et al. (2017). Hypodontia: An update on its etiology, classification, and clinical management. *Biomed Research International* 2017: 9378325.

Albhaisi, Z., Al-Khateeb, S.N., and Abu Alhaija, E.S. (2020). Enamel demineralization during clear aligner orthodontic treatment compared with fixed appliance therapy, evaluated with quantitative light-induced fluorescence: A randomized clinical trial. *American Journal of Orthodontics and Dentofacial Orthopedics* 157: 594–601.

Alcan, T. (2006). A miniature tooth-borne distractor for the alignment of ankylosed teeth. *Angle Orthodontist* 76: 77–83.

Allison, J.S., Stone, S.J., and Pigg, M. (2020). The painful tooth: Mechanisms, presentation and differential diagnosis of odontogenic pain. *Oral Surgery* 13: 309–320.

Almpani, K., Papageorgiou, S.N., and Papadopoulos, M.A. (2015). Autotransplantation of teeth in humans: A systematic review and meta-analysis. *Clinical Oral Investigations* 19: 1157–1179.

Alp, S., and Baka, Z.M. (2018). Effects of probiotics on salivary Streptecoccus mutans and Lactobacillus levels in orthodontic patients. *American Journal of Orthodontics and Dentofacial Orthopedics* 154: 517–523.

Al Rushaid, S., Chandhoke, T., Utreja, A. et al. (2016). Three-dimensional evaluation of root dimensions and alveolar ridge width of maxillary lateral incisors in patients with unilateral agenesis. *Progress in Orthodontics* 17: 30.

Amaechi, B.T., Alshareif, D.O., Azees, P.A.A. et al. (2021). Anti-caries evaluation of a nano-hydroxyapatite dental lotion for use after toothbrushing: An in situ study. *Journal of Dentistry* 115: 103863.

Amemiya, K., Kaneko, Y., Muramatsu, T. et al. (2003). Pulp cell responses during hypoxia and reoxygeneration in vitro. *European*

Journal of Oral Sciences 111: 332–338.

American Academy of Pediatric Dentistry (2004). Clinical guideline on management of acute dental trauma. *Pediatric Dentistry* 26: 120–127.

American Academy of Pediatric Dentistry (2014). *Guideline on Pediatric Oral Surgery*. *Reference Manual*, vol. 36, no. 6. Chicago, IL: American Academy of Pediatric Dentistry.

American Academy of Pediatric Dentistry (2021). Caries-risk assessment and management for infants, children, and adolescents. In: *The Reference Manual of Pediatric Dentistry*. Chicago, IL: American Academy of Pediatric Dentistry, pp. 252–257.

Amos, M.J., Day, P., and Littlewood, S.J. (2009). Autotransplantation of teeth: An overview. *Dental Update* 36: 102–113.

Andersson, L. (2007). Tooth avulsion and replantation. *Dental Traumatology* 23: 129.

Andersson, L., Andreasen, J.O., Day, P. et al. (2012). International Association of Dental Traumatology guidelines for the management of traumatic dental injuries: 2. Avulsion of permanent teeth. *Dental Traumatology* 28: 88–96.

Andreasen, F.M., Andreasen, J.O., and Tsukiboshi, M. (2007). Examination and diagnosis of dental injuries. In: J.O. Andreasen, F.M. Andreasen, and L. Andersson (eds.), *Textbook and Color Atlas of Traumatic Injuries to the Teeth*. Oxford: Blackwell/Munksgaard, pp. 255–274.

Andreasen, J.O. (1992). *Atlas of Replantation and Transplantation of Teeth*. Philadelphia, PA: W.B. Saunders.

Andreasen, J.O., and Andreasen, F.M. (2000). *Essentials of Traumatic Injuries to the Teeth*, 2nd ed. Copenhagen: Munksgaard/Mosby.

Andreasen, J.O., and Andreasen, F.M. (2007). Avulsions. In: J.O. Andreasen, F.M. Andreasen, and L. Andersson (eds.), *Textbook and Color Atlas of Traumatic Injuries to the Teeth*, 4th ed. Oxford: Blackwell/Munksgaard, pp. 444–480.

Andreasen, J.O., Andreasen, F.M., and Tsilingaridis, G. (2019). Avulsions. In: J.O. Andreasen, F.M. Andreasen, and L. Andersson (eds.), *Textbook and Color Atlas of Traumatic Injuries to the Teeth*, 5th ed. Oxford: Wiley Blackwell, pp. 486–520.

Andreasen, J.O., Borum, M.K., Jacobsen, H.L. et al. (1995a). Replantation of 400 avulsed permanent incisors. 1. Diagnosis of healing complications. *Endodontics and Dental Traumatology* 11: 51–58.

Andreasen, J.O., Borum, M.K., Jacobsen, H.L. et al. (1995b). Replantation of 400 avulsed permanent incisors. 2. Factors related to pulpal healing. *Endodontics and Dental Traumatology* 11: 59–68.

Andreasen, J.O., Farik, B., and Munksgaard, E.C. (2002). Long-term calcium hydroxide as a root canal dressing may increase risk of root fracture. *Dental Traumatology* 18: 134–137.

Andreasen, J.O., and Hjorting-Hansen, E. (1966). Replantation of teeth. I. Radiographic and clinical study of 110 human teeth replanted after accidental loss. *Acta Odontologica Scandinavia* 24: 263–286.

Andreasen, J.O., Munksgaard, E.C., and Bakland, L.K. (2006). Comparison of fracture resistance in root canals of immature sheep teeth after filling with calcium hydroxide or MTA. *Dental Traumatology* 22: 154–156.

Andreasen, J.O., Paulsen, H.U., Yu, Z. et al. (1990). A long-term study of 370 autotransplanted premolars. Part II. Tooth survival and pulp healing subsequent to transplantation. *European Journal of Orthodontics* 12: 14–24.

Andreasen, J.O., Schwartz, O., Kofoed, T. et al. (2009). Transplantation of premolars as an approach for replacing

avulsed teeth. *Pediatric Dentistry* 31: 129–132.

Anstendig, H., and Kronman, J. (1972). A histologic study of pulpal reaction to orthodontic tooth movement in dogs. *Angle Orthodontist* 42: 50–55.

Anthony, D.R. (1986). Apexification during active orthodontic movement. *Journal of Endodontics* 12: 419–421.

Antoniadou, M., and Varzakas, T. (2021). Probiotics and prebiotics and their effect on food and human health: New perspectives. In: H.A. El Enshasy and S.T. Yang (eds.), *Probiotics, the Natural Microbiota in Living Organisms: Fundamentals and Applications*. Boca Raton, FL: CRC Press, ch. 1.

Arhun, N., Arman, N., Çehreli, S.B. et al. (2006a). Microleakage beneath metal and ceramic brackets bonded with a conventional and an antibacterial adhesive system. *Angle Orthodontist* 76: 1028–1034.

Arhun, N., Arman, A., Ungor, M. et al. (2006b). A conservative multidisciplinary approach for improved aesthetic results with traumatised anterior teeth. *British Dental Journal* 201: 509–512.

Arhun, N., and Ungor, M. (2007). Re-attachment of a fractured tooth: A case report. *Dental Traumatology* 23(5): 322–326.

Arıkan, S., Arhun, N., Arman, A. et al. (2006). Microleakage beneath ceramic and metal brackets photopolymerized with LED or conventional light curing units. *Angle Orthodontist* 76: 1035–1040.

Arkutu, N., Gadhia, K., McDonald, S. et al. (2012). Amelogenesis imperfecta: The orthodontic perspective. *British Dental Journal* 212: 485–489.

Armbruster, P.C., Gardiner, D.M., Whitley, J.B., Jr. et al. (2005a). The congenitally missing maxillary lateral incisor. Part I: Esthetic judgement of treatment options. *World Journal of Orthodontics* 6: 369–375.

Armbruster, P.C., Gardiner, D.M., Whitley, J.B., Jr. et al. (2005b). The congenitally missing maxillary lateral incisor. Part 2: Assessing dentists' preferences for treatment. *World Journal of Orthodontics* 6: 376–381.

Arte, S., Awadh, W., Nieminen, P. et al. (2017). Tooth agenesis. In: M. Cobourne (ed.), *Orthodontic Management of the Developing Dentition*. Cham: Springer, pp. 67–84.

Arte, S., Nieminen, P., Apajalahti, S. et al. (2001). Characteristics of incisor-premolar hypodontia in families. *Journal of Dental Research* 80: 1445–1450.

Artun, J. (1987). A post-treatment evaluation of multibonded lingual appliances in lingual orthodontics. *European Journal of Orthodontics* 9: 204–210.

Artun, J., and Brobakken, B.O. (1986). Prevalence of carious white spots after orthodontic treatment with multibonded appliances. *European Journal of Orthodontics* 8: 229–234.

Artun, J., and Thylstrup, A. (1986). Clinical and scanning electron microscopic study of surface changes of incipient caries lesions after debonding. *Scandinavian Journal of Dental Research* 94: 193–201.

Asgary, S., and Eghbal, M.J. (2010). The effect of pulpotomy using a calcium-enriched mixture cement versus one-visit root canal therapy on postoperative pain relief in irreversible pulpitis: A randomized clinical trial. *Odontology* 98: 126–133.

Ashcraft, M.B., Southard, K.A., and Tolley, E.A. (1992). The effect of corticosteroid-induced osteoporosis on orthodontic tooth movement. *American Journal of Orthodontics and Dentofacial Orthopedics* 102: 310–319.

Azeem, M., and Ul Hamid, W. (2017). Incidence of white spot lesions during orthodontic clear aligner therapy. *Journal of World Federation of Orthodontics* 6: 127–130.

Baek, S.H., Plenk, H., Jr., and Kim, S. (2005). Periapical tissue responses and cementum regeneration with amalgam, superEBA and MTA as root-end filling materials. *Journal of Endodontics* 31: 444–449.

Baka, Z.M., Basciftci, F.A., and Arslan, U. (2013). Effects of 2 bracket and ligation types on plaque retention: A quantitative microbiologic analysis with real-time polymerase chain reaction. *American Journal of Orthodontics and Dentofacial Orthopedics* 144: 260–267.

Bakti, I., Santosa, A.S., Irawan, B. et al. (2018). Chameleon effect of nano-filled composite resin restorations in artificial acrylic teeth of various shades. *Journal of Physics: Conference Series* 1073: 052011.

Banchs, F., and Trope, M. (2004). Revascularization of immature permanent teeth with apical periodontitis: New treatment protocol? *Journal of Endodontics* 30: 196–200.

Barbizam, J.V.B., Massarwa, R., da Silva, L.A.B. et al. (2015). Histopathological evaluation of the effects of variable extraoral dry times and enamel matrix proteins (enamel matrix derivatives) application on replanted dogs' teeth. *Dental Traumatology* 31: 29–34.

Baroni, C., and Marchionni, S. (2011). MIH supplementation strategies: Prospective clinical and laboratory trial. *Journal of Dental Research* 90: 371–376.

Barros, M.M.A.F., De Queiroz Rodrigues, M.I., Muniz, F.W.M.G. et al. (2020). Selective, stepwise, or nonselective removal of carious tissue: Which technique offers lower risk for the treatment of dental caries in permanent teeth? A systematic review and meta-analysis. *Clinical Oral Investigations* 24: 521–532.

Bassett, J. (2020). Applying classical esthetic principles to create a predictable illusion of symmetry while using digital technology. *Compendium of Continuing Education in Dentistry* 41: 204–209.

Bauss, O., Sadat-Khonsari, R., Engelke, W. et al. (2003). Results of transplanting developing third molars as part of orthodontics space management. Part 2: Results following the orthodontic treatment of transplanted developing third molars in cases of aplasia and premature loss of teeth with atrophy of the alveolar process. *Journal of Orofacial Orthopedics* 64: 40–47.

Bauss, O., Schwestka-Polly, R., and Kiliaridis, S. (2004). Influence of orthodontic derotation and extrusion on pulpal and periodontal condition of autotransplanted immature third molars. *American Journal of Orthodontics and Dentofacial Orthopedics* 125: 488–496.

Baysal, A., Uysal, T., and Usumez, S. (2007). Temperature rise in the pulp chamber during different stripping procedures. *Angle Orthodontist* 3: 478–482.

Becker, A., and Karnei-R'em, R.M. (1992a). The effects of infraocclusion: Part 1. Tilting of the adjacent teeth and local space loss. *American Journal of Orthodontics Dentofacial Orthopedics* 102: 256–264.

Becker, A., and Karnei-R'em, R.M. (1992b). The effects of infraocclusion: Part 2. The type of movement of the adjacent teeth and their vertical development. *American Journal of Orthodontics and Dentofacial Orthopedics* 102: 302–309.

Becker, A., Karnei-R'em, R.M., and Steigman, S. (1992). The effects of infraocclusion: Part 3. Dental arch length and the midline. *American Journal of Orthodontics and Dentofacial Orthopedics* 102: 427–433.

Benington, P., Gillgrass, T., Foye, R. et al. (2001). Daily exposure to fluoride mouthrinse produces sustained fluoride release from orthodontic adhesives in vitro. *Journal of Dentistry* 29: 23–29.

Benson, P.E., Parkin, N., Millett, D.T. et al. (2004). Fluorides for the prevention of white spots on teeth during fixed brace treatment. *Cochrane Database of Systematic Reviews* 3: CD003809. doi: 10.1002/14651858.CD003809.pub2.

Benson, P.E., Parkin, N., Dyer, F. et al. (2019). Fluorides for preventing early tooth decay (demineralised lesions) during fixed brace treatment. *Cochrane Database of Systematic Reviews* 11: CD003809. doi: 10.1002/14651858.CD003809.pub4.

Berggreen, E., and Heyeraas, K.J. (1999). The role of sensory neuropeptides and nitric oxide on pulpal blood flow and tissue pressure in the ferret. *Journal of Dental Research* 78: 1535–1543.

Berglund, L., Kurol, J., and Kvint, S. (1996). Orthodontic pre-treatment prior to autotransplantation of palatally impacted maxillary canines: Case reports on a new approach. *European Journal of Orthodontics* 18: 449–456.

Bernabe, E., and Flores-Mir, C. (2007). Influence of anterior occlusal characteristics on self-perceived dental appearance in young adults. *Angle Orthodontist* 77: 831–836.

Bidra, A.S., and Almas, K. (2013). Mini implants for definitive prosthodontic treatment: A systematic review. *Journal of Prosthetic Dentistry* 109: 156–164.

Bilgin Yener, S., and Polat Özsoy, O. (2020). Quantitative analysis of biofilm formation on labial and lingual bracket surfaces. *Angle Orthodontist* 90: 100–108.

Bishara, S.E., and Ostby, A.W. (2008). White spot lesions: Formation, prevention and treatment. *Seminars in Orthodontics* 14: 174–182.

Bishara, S.E., Ostby, A.W., Laffoon, J. et al. (2007). Shear bond strength comparison of two adhesive systems following thermocycling: A new self-etch primer and resin modified glass ionomer. *Angle Orthodontist* 77: 337–341.

Bjørndal, L. (2018). Caries pathology and management in deep stages of lesion formation. In: L. Bjørndal, L.-L. Kirkevang, J. Whitworth (eds.), *Textbook of Endodontology*, 3rd ed. Oxford: Wiley Blackwell, pp. 61–78.

Bjørndal, L., Fransson, H., Bruun, G. et al. (2017). Randomized clinical trials on deep carious lesions: 5-year follow-up. *Journal of Dental Research* 96: 747–753.

Bjørndal, L., Simon, S., Tomson, P.L. et al. (2019). Management of deep caries and the exposed pulp. *International Endodontic Journal* 52: 949–973.

Boersma, J.G., van der Veen, M.H., Lagerweij, M.D. et al. (2005). Caries prevalence measured with QLF after treatment with fixed orthodontic appliances: influencing factors. *Caries Research* 39: 41–47.

Borum, M.K., and Andreasen, J.O. (2001). Therapeutic and economic implications of traumatic dental injuries in Denmark: An estimate based on 7549 patients treated at a major trauma centre. *International Journal of Pediatric Dentistry* 11: 249–258.

Bose, R., Nummikoski, P., and Hargreaves, K. (2009). A retrospective evaluation of radiographic outcomes in immature teeth with necrotic root canal systems treated with regenerative endodontic procedures. *Journal of Endodontics* 35: 1343–1349.

Botelho, M.G., Chan, A.W., Leung, N.C. et al. (2016). Long-term evaluation of cantilevered versus fixed–fixed resin-bonded fixed partial dentures for missing maxillary incisors. *Journal of Dentistry* 45: 59–66.

Bourguignon, C., Cohenca, N., Lauridsen, E. et al. (2020). International Association of Dental Traumatology guidelines for the management of traumatic dental injuries: 1. *Fractures and luxations. Dental Traumatology* 36: 314–330.

Bourouni, S., Dritsas, K., Kloukos, D. et al. (2021). Efficacy of resin infiltration to mask post-orthodontic or non-post-orthodontic white spot lesions or fluorosis—a systematic review and meta-analysis. *Clinical Oral Investigations* 25: 4711–4719.

Boyd, R.L., and Chun, Y.S. (1994). Eighteen-month evaluation of the effects of a 0.4% stannous fluoride gel on gingivitis in orthodontic

patients. *American Journal of Orthodontics and Dentofacial Orthopedics* 105: 35–41.

Branemark, P.I., Hansson, B.O., Adell, R. et al. (1977). Osseointegrated implants in the treatment of the edentulous jaw. Experience from a 10-year period. *Scandinavian Journal of Plastic and Reconstructive Surgery Supplementum* 16: 1–132.

Bratthall, D. (1996). Dental caries: Intervened—interrupted—interpreted. Concluding remarks and cariograph. *European Journal of Oral Sciences* 104: 486–491.

Bratthall, D., and Petersson, G.H. (2005). Cariogram—a multifactorial risk assessment model for a multifactorial disease. *Community Dentistry and Oral Epidemiology* 33: 256–264.

Brezniak, N., and Wasserstein, A. (2002). Orthodontically induced inflammatory root resorption. Part II: The clinical aspects. *Angle Orthodontist* 72: 180–184.

Briggs, P.F., and Scott, B.J. (1997). Evidence based dentistry; endodontic failure – now should it be managed? *British Dental Journal* 183: 159–164.

Brudvik, P., and Rygh, P. (1993). The initial phase of orthodontic root resorption incident to local compression of the periodontal ligament. *European Journal of Orthodontics* 15: 249–263.

Brudvik, P., and Rygh, P. (1994a). Root resorption beneath the main hyalinized zone. *European Journal of Orthodontics* 16: 249–263.

Brudvik, P., and Rygh, P. (1994b). Multi-nucleated cells remove the main hyalinized tissue and start resorption of adjacent root surfaces. *European Journal of Orthodontics* 16: 265–273.

Bryson, E.C., Levin, L., Banchs, F. et al. (2002). Effect of immediate intracanal placement of ledermix paste on healing of replanted dog teeth after extended dry times. *Dental Traumatology* 18: 316–321.

Burden, D.J. (1995). An investigation of the association between overjet size, lip coverage, and traumatic injury to maxillary

incisors. *European Journal of Orthodontics* 17: 513–517.

Butcher, E.O., and Taylor, A.C. (1951). The effects of denervation and ischemia upon the teeth of the monkey. *Journal of Dental Research* 30: 265–275.

Büyükyılmaz, T., Tangugsorn, V., Ogaard, B. et al. (1994). The effect of titatium tetrafluoride (TiF4) application around orthodontic brackets. *American Journal of Orthodontics and Dentofacial Orthopedics* 105: 293–296.

Buzalaf, M.A.R. (2018). Review of fluoride intake and appropriateness of current guidelines. *Advances in Dental Research* 29: 157–166.

Cagetti, M.G., Bontà, G., Cocco, F. et al. (2018). Are standardized caries risk assessment models effective in assessing actual caries status and future caries increment? A systematic review. *BMC Oral Health* 18: 123.

Çağlar, E., Sandalli, N., Twetman, S. et al. (2005). Effect of yogurt with Bifidobacterium DN-173 010 on salivary mutans streptococci and lactobacilli in young adults. *Acta Odontologica Scandinavica* 63: 317–320.

Calamia, V., and Pantzis, A. (2015). Simple case treatment planning: Diastema closure. *Dental Clinics of North America* 59: 655–664.

Caniklioglu, C., and Ozturk, Y. (2005). Patient discomfort: A comparison between lingual and labial fixed appliances. *Angle Orthodontist* 75: 86–91.

Casagrande, L., Seminario, A.T., Correa, M.B. et al. (2017). Longevity and associated risk factors in adhesive restorations of young permanent teeth after complete and selective caries removal: A retrospective study. *Clinical Oral Investigations* 21: 847–855.

Cengiz, S.B., Atac, A.S., Cehreli, Z.C. (2006). Biomechanical effects of splint types on traumatized tooth: A photoelastic stress analysis. *Dental Traumatology* 22: 133–138.

Cengiz, S.B., Kocadereli, I., Gungor, H.C. et al. (2005). Adhesive fragment reattachment after orthodontic extrusion: A case report. *Dental Traumatology* 21: 60–64.

Chadwick, B.L., Roy, J., Knox, J. et al. (2005). The effect of topical fluorides on decalcification in patients with fixed orthodontic appliances: A systematic review. *American Journal of Orthodontics and Dentofacial Orthopedics* 128: 601–606.

Chaushu, S., Becker, A., and Chaushu, G. (2004a). Orthosurgical treatment with lingual orthodontics of an infraoccluded maxillary first molar in an adult. *American Journal of Orthodontics and Dentofacial Orthopedics* 125: 379–387.

Chaushu, S., Shapira, J., Heling, I. et al. (2004b). Emergency orthodontic treatment after the traumatic intrusive luxation of maxillary incisors. *American Journal of Orthodontics and Dentofacial Orthopedics* 126: 162–172.

Chen, H., Teixeira, F.B., Ritter, A.L. et al. (2008). The effect of intracanal anti-inflammatory medicaments on external root resorption of replanted dog teeth after extended extra-oral dry time. *Dental Traumatology* 24: 74–78.

Chen, L., Hong, J., Xiong, D. et al. (2020). Are parents' education levels associated with either their oral health knowledge or their children's oral health behaviors? A survey of 8446 families in Wuhan. *BMC Oral Health* 20: 203.

Chen, M.Y., Chen, K.L., Chen, C.A. et al. (2012). Responses of immature permanent teeth with infected necrotic pulp tissue and apical periodontitis/abscess to revascularization procedures. *International Endodontic Journal* 45: 294–305.

Christian, B., Armstrong, R., Calache, H. et al. (2019). A systematic review to assess the methodological quality of studies on measurement properties for caries risk assessment tools for young children. *International Journal of Paediatric Dentistry* 29: 106–116.

Chu, C.H., Zhang, C.F., and Jin, L.J. (2011). Treating a maxillary midline diastema in adult patients: A general dentist's perspective. *Journal of American Dental Association* 142: 1258–1264.

Chutimanutskul, W., Ali Darendeliler, M., Shen, G. et al. (2006). Changes in the physical properties of human premolar cementum after application of 4 weeks of controlled orthodontic forces. *European Journal of Orthodontics* 28: 313–318.

Ciarlantini, R., and Melsen, B. (2017). Semipermanent replacement of missing maxillary lateral incisors by mini-implant retained pontics: A follow-up study. *American Journal of Orthodontics and Dentofacial Orthopedics* 151: 989–994.

Cildir, S.K., Germec, D., Sandalli, N. et al. (2009). Reduction of salivary mutans streptococci in orthodontic patients during daily consumption of yoghurt containing probiotic bacteria. *European Journal of Orthodontics* 31: 407–411.

Cobourne, M.T. (2007). Familial human hypodontia—is it all in the genes? *British Dental Journal* 203: 203–208.

Cocconi, R. (2020). Essay II: Space closure vs space preservation as it relates to craniofacial classification. *International Journal of Esthetic Dentistry* 15(Suppl): S32–S45.

Cochrane, N.J., Cai, F., Huq, N.L. et al. (2010). New approaches to enhanced remineralization of tooth enamel. *Journal of Dental Research* 89: 1187–1197.

Cochrane, N.J., Lo, T.W., Adams, G.G. et al. (2017). Quantitative analysis of enamel on debonded orthodontic brackets. *American Journal of Orthodontics and Dentofacial Orthopedics* 152: 312–319.

Coelho-de-Souza, F.H., Gonçalves, D.S., Sales, M.P. et al. (2015). Direct anterior composite veneers in vital and non-vital teeth: A retrospective clinical evaluation. *Journal of Dentistry* 43: 1330–1336.

Comba, A., Vergano, E.A., Baldi, A. et al. (2021). 5-year retrospective evaluation of direct composite restorations in orthodontically treated patients. *Journal of Dentistry* 104: 1–7.

Consolaro, A., and Consolaro, R.B. (2013). Orthodontic movement of endodontically treated teeth. *Dental Press Journal of Orthodontics* 18: 2–7.

Consolaro, A., Miranda, D.A.O., and Consolaro, R.B. (2020). Orthodontics and endodontics: Clinical decision-making. *Dental Press Journal of Orthodontics* 25: 20–29.

Cope, J.B., and McFadden, D. (2014). Temporary replacement of missing maxillary lateral incisors with orthodontic miniscrew implants in growing patients: Rationale, clinical technique, and long-term results. *Journal of Orthodontics* 41(Suppl 1): s62–s74.

Coyle, M., Toner, M., and Barry, H. (2006). Multiple teeth showing invasive cervical resorption—an entitiy with little known histologic features. *Journal of Oral Pathology and Medicine* 35: 55–57.

Crawford, P.J., Aldred, M., and Bloch-Zupan, A. (2007). Amelogenesis imperfecta. *Orphanet Journal of Rare Diseases* 2: 17.

Croll, T.P., and Bullock, G.A. (1994). Enamel microabrasion for removal of smooth surface decalcification lesions. *Journal of Clinical Orthodontics* 28: 365–370.

Croll, T.P., and Helpin, M.L. (2000). Enamel microabrasion: A new approach. *Journal of Esthetic Dentistry* 12: 64–71.

Croll, T.P., Killian, C.M., and Miller, A.S. (1990). Effect of enamel microabrasion compound on human gingiva: Report of a case. *Quintessence International* 21: 959–963.

Crystal, Y.O., and Niederman, R. (2019). Evidence-based dentistry update on silver diamine fluoride. *Dental Clinics of North America* 63: 45–68.

Curtis, A.R., Palin, W.M., Fleming, G.J. et al. (2009). The mechanical properties of nanofilled resin-based composites: The impact of dry and wet cyclic pre-loading on bi-axial flexure strength, *Dental Materials* 25: 188–197.

Cvek, M. (1978). A clinical report on partial pulpotomy and capping with calcium hydroxide in permanent incisors with complicated crown fracture. *Journal of Endodontics* 4: 232–237.

Cvek, M. (1992). Prognosis of luxated non-vital maxillary incisors treated with calcium hydroxide and filled with gutta-percha. A retrospective clinical study. *Endodontics and Dental Traumatology* 8: 45–55.

Da Cunha, L.F., Pedroche, L.O., Gonzaga, C.C. et al. (2014). Esthetic, occlusal, and periodontal rehabilitation of anterior teeth with minimum thickness porcelain laminate veneers. *Journal of Prosthetic Dentistry* 112: 1315–1318.

Davidovitch, Z. (1996). Etiologic factors in force-induced root resorption. In: Z. Davidovitch and L.A. Norton (eds.), *Biological Mechanisms of Tooth Movement and Craniofacial Adaptation*. Boston, MA: Harvard Society for the Advancement of Orthodontics, pp. 349–355.

Davidovitch, Z., Lee, Y.J., Counts, A.L. et al. (2000). The immune system possibly modulates orthodontic root resorption. In: Z. Davidovitch and J. Mah (eds.), *Biological Mechanisms of Tooth Movement and Craniofacial Adaptation*. Boston, MA: Harvard Society for the Advancement of Orthodontics, pp. 207–217.

Day, P.F., Duggal, M., and Nazzal, H. (2019). Interventions for treating traumatised permanent front teeth: Avulsed (knocked out) and replanted. *Cochrane Database of Systematic Reviews* 2: CD006542. doi: 10.1002/14651858.CD006542.pub3.

de Alencar, A.H., Lustosa-Pereira, A., de Sousa, H.A. et al. (2007). Intrusive luxation: A case report. *Dental Traumatology* 23: 307–312.

De Angelis, V., and Davidovitch, Z. (2009). Biologically and clinically, what are optimal orthodontic forces and how are they applied in selective common malocclusions? In: V. Krishnan and Z. Davidovitch (eds.), *Biological Mechanisms of Tooth Movement*. Oxford: Wiley-Blackwell, pp. 180–200.

De Coster, P.J., Marks, L.A., Martens, L.C. et al. (2009). Dental agenesis: Genetic and clinical perspectives. *Journal of Oral Pathology & Medicine* 38: 1–17.

Del Monte S, Afrashtehfar KI, Emami E, et al. (2017) Lay preferences for dentogingival esthetic parameters: a systematic review. *Journal of Prosthetic Dentistry* 118: 717–24.

Delivanis, H.P., and Gauer, G.J. (1980). Incidence of canal calcification in the orthodontic patient. *American Journal of Orthodontics* 82: 58–61.

Delli, K., Livas, C., Sculean, A. et al. (2013). Facts and myths regarding the maxillary midline frenum and its treatment: A systematic review of the literature. *Quintessence International* 44: 177–187.

Demir, O., and Arici, N. (2021). Dose-related effects of extracorporeal shock waves on orthodontic tooth movement in rabbits. *Scientific Reports* 11: 3405.

Demirci, M., Tuncer, S., Öztaş, E. et al. (2015). A 4-year clinical evaluation of direct composite build-ups for space closure after orthodontic treatment. *Clinical Oral Investigations* 19: 2187–2199.

Derks, A., Katsaros, C., Frencken, J.E. et al. (2004). Caries inhibiting effect of fluoride measures during orthodontic treatment with fixed appliances: A systematic review. *Caries Research* 38: 413–420.

Desai, S., and Chandler, N. (2009). The restoration of permanent immature anterior teeth, root filled using MTA: A review. *Journal of Dentistry* 37: 652–657.

De Villiers, J.A., Houreld, N.N., and Abrahamse, H. (2011). Influence of low intensity laser irradiation on isolated human adipose derived stem cells over 72 hours and their differentiation potential into smooth muscle cells using retinoic acid. *Stem Cell Reviews and Reports* 7: 869–882.

Dewhirst, F.E., Chen, T., Izard, J. et al. (2010). The human oral microbiome. *Journal of Bacteriology* 192: 5002–5017.

Dhanrajani, P.J. (2002). Hypodontia: Etiology, clinical features, and management. *Quintessence International* 33: 294–302.

Dolanmaz, D., Karaman, A.I., Pampu, A.A. et al. (2010) Orthodontic treatment of an ankylosed maxillary central incisor through osteogenic distraction. *Angle Orthodontist* 80: 391–395.

Donly, K.J., and Sasa, I.S. (2008). Potential remineralization of postorthodontic demineralized enamel and the use of enamel microabrasion and bleaching for esthetics. *Seminars in Orthodontics* 14: 220–225.

Dougherty, H.L. (1968). The effect of mechanical forces upon the mandibular buccal segments during orthodontic treatment. Part II. *American Journal of Orthodontics* 54: 83–103.

Dudic, A., Giannopoulou, C., Leuzinger, M. et al. (2009). Detection of apical root resorption after orthodontic treatment by using panoramic radiography and cone-beam computed tomography of super-high resolution. *American Journal of Orthodontics and Dentofacial Orthopedics* 135: 434–437.

Dudic, A., Giannopoulou, C., Meda, P. et al. (2017). Orthodontically induced cervical root resorption in humans is associated with the amount of tooth movement. *European Journal of Orthodontics* 39(5): 534–540.

Duncan, H.F., Cooper, P.R., and Smith, A.J. (2019). Dissecting dentine-pulp injury and wound healing responses: Consequences for regenerative endodontics. *International Endodontic Journal* 52: 261–266.

Edwards, D., Stone, S., Bailey, O. et al. (2021) Preserving pulp vitality: Part one – strategies for managing deep caries in permanent teeth. *British Dental Journal* 230: 77–82.

Elfrink, M.E.C., Ghanim, A., Manton, D.J. et al. (2015). Standardised studies on molar incisor hypomineralisation (MIH) and hypomineralised second primary molars (HSPM): A need. *European Archives of Paediatric Dentistry* 16: 247–255.

Eliasson, S., Laftman, A.C., and Strindberg, L. (1988). Autotransplanted teeth with early-stage endodontic treatment: A radiographic evaluation. *Oral Surgery, Oral Medicine, Oral Pathology* 65: 598–603.

ElSherifa, M.T., Shamaa, M.S., and Montasser, M.A. (2020). Enamel around orthodontic brackets coated with flash-free and conventional adhesives. *Journal of Orofacial Orthopedics* 81: 419–426.

Eminkahyagil, N., Arman, A., Çetinşahin, A. et al. (2006). Effect of resin-removal methods on enamel and shear bond strength of rebonded brackets. *Angle Orthodontist* 76: 314–321.

Endo, T., Finger, W.J., Kanehira, M. et al. (2010). Surface texture and roughness of polished nanofill and nanohybrid resin composites. *Dental Materials Journal* 29: 213–223.

Erdemir, A., Ungor, M., and Erdemir, E.O. (2005). Orthodontic movement of a horizontally fractured tooth: A case report. *Dental Traumatology* 21: 160–164.

Eriksen, H.M., Kirkevang, L.L., and Petersson, K. (2002). Endodontic epidemiology and treatment outcome: General considerations. *Endodontic Topics* 2: 1–9.

Estrela, C., and Holland, R. (2003). Calcium hydroxide: Study based on scientific evidences. *Journal of Applied Oral Science* 11: 269–282.

European Society of Endodontology (2006). Quality guidelines for endodontic treatment: Consensus report of the European Society

of Endodontology. *International Endodontic Journal* 39: 921–930.

European Society of Endodontology, Duncan, H.F., Galler, K.M. et al. (2019). European Society of Endodontology position statement: Management of deep caries and the exposed pulp. *International Endodontic Journal* 52: 923–934.

Fang, X., Qi, R., Liu, C. (2019). Root resorption in orthodontic treatment with clear aligners: A systematic review and meta-analysis. *Orthodontics & Craniofacial Research* 22: 259–269.

Farronato, G., Giannini, L., Riva, R. et al. (2012). Correlations between malocclusions and dyslalias. *European Journal of Paediatric Dentistry* 13: 13–18.

Fayle, S.A. (2003). Molar incisor hypomineralisation: Restorative management. *European Journal of Pediatric Dentistry* 4: 121–126.

Felippe, W.T., Felippe, M.C., and Rocha, M.J. (2006). The effect of mineral trioxide aggregate on the apexification and periapical healing of teeth with incomplete root formation. *International Endodontic Journal* 39: 2–9.

Feller, L., Khammissa, R.A., Thomadakis, G. et al. (2016). Apical external root resorption and repair in orthodontic tooth movement: Biological events. *BioMed Research International* 26: 7.

Fisher-Owens, S.A., Gansky, S.A., Platt, L.J. et al. (2007). Influences on children's oral health: A conceptual model. *Pediatrics* 120: e510–e520.

Fjeld, M., and Ogaard, B. (2006). Scanning electron microscopic evaluation of enamel surfaces exposed to 3 orthodontic bonding systems. *American Journal of Orthodontics and Dentofacial Orthopedics* 130: 575–581.

Flores, M.T. (2002). Traumatic injuries in the primary dentition. *Dental Traumatology* 18: 287–298.

Flores, M.T., Andersson, L., Andreasen, J.O. et al. (2007). Guidelines for the management of traumatic dental injuries. I. Fractures and luxations of permanent teeth. *Dental Traumatology* 23: 66–71.

Foersch, M., Schuster, C., Rahimi, R.K. et al. (2016). A new flash-free orthodontic adhesive system: A first clinical and stereomicroscopic study. *Angle Orthodontist* 86: 260–264.

Forsberg, C.M., and Tedestam, G. (1993). Etiological and predisposing factors related to traumatic injuries to permanent teeth. *Swedish Dental Journal* 17: 183–190.

Fouad, A.F., Abbott, P.V., Tsilingaridis, G. et al. (2020). International Association of Dental Traumatology guidelines for the management of traumatic dental injuries: 2. Avulsion of permanent teeth. *Dental Traumatology* 36: 331–342.

Frank, A.L. (1981). External-internal progressive resorption and its non-surgical correction. *Journal of Endodontics* 7: 473–476.

Frank, A.L., and Blakland, L.K. (1987). Nonendodontic therapy for supra osseous extra-canal invasive resorption. *Journal of Endodontics* 13: 348–387.

Frank, A.L., and Torabinejad, M. (1998). Diagnosis and treatment of extracanal invasive resorption. *Journal of Endodontics* 24: 500–504.

Frencken, J.E., Peters, M.C., Manton, D.J. et al. (2012). Minimal intervention dentistry for managing dental caries – a review: Report of a FDI task group. *International Dental Journal* 62: 223–243.

Frenken, J.W., Baart, J.A., and Jovanovic, A. (1998). Autotransplantation of premolars. A retrospective study. *International Journal of Oral and Maxillofacial Surgery* 27: 181–185.

Frese, C., Schiller, P., Staehle, H.J. et al. (2013). Recontouring teeth and closing diastemas with direct composite buildups: A 5-year follow-up. *Journal of Dentistry* 41: 979–985.

Fricker, J.P. (2022). Therapeutic properties of glass-ionomer cements: Their application to orthodontic treatment. *Australian Dental Journal* 67: 12–20.

Fujita, K., Kanno, Z., Otsubo, K. et al. (2008). Autotransplantation combined with orthodontic treatment in adult patients. *Orthodontic Waves* 67: 128–134.

Fuks, A.B., Cosack, A., Klein, H. et al. (1987). Partial pulpotomy as a treatment alternative for exposed pulps in crown-fractured permanent incisors. *Endodontics and Dental Traumatology* 3: 100–102.

Fukui, T., Choi, Y.B., Yamaguchi, H. et al. (2009). Treatment of a horizontal open bite with an invisible multiloop appliance in a girl with tooth trauma. *American Journal of Orthodontics and Dentofacial Orthopedics* 136: 596–606.

Gadhia, K., McDonald, S., Arkutu, N., et al. (2012). Amelogenesis imperfecta: An introduction. *British Dental Journal* 212: 377–379.

Galler, K.M., Grätz, E.M., Widbiller, M. et al. (2021). Pathophysiological mechanisms of root resorption after dental trauma: A systematic scoping review. *BMC Oral Health* 21: 163.

Garcia-Godoy, F., and Murray, P.E. (2012). Recommendations for using regenerative endodontic procedures in permanent immature traumatized teeth. *Dental Traumatology* 28: 33–41.

Gass, J.R., Valiathan, M., Tiwari, H.K. et al. (2003). Familial correlations and heritability of maxillary midline diastema. *American Journal of Orthodontics and Dentofacial Orthopedics* 123: 35–39.

Gault, P.C., and Warocquier-Clerout, R. (2002). Tooth auto-transplantation with double periodontal ligament stimulation to replace periodontally compromised teeth. *Journal of Periodontology* 73: 575–583.

Gholston, L., and Mattison, G. (1983). An endodontic-orthodontic technique for esthetic stabilization of externally resorbed teeth. *American Journal of Orthodontics* 83: 435–440.

Giannopoulou, C., Dudic, A., Pandis, N. et al. (2016). Slow and fast orthodontic tooth movement: An experimental study on humans. *European Journal of Orthodontics* 38: 404–408.

Gillen, B.M., Looney, S.W., Gu, L.S. et al. (2011). Impact of the quality of coronal restoration versus the quality of root canal fillings on success of root canal treatment: A systematic review and meta-analysis. *Journal of Endodontics* 37: 895–902.

Giuca, M.R., Lardani, L., Pasini, M. et al. (2020). State-of-the-art on MIH. Part 1 Definition and aepidemiology. *European Journal of Paediatric Dentistry* 21: 80–82.

Gkantidis, N., Kolokitha, O.E., and Topouzelis, N. (2008). Management of maxillary midline diastema with emphasis on etiology. *Journal of Clinical Pediatric Dentistry* 32: 265–272.

Gladwin, M., and Bagby, M. (2004). *Clinical Aspects of Dental Materials: Theory, Practice and Cases*. Baltimore, MD: Lippincott Williams & Wilkins.

Glendor, U., Marcenes, W., and Andreasen, J.O. (2007). Classification, epidemiology and etiology. In: J.O. Andreasen and F.M. Andreasen (eds.), *Textbook and Color Atlas of Traumatic Injuries to the Teeth*. Oxford: Blackwell/Munksgaard, pp. 217–244.

Goldson, L., and Henrikson, C.O. (1975). Root resorption during Begg treatment. A longitudinal roentgenologic study. *American Journal of Orthodontics* 68: 55–66.

Goodman, J.R., Jones, S.P., Hobkirk, J.A. et al. (1994). Hypodontia: 1. Clinical features and the management of mild to moderate hypodontia. *Dental Update* 21: 381–384.

Gorelick, L., Geiger, A.M., and Gwinnett, A.J. (1982). Incidence of white spot formation after bonding and banding. *American Journal of Orthodontics* 81: 93–98.

Graham, J.W. (2007). Temporary replacement of maxillary lateral incisors with miniscrews and bonded pontics. *Journal of Clinical Orthodontics* 41: 321–325.

Gregg, T.A., and Boyd, D.H. (1998). Treatment of avulsed permanent teeth in children. UK National Guidelines in Paediatric Dentistry. Royal College of Surgeons, Faculty of Dental Surgery. *International Journal of Pediatric Dentistry* 8: 75–81.

Gresnigt, M.M., Kalk, W., and Ozcan, M. (2012). Randomized controlled split-mouth clinical trial of direct laminate veneers with two micro-hybrid resin composites. *Journal of Dentistry* 40: 766–775.

Grossmann, Y., Nissan, J., and Levin, L. (2009). Clinical effectiveness of implant-supported removable partial dentures—a review of the literature and retrospective case evaluation. *Journal of Oral and Maxillofacial Surgery* 67: 1941–1946.

Gruner, D., Paris, S., and Schwendicke, F. (2016). Probiotics for managing caries and periodontitis: Systematic review and meta-analysis. *Journal of Dentistry* 48: 16–25.

Gulabivala, K., and Searson, L.J. (1995). Clinical diagnosis of internal resorption: An exception to the rule. *International Endodontic Journal* 28: 255–260.

Gülşahı, A. (2014). Clinical and radiologic appereances of invasive cervical resorption. *Oral Health and Dental Management* 13: 934–939.

Gulsahi, A., Gulsahi, K., and Ungor, M. (2007). Invasive cervical resorption: Clinical and radiological diagnosis and treatment of 3 cases. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics* 103: e65–e72.

Gwinnett, A.J., and Ceen, F. (1979). Plaque distribution on bonded brackets: A scanning microscope study. *American Journal of Orthodontics* 75: 667–677.

Hadj-Hamou, R., Senok, A.C., Athanasiou, A.E. et al. (2020). Do probiotics promote oral health during orthodontic treatment with fixed appliances? A systematic review. *BMC Oral Health* 20: 126.

Hamersky, P., Weimar, A.D., and Taintor, J. (1980). The effect of orthodontic force application on the pulpal tissue respiration rate in the human premolar. *American Journal of Orthodontics* 77: 368–378.

Hamilton, R.S., and Gutmann, J.L. (1999). Endodontic-orthodontic relationships: A review of integrated treatment planning challenges. *International Endodontic Journal* 32: 343–360.

Hashem, D., Mannocci, F., Patel, S. et al. (2019). Evaluation of the efficacy of calcium silicate vs. glass ionomer cement indirect pulp capping and restoration assessment criteria: A randomized controlled clinical trial—2-year results. *Clinical Oral Investigations* 23: 1931–1939.

Heide, S. (1991). The effect of pulp capping and pulpotomy on hard tissue bridges of contaminated pulps. *International Endodontic Journal* 24: 126–134.

Heithersay, G.S. (1999). Clinical, radiologic, and histopathologic features of invasive cervical resorption. *Quintessence International* 30: 27–37.

Heithersay, G.S. (2004). Invasive cervical resorption. *Endodontic Topics* 7: 73–92.

Heithersay, G.S., and Moule, A.J. (1982). Anterior subgingival fractures: A review of treatment alternatives. *Australian Dental Journal* 27: 368–376.

Hicks, M.J., Flaitz, C.M., Westerman, G.H. et al. (1995). Enamel caries initiation and progression following low fluence (energy) argon laser and fluoride treatment. *Journal of Clinical Pediatric Dentistry* 20: 9–13.

Hicks, M.J., Silverstone, L.M., and Flaitz, C.M. (1984). A scanning electron microscopic and polarized light study of acid etching of

caries like lesions in human enamel treated with sodium fluoride in vitro. *Archives of Oral Biology* 29: 765–772.

Hinckfuss, S., and Messer, L.B. (2009a). Splinting duration and periodontal outcomes for replanted avulsed teeth: A systematic review. *Dental Traumatology* 25: 150–157.

Hinckfuss, S.E., and Messer, L.B. (2009b). An evidence-based assessment of the clinical guidelines for replanted avulsed teeth. Part I: Timing of pulp extirpation. *Dental Traumatology* 25: 32–42.

Hiraishi, N., Yiu, C.K., and King, N.M. (2008). Effect of acid etching time on bond strength of an etch-and-rinse adhesive to primary tooth dentine affected by amelogenesis imperfecta. *International Journal of Paediatric Dentistry* 18: 224–230.

Hobkirk, J.A., Gill, D.S., Jones, S.P. et al. (2010). *Hypodontia: A Team Approach to Management*. Chichester: Wiley.

Hobkirk, J.A., King, P.A., Googman, J.R. et al. (1995). Hypodontia: 2. The management of severe hypodontia. *Dental Update* 22: 8–11.

Horst, J.A., Ellenikiotis, H., and Milgrom, P.L. (2016). UCSF protocol for caries arrest using silver diamine fluoride: Rationale, indications and consent. *Journal of the Californian Dental Association* 44: 16–28.

Hovland, E.J. (1992). Horizontal root fractures. Treatment and repair. *Dental Clinics of North America* 36: 509–525.

Hovland, E.J., Dumsha, T.C., and Gutmann, J.L. (1983). Orthodontic movement of a horizontal root fractured tooth. *British Journal of Orthodontics* 10: 32–33.

Hsu, J.A., and Lee, L.H. (2019). Orthodontic treatment for congenitally missing maxillary lateral incisors with canine substitution: A case report. *Advancements in Case Studies l*: 1–5.

Hu, W., and Featherstone, J.D. (2005). Prevention of enamel demineralization: An in-vitro study using light-cured filled

sealant. *American Journal of Orthodontics and Dentofacial Orthopedics* 128: 592–600; quiz 670.

Hua, F., He, H., Ngan, P. et al. (2013). Prevalence of peg-shaped maxillary permanent lateral incisors: A meta-analysis. *American Journal of Orthodontics and Dentofacial Orthopedics* 144: 97–109.

Huang, J.C., King, G., and Kapila, S. (2005). Biologic mechanisms in orthodontic tooth movement. In: R. Nanda (ed.), *Biomechanics and Esthetic Strategies in Clinical Orthodontics*. St. Louis, MO: Elsevier, pp. 17–37.

Huang, W.J., and Creath, C.J. (1995). The midline diastema: A review of its etiology and treatment. *Pediatric Dentistry* 17: 171–179.

Imazato, S. (2009). Bio-active restorative materials with antibacterial effects: New dimension of innovation in restorative dentistry. *Dental Materials Journal* 28: 11–19.

Ingber, J.S. (1974). Forced eruption. I. A method of treating isolated one and two wall infrabony osseous defects—rationale and case report. *Journal of Periodontology* 45: 199–206.

Iniesta, M., Herrera, D., Montero, E. et al. (2012). Probiotic effects of orally administered Lactobacillus reuteri-containing tablets on the subgingival and salivary microbiota in patients with gingivitis. A randomized clinical trial. *Journal of Clinical Periodontology* 39: 736–744.

Innes, N.P., Frencken, J.E., Bjørndal, L. et al. (2016). Managing carious lesions: Consensus recommendations on terminology. *Advances in Dental Research* 28: 49–57.

Iqbal, M., Kim, S., and Yoon, F. (2007). An investigation into diferential diagnosis of pulp and periapical pain: A PennEndo database study. *Journal of Endodontics* 33: 548–551.

Isaacson, R.J., Strauss, R.A., Bridges-Poquis, A. et al. (2001). Moving an ankylosed central incisor using orthodontics, surgery and

distraction osteogenesis. *Angle Orthodontist* 71: 411–418.

Iwamoto, C.E., Adachi, E., Pameijer, C.H. et al. (2006). Clinical and histological evaluation of white ProRoot MTA in direct pulp capping. *American Journal of Dentistry* 19: 85–90.

Iwaya, S.I., Ikawa, M., and Kubota, M. (2001). Revascularization of an immature permanent tooth with apical periodontitis and sinus tract. *Dental Traumatology* 17: 185–187.

Jälevik, B., and Klingberg, G. (2002). Dental treatment, dental fear and behaviour management problems in children with severe enamel hypomineralization of their permanent first molars. *International Journal of Paediatric Dentistry* 12: 24–32.

Jälevik, B., and Möller, M. (2007). Evaluation of spontaneous space closure and development of permanent dentition after extraction of hypomineralized permanent first molars. *International Journal of Paediatric Dentistry* 17: 328–335.

Jamilian, A., Perillo, L., and Rosa, M. (2015). Missing upper incisors: A retrospective study of orthodontic space closure versus implant. *Progress in Orthodontics* 16: 2.

Javed, F., Al-Kheraif, A.A., Romanos, E.B. et al. (2015). Influence of orthodontic forces on human dental pulp: A systematic review. *Archives of Oral Biology* 60: 347–356.

Javed, F., Ramalingam, S., Ahmed, H.B. et al. (2014). Oral manifestations in patients with neurofibromatosis type-1: A comprehensive literature review. *Critical Reviews in Oncology/Hematology* 91: 123–129.

Jeeruphan, T., Jantarat, J., Yanpiset, K. et al. (2012). Mahidol study 1: Comparison of radiographic and survival outcomes of immature teeth treated with either regenerative endodontic or apexification methods: A retrospective study. *Journal of Endodontics* 38: 1330–1336.

Jeong, J.S., Lee, S.Y., and Chang, M. (2016). Alterations of papilla dimensions after orthodontic closure of the maxillary midline

diastema: A retrospective longitudinal study. *Journal of Periodontal & Implant Science* 46: 197–206.

Jespersen, J.J., Hellstein, J., Williamson, A. et al. (2014). Evaluation of dental pulp sensibility tests in a clinical setting. *Journal of Endodontics* 40: 351–354.

Johal, A., Huang, Y., and Toledano, S. (2021). Hypodontia and its impact on a young person's quality of life, esthetics, and self-esteem. *American Journal of Orthodontics and Dentofacial Orthopedics* 161: 220–227.

Johal, A., Katsaros, C., Kuijpers-Jagtman, A.M. et al. (2013). State of the science on controversial topics: Missing maxillary lateral incisors—a report of the Angle Society of Europe 2012 meeting. *Progress in Orthodontics* 14: 20.

Jonsson, T., and Sigurdsson, T.J. (2004). Autotransplantation of premolars to premolar sites. A long-term follow-up study of 40 consecutive patients. *American Journal of Orthodontics and Dentofacial Orthopedics* 125: 668–675.

Kabbach, W., Sampaio, C.S., and Hirata, R. (2018). Diastema closure: A novel technique to ensure dental proportion. *Journal of Esthetics and Restorative Dentistry* 30: 275–280.

Kahler, B., Rossi-Fedele, G., Chugal, N. et al. (2017). An evidence-based review of the efficacy of treatment approaches for immature permanent teeth with pulp necrosis. *Journal of Endodontics* 43: 1052–1057.

Kalia, A.J. (2015). Mini screw orthodontic implant as temporary crown restoration to replace unilateral missing lateral incisor post-orthodontic treatment. *Journal of Oral Implantology* 41: 306–309.

Kavadia, S., Papadiochou, S., Papadiochos, I. et al. (2011). Agenesis of maxillary lateral incisors: A global overview of the clinical problem. *Orthodontics: The Art and Practice of Dentofacial Enhancement* 12: 296–317.

Kayhan, F., Küçükkeleş, N., and Demirel, D. (2000). A histologic and histomorphometric evaluation of pulpal reactions following rapid palatal expansion. *American Journal of Orthodontics and Dentofacial Orthopedics* 117: 465–473.

Kenny, D.J., and Barrett, E.J. (2001). Recent developments in dental traumatology. *Pediatric Dentistry* 23: 464–468.

Kerezoudis, N.P., Fried, K., and Olgart, L. (1995). Haemodynamic and immunohistochemical studies of rat incisor pulp after denervation and subsequent re-innervation. *Archives of Oral Biology* 40: 815–823.

Khalaf, K., Miskelly, J., Voge, E. et al. (2014). Prevalence of hypodontia and associated factors: A systematic review and meta-analysis. *Journal of Orthodontics* 41: 299–316.

Khalaf, K., Mustafa, S., and Maarouf, T. (2022). Is orthodontic treatment a risk factor of cervical root resorption? A systematic review. *European Journal of Dentistry* 16(4): 729–736.

Khetarpal, A., Talwar, S., and Verma, M. (2013). Creating a single-visit, fibre-reinforced, composite resin bridge by using a natural tooth pontic: A viable alternative to a PFM bridge. *Journal of Clinical and Diagnostic Research* 7: 772–775.

Kida, M., Ariga, T., Shirakawa, T. et al. (2002). Autosomal-dominant hypoplastic form of amelogenesis imperfecta caused by an enamelin gene mutation at the exon-intron boundary. *Journal of Dental Research* 81: 738–742.

Kidd, E.A. (2004). How “clean” must a cavity be before restoration? *Caries Research* 38: 305–313.

Kim, D.S., Park, H.J., Yeom, J.H. et al. (2012). Long-term follow-ups of revascularized immature necrotic teeth: Three case reports. *International Journal of Oral Science* 4: 109–113.

Kim, E., Kim, K.D., Roh, B.D. et al. (2003). Computed tomography as a diagnostic aid for extracanal invasive resorption. *Journal of Endodontics* 29: 463–465.

Kim, Y.K. (2017). Complications associated with orthognathic surgery. *Journal of the Korean Association of Oral and Maxillofacial Surgeons* 43: 3–15.

Kinzinger, G.S., Jänicke, S., Riediger, D. et al. (2003). Orthodontic fine adjustment after vertical callus distraction of an ankylosed incisor using the floating bone concept. *American Journal of Orthodontics and Dentofacial Orthopedics* 124: 582–590.

Kirschneck, C., and Proff, P. (2016). Kieferorthopädische Extraktionstherapie bei Molaren-Inzisiven-Hypomineralisation (MIH). *ZMK* 32: 2–10.

Kling, M., Cvek, M., and Mejare, I. (1986). Rate and predictability of pulp revascularization in therapeutically reimplanted permanent incisors. *Endodontics and Dental Traumatology* 2: 83–89.

Kocak, M.M., Ozcan, S., Kocak, S. et al. (2009). Comparison of the efficacy of three different mouthrinse solutions in decreasing the level of *S. mutans* in saliva. *European Journal of Dentistry* 3: 57–61.

Kofod, T., Würtz, V., and Melsen, B. (2005). Treatment of an ankylosed central incisor by single tooth dento-osseous osteotomy and a simple distraction device. *American Journal of Orthodontics and Dentofacial Orthopedics* 127: 72–80.

Kojima, Y., Ohshima, T., Seneviratne, C.J. et al. (2016). Combining prebiotics and probiotics to develop novel synbiotics that suppress oral pathogens. *Journal of Oral Biosciences* 58: 27–32.

Kokai, S., Kanno, Z., Koike, S. et al. (2015). Retrospective study of 100 autotransplanted teeth with complete root formation and subsequent orthodontic treatment. *American Journal of Orthodontics and Dentofacial Orthopedics* 148: 982–989.

Kokich, V.G. (2002). The role of orthodontics as an adjunct to periodontal therapy. In: M.G. Newman, H.H. Takei, and F.A. Carranza (eds.), *Carranza's Clinical Periodontology*. Philadelphia, PA: W.B. Saunders, pp. 704–718.

Kokich, V.G. (2004). Maxillary lateral incisor implants: Planning with the aid of orthodontics. *Journal of Oral and Maxillofacial Surgery* 62(Suppl 2): 48–56.

Kokich, V.O., Jr., Kinzer, G.A., and Janakievski, J. (2011). Congenitally missing maxillary lateral incisors: Restorative replacement. Counterpoint. *American Journal of Orthodontics and Dentofacial Orthopedics* 139: 435–439.

Kokich, V.O., Jr., Kiyak, H.A., and Shapiro, P.A. (1999). Comparing the perception of dentists and lay people to altered dental esthetics. *Journal of Esthetic and Restorative Dentistry* 11: 311–324.

Korkut, B., and Türkmen, C. (2021). Longevity of direct diastema closure and recontouring restorations with resin composites in maxillary anterior teeth: A 4-year clinical evaluation. *Journal of Esthetic and Restorative Dentistry* 33: 590–604.

Krasse, P., Carlsson, B., Dahl, C. et al. (2006). Decreased gum bleeding and reduced gingivitis by the probiotic Lactobacillus reuteri. *Swedish Dental Journal* 30: 55–60.

Krassnig, M., and Fickl, S. (2011). Congenitally missing lateral incisors—a comparison between restorative, implant, and orthodontic approaches. *Dental Clinics of North America* 55: 283–299.

Krishnan, V. (2017). Root resorption with orthodontic mechanics: Pertinent areas revisited. *Australian Dental Journal* 62(Suppl 1): 71–77.

Krishnan, V., and Davidovitch, Z. (2009). *Biologic Mechanisms of Tooth Movement*. London: Wiley Blackwell.

Küçükkeleş, N., and Okar, I. (1994). RME sonucu kök yüzeyinde oluşan rezorpsiyon alanlarının SEM ve ışık mikroskobu ile incelenmesi [Examination of the resorption areas formed on the root surface as a result of RME by SEM and light microscopy]. *Journal of Marmara University* 2: 404–408.

Kudiyirickal, M.G., and Ivancaková, R. (2008). Early enamel lesion part II. Histomorphology and prevention. *Acta Medica* 51: 151–156.

Kumar, A., Goyal, A., Gauba, K. et al. (2022). An evaluation of remineralised MIH using CPP-ACP and fluoride varnish: An in-situ and in-vitro study. *European Archives of Paediatric Dentistry* 23: 79–87.

Kurol, J. (2002). Early treatment of tooth-eruption disturbances. *American Journal of Orthodontics and Dentofacial Orthopedics* 121: 588–591.

Kurol, J. (2006). Impacted and ankylosed teeth: Why, when, and how to intervene. *American Journal of Orthodontics and Dentofacial Orthopedics* 129: 86–90.

Kurol, J., and Koch, G. (1985). The effect of extraction of infraoccluded deciduous molars: A longitudinal study. *American Journal of Orthodontics* 87: 46–55.

Kurol, J., and Thilander, B. (1984). Infraocclusion of primary molars with aplasia of the permanent successor. A longitudinal study. *Angle Orthodontist* 54: 283–294.

Kusku, O.O., Caglar, E., and Sandalli, N. (2008). The prevalence and aetiology of molar-incisor hypomineralisation in a group of children in Istanbul. *European Journal of Paediatric Dentistry* 9: 139–144.

Kvinnsland, S., Heyeraas, K., and Ofjord, E.S. (1989). Effect of experimental tooth movement on periodontal and pulpal blood flow. *European Journal of Orthodontics* 11: 200–205.

Kvint, S., Lindsten, R., Magnusson, A. et al. (2010). Autotransplantation of teeth in 215 patients. *Angle Orthodontist* 80: 446–451.

Kwan, S.C., Johnson, J.D., and Cohenca, N. (2012). The effect of splint material and thickness on tooth mobility after extraction

and replantation using a human cadaveric model. *Dental Traumatology* 28: 277–281.

Lacerda-Santos, R., Canutto, R.F., Araújo, J.L.D.S. et al. (2020). Effect of orthodontic treatment on tooth autotransplantation: Systematic review of controlled clinical trials. *European Journal of Dentistry* 14: 467–482.

Lagerström, L., and Kristerson, L. (1986). Influence of orthodontic treatment on root development of autotransplanted premolars. *American Journal of Orthodontics* 89: 146–150.

Lally, U. (2012). Resin-bonded fixed partial dentures past and present—an overview. *Journal of the Irish Dental Association* 58: 294–300.

Lammi, L., Arte, S., Somer, M. et al. (2004). Mutations in AXIN2 cause familial tooth agenesis and predispose to colorectal cancer. *American Journal of Human Genetics* 74: 1043–1050.

Larsen, M.J. (1990). Chemical events during tooth dissolution. *Journal of Dental Research* 69(Spec): 575–580.

Laurent, P., Camps, J., About, I. (2012). Biodentine(TM) induces TGF-β1 release from human pulp cells and early dental pulp mineralization. *International Endodontic Journal* 45: 439–448.

Lebon, N., Tapie, L., Vennat, E. et al. (2015). Influence of CAD/CAM tool and material on tool wear and roughness of dental prostheses after milling. *Journal of Prosthetic Dentistry* 114: 236–247.

Lee, J.Y., Vann, W.F., Jr., and Sigurdsson, A. (2001). Management of avulsed permanent incisors: A decision analysis based on changing concepts. *Pediatric Dentistry* 23: 357–360.

Lee, K.J., Joo, E., Yu, H.S. et al. (2009). Restoration of an alveolar bone defect caused by an ankylosed mandibular molar by root movement of the adjacent tooth with miniscrew implants. *American Journal of Orthodontics and Dentofacial Orthopedics* 136: 440–449.

Lempel, E., Lovász, B.V., Meszarics, R. et al. (2017). Direct resin composite restorations for fractured maxillary teeth and diastema closure: A 7-years retrospective evaluation of survival and influencing factors. *Dental Materials* 33: 467–476.

Leone, A., Mauro, A., Spatola, G.F. et al. (2009). MMP-2, MMP-9, and INOS expression in human dental pulp subjected to orthodontic traction. *Angle Orthodontist* 79: 1119–1125.

Levander, E., and Malmgren, O. (1988). Evaluation of the risk of root resorption during orthodontic treatment: A study of upper incisors. *European Journal of Orthodontics* 10: 30–38.

Li, W.T., Leu, Y.C., and Wu, J.L. (2010). Red-light light-emitting diode irradiation increases the proliferation and osteogenic differentiation of rat bone marrow mesenchymal stem cells. *Photomedicine and Laser Surgery* 28(Suppl 1): S157–S165.

Lim, E., Belton, D., Petocz, P. et al. (2011). Physical properties of root cementum: Part 15. Analysis of elemental composition by using proton-induced X-ray and gamma-ray emissions in orthodontically induced root resorption craters of rat molar cementum after exposure to systemic fluoride. *American Journal of Orthodontics and Dentofacial Orthopedics* 139: e193–e202.

Lim, W.H., Kim, H.J., and Chun, Y.S. (2008). Treatment of ankylosed mandibular first permanent molar. *American Journal of Orthodontics and Dentofacial Orthopedics* 133: 95–101.

Lima, T.J., Ribeiro, C.C.C., Tenuta, L.M. et al. (2008). Low fluoride dentifrice and caries lesions control in children with different caries experience: A randomized clinical trial. *Caries Research* 42: 46–50.

Lin, L.M., Ricucci, D., and Huang, G.T. (2014). Regeneration of the dentine-pulp complex with revitalization/revascularization therapy: Challenges and hopes. *International Endodontic Journal* 47: 713–724.

Linge, B.O., and Linge, L. (1983). Apical root resorption in upper anterior teeth. *European Journal of Orthodontics* 5: 173–183.

Linge, L., and Linge, B.O. (1991). Patient characteristics and treatment variables associated with apical root resorption during orthodontic treatment. *American Journal of Orthodontics and Dentofacial Orthopedics* 99: 35–43.

Linton, L.J. (1996). Quantitative measurements of remineralization of incipient caries. *American Journal of Orthodontics and Dentofacial Orthopedics* 104: 590–597.

Liu, L., Igarashi, K., Haruyama, N. et al. (2004). Effects of local administration of clodronate on orthodontic tooth movement and root resorption in rats. *European Journal of Orthodontics* 26: 469–473.

Loison-Robert, L.S., Tassin, M., Bonte, E. et al. (2018). In vitro effects of two silicate-based materials, biodentine and BioRoot RCS, on dental pulp stem cells in models of reactionary and reparative dentinogenesis. *PLoS One* 13: e0190014.

Lombardo, L., Ortan, Y.Ö., Gorgun, Ö. et al. (2013). Changes in the oral environment after placement of lingual and labial orthodontic appliances. *Progress in Orthodontics* 14: 28.

Lucchese, A., Bondemark, L., Marcolina, M. et al. (2018). Changes in oral microbiota due to orthodontic appliances: A systematic review. *Journal of Oral Microbiology* 10: 1.

Lundberg, T., and Isaksson, S. (1996). A clinical follow-up study of 278 autotransplanted teeth. *British Journal of Oral and Maxillofacial Surgery* 34: 181–185.

Luo, Z., Li, D., Kohli, M.R. et al. (2014). Effect of biodentine™ on the proliferation, migration and adhesion of human dental pulp stem cells. *Journal of Dentistry* 42: 490–497.

Luso, S., and Luder, H.U. (2012). Resorption pattern and radiographic diagnosis of invasive cervical resorption. *Schweizer Monatsschrift für Zahnmedizin* 122: 914–922.

Lustmann, J., and Ehrlich, J. (1974). Deep external resorption: Treatment by combined endodontic and surgical approach. A

report of 2 cases. *Journal of Dentistry* 24: 203–206.

Lygidakis, N.A., Wong, F., Jälevik, B. et al. (2010). Best clinical practice guidance for clinicians dealing with children presenting with molar-incisor-hypomineralisation (MIH): An EAPD policy document. *European Archives of Paediatric Dentistry* 11: 75–81.

Ma, T., Marangoni, R.D., and Flint, W. (1997). In vitro comparison of debonding force and intrapulpal temperature changes during ceramic orthodontic bracet removal using a carbondioxide laser. *American Journal of Orthodontics and Dentofacial Orthopedics* 111: 203–210.

Machado, L.A., do Nascimento, R.R., Ferreira, D.M.T.P. et al. (2016). Long-term prognosis of tooth autotransplantation: A systematic review and meta-analysis. *International Journal of Oral and Maxillofacial Surgery* 45: 610–617.

Machiulskiene, V., Campus, G., Carvalho, J.C. et al. (2020). Terminology of dental caries and dental caries management: Consensus report of a workshop organized by ORCA and Cariology Research Group of IADR. *Caries Research* 54: 7–14.

Mackie, I.C., and Warren, V.N. (1988). Dental trauma: 3 splinting, displacement injuries, and root fracture of immature permanent incisor teeth. *Dental Update* 15: 332–335.

Mah, J., and Prasad, N. (2004). Dentine phosphoproteins in gingival crevicular fluid during root resorption. *European Journal of Orthodontics* 26: 25–30.

Mainjot, A.K.J. (2020). The one step-no prep technique: A straightforward and minimally invasive approach for full-mouth rehabilitation of worn dentition using polymer-infiltrated ceramic network (PICN) CAD-CAM prostheses. *Journal of Esthetic and Restorative Dentistry* 32: 141–149.

Malkondu, Ö., Karapinar Kazandağ, M., and Kazazoğlu, E. (2014). A review on biodentine, a contemporary dentine replacement and repair material. *BioMed Research International* 2014: 160951.

Malmgren, B., Cvek, M., Lundberg, M. et al. (1984). Surgical treatment of ankylosed and infrapositioned reimplanted incisors in adolescents. *Scandinavian Journal of Dental Research* 92: 391–399.

Malmgren, O., Goldson, L., Hill, C. et al. (1982). Root resorption after orthodontic treatment of traumatized teeth. *American Journal of Orthodontics* 82: 487–491.

Malmgren, O., Malmgren, B., and Goldson, L. (1994). Orthodontic management of the traumatized dentition. In: J.O. Andreasen and F.M. Andreasen (eds.), *Textbook and Color Atlas of Traumatic Injuries to the Teeth*. Copenhagen: Munksgaard, pp. 587–633.

Maltz, M., Garcia, R., Jardim, J.J. et al. (2012). Randomized trial of partial vs. stepwise caries removal: 3-year follow-up. *Journal of Dental Research* 91: 1026–1031.

Maltz, M., Koppe, B., Jardim, J.J. et al. (2018). Partial caries removal in deep caries lesions: A 5-year multicenter randomized controlled trial. *Clinical Oral Investigations* 22: 1337–1343.

Manhart, J., Chen, H., Hamm, G. et al. (2004). Buonocore memorial lecture. Review of the clinical survival of direct and indirect restorations in posterior teeth of the permanent dentition. *Operative Dentistry* 29: 481–508.

McCarthy, M.F., and Hondrum, S.O. (1994). Mechanical and bond strength properties of light-cured and chemically cured glass ionomer cements. *American Journal of Orthodontics and Dentofacial Orthopedics* 105: 135–141.

McCourt, J.W., Cooley, R.L., and Huddleston, A.M. (1990). Fluoride release from fluoride containing liners/bases. *Quintessence International* 21: 41–45.

McDonald, F., and Pitt Ford, T.R. (1994). Blood flow changes in permanent maxillary canines during retraction. *European Journal of Orthodontics* 16: 1–9.

McNab, S., Battistutta, D., Taverne, A. et al. (1999). External apical root resorption of posterior teeth in asthmatics after orthodontic

treatment. *American Journal of Orthodontics and Dentofacial Orthopedics* 116: 545–551.

Meaney, S., Anweigi, L., Ziada, H. et al. (2012). The impact of hypodontia: A qualitative study on the experiences of patients. *European Journal of Orthodontics* 34: 547–552.

Medeiros, P.J., and Bezerra, A.R. (1997). Treatment of an ankylosed central incisor by single tooth dento-osseous osteotomy. *American Journal of Orthodontics and Dentofacial Orthopedics* 112: 496–501.

Medeiros, R.B., and Mucha, J.N. (2009). Immediate vs late orthodontic extrusion of traumatically intruded teeth. *Dental Traumatology* 25: 380–385.

Mejàre, I., Axelsson, S., Dahlén, G. et al. (2014). Caries risk assessment. A systematic review. *Acta Odontologica Scandinavica* 72: 81–91.

Melo, M.E., Silva, C.A., de Souza Gomes, W.D. et al. (2016). Immediate tooth replantation in rats: Effect of systemic antibiotic therapy with amoxicillin and tetracycline. *Clinical Oral Investigations* 20: 523–532.

Meurman, J.H., and Stamatova, I. (2007). Probiotics: Contributions to oral health. *Oral Diseases* 13: 443–451.

Meyer-Lueckel, H., and Paris, S. (2008). Improved resin infiltration of natural caries lesions. *Journal of Dental Research* 87: 1112–1116.

Meyer-Lueckel, H., Paris, S., and Kielbassa, A.M. (2007). Surface layer erosion of natural caries lesions with phosphoric and hydrochloric acid gels. *Caries Research* 41: 223–230.

Mielczarek, A., and Michalik, J. (2014). The effect of nano-hydroxyapatite toothpaste on enamel surface remineralization. An in vitro study. *American Journal of Dentistry* 27: 287–290.

Miguel, J.A., Almeida, M.A., and Chevitarese, O. (1995). Clinical comparison between a glass ionomer cement and a composite for

direct bonding of orthodontic brackets. *American Journal of Orthodontics and Dentofacial Orthopedics* 107: 484–487.

Miller, J.R., Mancl, L., Arbuckle, G. et al. (1996). A three-year clinical trial using a glass ionomer cement for the bonding of orthodontic brackets. *Angle Orthodontist* 66: 309–312.

Mirabella, A.D., Kokich, V.G., and Rosa, M. (2012). Analysis of crown widths in subjects with congenitally missing maxillary lateral incisors. *European Journal Orthodontics* 34: 783–787.

Mitsui, S.N., Yasue, A., Masuda, K. et al. (2014). Novel PAX9 mutations cause non-syndromic tooth agenesis. *Journal of Dental Research* 93: 245–249.

Mizrahi, E. (1982). Enamel demineralization following orthodontic treatment. *American Journal of Orthodontics* 82: 62–67.

Mostafa, Y.A., Iskander, K.G., and El-Mangoury, N.H. (1991). Iatrogenic pulpal reactions to orthodontic extrusion. *American Journal of Orthodontics and Dentofacial Orthopedics* 99: 30–34.

Moule, A.J., and Moule, C.A. (2009). Minor traumatic injuries to the permanent dentition. *Dental Clinics of North America* 53: 639–659.

Mullally, B.H., Blakely, D., and Burden, D.J. (1995). Ankylosis: An orthodontic problem with a restorative solution. *British Dental Journal* 179: 426–429.

Murray, P.E., Garcia-Godoy, F., and Hargreaves, K.M. (2007). Regenerative endodontics: A review of current status and a call for action. *Journal of Endodontics* 33: 377–390.

Nagarajappa, R., Daryani, H., Sharda, A.J. et al. (2015). Effect of chocobar ice cream containing bifidobacterium on salivary Streptococcus mutans and Lactobacilli: A randomised controlled trial. *Oral Health & Preventive Dentistry* 13: 213–218.

Naguib, A., Fahmy, N., Hamdy, A. et al. (2021). Fracture resistance of different designs of a resin-bonded fixed dental prosthesis: An

in vitro study. *International Journal of Prosthodontics* 34: 348–356.

Nanekrungsan, K., Patanaporn, V., Janhom, A. et al. (2012). External apical root resorption in maxillary incisors in orthodontic patients: Associated factors and radiographic evaluation. *Imaging Science in Dentistry* 42: 147–154.

Näse, L., Hatakka, K., Savilahti, E. et al. (2001). Effect of long-term consumption of a probiotic bacterium, Lactobacillus rhamnosus GG, in milk on dental caries and caries risk in children. *Caries Research* 35: 412–420.

Natera, M., and Mukherjee, P.M. (2018). Regenerative endodontic treatment with orthodontic treatment in a tooth with dens evaginatus: A case report with a 4-year follow-up. *Journal of Endodontics* 44: 952–955.

Negi, A., and Amita (2020). Interdisciplinary management of congenitally missing maxillary lateral incisors. *Journal of Oral Biology and Craniofacial Research* 10: 184–188.

Ngo, H., and Opsahl-Vital, S. (2014). Minimal intervention dentistry II: Part 7. Minimal intervention in cariology: The role of glass-ionomer cements in the preservation of tooth structures against caries. *British Dental Journal* 216: 561–565.

Nimčenko, T., Omerca, G., Varinauskas, V. et al. (2013). Tooth auto-transplantation as an alternative treatment option: A literature review. *Dental Research Journal (Isfahan)* 10: 1–6.

Nishimura, K., Amano, S., Nakao, K. et al. (2009). Orthodontic treatment including autotransplantation of a mature tooth. *Angle Orthodontist* 79: 387–393.

Nixon, C.E., Saviano, J.A., King, G.J. et al. (1993). Histomorphometric study of dental pulp during orthodontic tooth movement. *Journal of Endodontics* 19: 13–16.

Nongonierma, A.B., and Fitzgerald, R.J. (2012). Biofunctional properties of caseinphosphopeptides in the oral cavity. *Caries*

Research 46: 234–267.

Ogaard, B. (1989). Prevelance of white spot lesions in 19-year-olds. A study on untreated and orthodontically treated persons 5 years after treatment. *American Journal of Orthodontics and Dentofacial Orthopedics* 96: 423–427.

Ogaard, B. (1990). Effects of fluoride on caries development and progression in vivo. *Journal of Dental Research* 69(Spec): 813–819.

Ogaard, B. (2001). Oral microbiological changes, long term enamel alterations due to decalcification, and caries prophylactic aspects. In: W.A. Brantley and T. Eliades (eds.), *Orthodontic Materials. Scientific and Clinical Aspects*. Stuttgart: Thieme, pp. 123–142.

Ogaard, B. (2008). White spot lesions during orthodontic treatment: Mechanisms and fluoride preventive aspects. *Seminars in Orthodontics* 14: 183–193.

Ogaard, B., Alm, A.A., Larsson, E. et al. (2006). A prospective randomized clinical study on the effects of an amine fluoride/stannous fluoride toothpaste/mouthrinse on plaque, gingivitis and initial caries lesion development in orthodontic patients. *European Journal of Orthodontics* 28: 8–12.

Ogaard, B., Bishara, S.E., and Duschner, H. (2004). Enamel effects during bonding-debonding and treatment with fixed orthodontic appliances. In: T.M. Graber, T. Eliades, and A.E. Athanasiou (eds.), *Risk Management in Orthodontics: Experts Guide to Malpractice*. Hanover Park, IL: Quintessence Publishing, pp. 19–46.

Ogaard, B., Gjermo, P., and Rolla, G. (1980). Plaque inhibiting effect in orthodontic patients of a dentifrice containing stannous fluoride. *American Journal of Orthodontics* 78: 266–272.

Ogaard, B., Larsson, E., Henriksson, T. et al. (2001). Effects of combined application of antimicrobial and fluoride varnishes in orthodontic patients. *American Journal of Orthodontics and Dentofacial Orthopedics* 120: 28–35.

Ogaard, B., Rolla, G., and Arends, J. (1988). Orthodontic appliances and enamel demineralization. Part I. Lesion development. *American Journal of Orthodontics and Dentofacial Orthopedics* 94: 68–73.

Ojeda-Gutierrez, F., Martinez-Marquez, B., Arteaga-Larios, S. et. al (2013). Management and followup of complicated crown fractures in young patients treated with partial pulpotomy. *Case Report in Dentistry* 2013: 597563.

Op Heij, D.G., Opdebeeck, H., Steenberghe, D.V. et al. (2006). Facial development, continuous tooth eruption and mesial drift as compromising factors for implant placement. *International Journal of Maxillofacial Implantology* 21: 867–878.

O'Reilly, M.M., and Featherstone, J.D. (1987). Demineralization and remineralization around orthodontic appliances: An in vivo study. *American Journal of Orthodontics and Dentofacial Orthopedics* 92: 33–40.

Oulis, C., Vadiakas, G., and Siskos, G. (1996). Management of intrusive luxation injuries. *Endodontic and Dental Traumatology* 12: 113–119.

Owman-Moll, P., and Kurol, J. (1998). The early reparative process of orthodontically induced root resorption in adolescents – location and type of tissue. *European Journal of Orthodontics* 20: 727–732.

Padavala, S., and Sukumaran, G. (2018). Molar incisor hypomineralization and its prevalence. *Contemporary Clinical Dentistry* 9(Suppl 2): S246–S250.

Paduano, S.I., Cioffi, R., Rongo, A. et al. (2014). Orthodontic management of congenitally missing maxillary lateral incisors: A case report. *Case Reports in Dentistry* 2014: 731074.

Pagán-Collazo, G.J., Oliva, J., Cuadrado, L. et al. (2014). Prevalence of hypodontia in 10- to 14-year-olds seeking orthodontic treatment at a group of clinics in Puerto Rico. *Puerto Rico Health Sciences Journal* 33: 9–13.

Palmer, R.J., Jr. (2014). Composition and development of oral bacterial communities. *Periodontology 2000* 64: 20–39.

Pamukçu, H., Polat Ozsoy, O., Gülşahi, A. et al. (2020). External apical root resorption after nonextraction orthodontic treatment with labial vs. lingual fixed appliances. *Journal of Orofacial Orthopedics* 81: 41–51.

Paquette, D.E. (2010). Miniscrew-supported transitional tooth replacement: An esthetic alternative. *Journal of Clinical Orthodontics* 44: 321–325.

Paravina, R.D., Westland, S., Imai, F.H. et al. (2006). Evaluation of blending effect of composites related to restoration size. *Dental Materials* 22: 299–307.

Paris, S., and Meyer-Lueckel, H. (2009). Masking of labial enamel white spot lesions by resin infiltration – a clinical report. *Quintessence International* 40: 713–718.

Paris, S., Meyer-Lueckel, H., and Kielbassa, A.M. (2007). Resin infiltration of natural caries lesions. *Journal of Dental Research* 86: 662–666.

Park, J.H., Tai, K., and Hayashi, D. (2010). Tooth autotransplantation as a treatment option: A review. *Journal of Clinical Pediatric Dentistry* 35: 129–135.

Parkin, N., Benson, P.E., Shah, A. et al. (2009a). Extraction of primary (baby) teeth for unerupted palatally displaced permanent canine teeth in children. *Cochrane Database of Systematic Reviews* 15: CD004621. doi: 10.1002/14651858.CD004621.pub3.

Parkin, N., Elcock, C., Smith, R.N. et al. (2009b). The aetiology of hypodontia: The prevalence, severity and locaiton of hypodontia within families. *Archives of Oral Biology* 54(Suppl 1): s52–s56.

Parrini, S., Rossini, G., Castroflorio, T. et al. (2016). Laypeople's perceptions of frontal smile esthetics: A systematic review. *American Journal of Orthodontics and Dentofacial Orthopedics* 150: 740–750.

Pasini, M., Giuca, M.R., Scatena, M. et al. (2018). Molar incisor hypomineralization treatment with casein phosphopeptide and amorphous calcium phosphate in children. *Minerva Stomatologica* 67: 20–25.

Paulsen, H.U., Andreasen, J.O., and Schwartz, O. (1995). Pulp and periodontal healing, root development and root resorption subsequent to transplantation and orthodontic rotation: A long-term study of autotransplanted premolars. *American Journal of Orthodontics and Dentofacial Orthopedics* 108: 630–640.

Peck, S., Peck, L., and Kataja, M. (1998). Mandibular lateral incisor-canine transposition, concomitant dental anomalies, and genetic control. *Angle Orthodontist* 68: 455–466.

Pereira Sanchez, N., Powers, J.M., and Paravina, R.D. (2019). Instrumental and visual evaluation of the color adjustment potential of resin composites. *Journal of Esthetic Restorative Dentistry* 31: 465–470.

Perinetti, G., Paolantonio, M., Serra, E. et al. (2004a) Longitudinal monitoring of subgingival colonization by Actinobacillus actinomycetemcomitans, and crevicular alkaline phosphatase and aspartate aminotransferase activities around orthodontically treated teeth. *Journal of Clinical Periodontology* 31: 60–67.

Perinetti, G., Varvara, G., Festa, F. et al. (2004b). Aspartate aminotransferase activity in pulp of orthodontically treated teeth. *American Journal of Orthodontics and Dentofacial Orthopedics* 125: 88–92.

Petrou, M.A., Alhamoui, F.A., Welk, A. et al. (2014). A randomized clinical trial on the use of medical portland cement, MTA and calcium hydroxide in indirect pulp treatment. *Clinical Oral Investigations* 18: 1383–1389.

Peumans, M., Kanumilli, P., De Munck, J. et al. (2005). Clinical effectiveness of contemporary adhesives: A systematic review of current clinical trials. *Dental Materials* 21: 864–881.

Pithon, M.M., Vargas, E.O.A., da Silva Coqueiro, R. et al. (2021). Impact of oral-health-related quality of life and self-esteem on patients with missing maxillary lateral incisor after orthodontic space closure: A single-blinded, randomized, controlled trial. *European Journal of Orthodontics* 43: 208–214.

Pitts, N.B., Twetman, S., Fisher, J. et al. (2021). Understanding dental caries as a non-communicable disease. *British Dental Journal* 231: 749–753.

Pizzo Reis, P.M., Lima, P., Pimentel Garcia, F.C. et al. (2020). Effect of maxillary median diastema on the esthetics of a smile. *American Journal of Orthodontics and Dentofacial Orthopedics* 158: e37–e42.

Pohl, Y., Filippi, A., and Kirschner, H. (2005). Results after replantation of avulsed permanent teeth. I. Endodontic considerations. *Dental Traumatology* 21: 80–92.

Poi, W.R., Manfrin, T.M., Holland, R. et al. (2002). Repair characteristics of horizontal root fracture: A case report. *Dental Traumatology* 18: 98–102.

Polat, O., and Karaman, A.I. (2005). Pain control during fixed orthodontic appliance therapy. *Angle Orthodontist* 75: 214–219.

Polat-Ozsoy, O., Gülsahi, K., and Veziroğlu, F. (2008). Treatment of horizontal root-fractured maxillary incisors – a case report. *Dental Traumatology* 24: e91–e95.

Polder, B.J., Van't Hof, M.A., Van der Linden, F.P. et al. (2004). A meta-analysis of the prevalence of dental agenesis of permanent teeth. *Community Dentistry and Oral Epidemiology* 32: 217–226.

Pontons-Melo, J.C., Atzeri, G., Collares, F.M. et al. (2019). Cosmetic recontouring for achieving anterior esthetics. *International Journal of Esthetic Dentistry* 14: 134–146.

Pontons-Melo, J.C., Garcia, I.M., Leitune, V.C.B. et al. (2021). The golden proportion concept: Smile makeover with an 18-month

follow-up. *International Journal of Esthetics and Restorative Dentistry* 16: 2–11.

Popp, T.W., Artun, J., and Linge, L. (1992). Pulpal response to orthodontic tooth movement in adolescents: A radiographic study. *American Journal of Orthodontics and Dentofacial Orthopedics* 101: 228–233.

Prabhu, R., Bhaskaran, S., Geetha Prabhu, K.R. et al. (2015). Clinical evaluation of direct composite restoration done for midline diastema closure – long-term study. *Journal of Pharmacy & Bioallied Sciences* 7: S559–S562.

Proffit, W.R. (1986). *Contemporary Orthodontics*. St. Louis, MO: Mosby.

Proffit, W.R. (2000). *Contemporary Orthodontics*, 3rd ed. St. Louis, MO: Mosby-Year Book.

Qadri, S., Parkin, N.A., and Benson, P.E. (2016). Space closing versus space opening for bilateral missing upper laterals – aesthetic judgments of laypeople: A web-based survey. *Journal of Orthodontics* 43: 137–146.

Rafter, M. (2005). Apexification: A review. *Dental Traumatology* 21: 1–8.

Raghoebar, G.M., Boering, G., Jansen, H.W. et al. (1989). Secondary retention of permanent molars: A histologic study. *Journal of Oral Pathology and Medicine* 18: 427–431.

Ram, D., and Cohenca, N. (2004). Therapeutic protocols for avulsed permanent teeth: Review and clinical update. *Pediatric Dentistry* 26: 251–255.

Ramaglia, L., Cicciù, M., Fiorentino, E. et al. (2019). Effectiveness of a piezoelectric-assisted distraction osteogenesis procedure for the treatment of ankylosed permanent front teeth. *Journal of Craniofacial Surgery* 30: e356–e359.

Rana, M.W., Pothisiri, V., Killiany, D.M. et al. (2001). Detection of apoptosis during orthodontic tooth movement in rats. *American*

Journal of Orthodontics and Dentofacial Orthopedics 119: 516–521.

Razdolsky, Y., El-Bialy, T.H., Dessner, S. et al. (2004). Movement of ankylosed permanent teeth with a distraction device. *Journal of Clinical Orthodontics* 38: 612–620.

Reeves, R., and Stanley, H.R. (1966). The relationship of bacterial penetration and pulpal pathosis in carious teeth. *Oral Surgery, Oral Medicine, and Oral Pathology* 22: 59–65.

Reichardt, E., Geraci, J., Sachse, S. et al. (2019). Qualitative and quantitative changes in the oral bacterial flora occur shortly after implementation of fixed orthodontic appliances *American Journal of Orthodontics and Dentofacial Orthopedics* 156: 735–744.

Reitan, K. (1964). Effects of force magnitude and direction of tooth movement on different alveolar bone types. *Angle Orthodontist* 34: 244–255.

Reitan, K. (1974). Initial tissue behavior during apical root resorption. *Angle Orthodontist* 44: 68–82.

Reitan, K. (1985). Biomechanical principles and reactions. In: T.M. Graber and B.F. Swain (eds.), *Orthodontics: Current Principles and Techniques*. St Louis, MO: Mosby, pp. 101–192.

Remington, D.N., Joondeph, D.R., Artun, J. et al. (1989). Long-term evaluation of root resorption occuring during orthodontic treatment. *American Journal of Orthodontics and Dentofacial Orthopedics* 96: 43–46.

Ren, W., Yang, L., Chen, X. et al. (2000). The effect of fibrin sealant in dental pulp capping in experimental dogs. *West China Journal of Stomatology* 18: 380–382.

Reynolds, E.C. (1987). The prevention of sub-surface demineralization of bovine enamel and change in plaque composition by casein in an intraoral model. *Journal of Dental Research* 66: 1120–1127.

Reynolds, E.C. (1997). Remineralization of enamel subsurface lesions by casein phosphopeptide-stabilized calcium phosphate solutions. *Journal of Dental Research* 76: 1587–1595.

Reynolds, E.C., Cai, F., Shen, P. et al. (2003). Retention and remineralization of enamel lesions by various forms of calcium in a mouthrinse or sugarfree chewing gum. *Journal of Dental Research* 82: 206–211.

Ricketts, D., Lamont, T., Innes, N.P. et al. (2013). Operative caries management in adults and children. *Cochrane Database of Systematic Reviews* 28: CD003808. doi: 10.1002/14651858.CD003808.pub3.

Ricucci, D., Loghin, S., and Siqueira, J.F., Jr. (2014). Correlation between clinical and histologic pulp diagnoses. *Journal of Endodontics* 40: 1932–1939.

Rizos, M., and Spyropoulos, M.N. (2004). Van der Woude syndrome: A review. Cardinal signs, epidemiology, associated features, differential diagnosis, expressivity, genetic counselling and treatment. *European Journal of Orthodontics* 26: 17–24.

Roberts, W.E. (2000). Bone physiology of tooth movement, ankylosis, and osseointegration. *Seminars in Orthodontics* 6: 173–182.

Robertson, A., Andreasen, F.M., Andreasen, J.O. et al. (2000). Long-term prognosis of crown-fractured permanent incisors. The effect of stage of root development and associated luxation injury. *International Journal of Paediatric Dentistry* 10: 191–199.

Robertson, S., and Mohlin, B. (2000). The congenitally missing upper lateral incisor. A retrospective study of orthodontic space closure versus restorative treatment. *European Journal of Orthodontics* 22: 697–710.

Robinson, P.P. (1983). An electrophysiological study of the reinnervation of reimplanted and autotransplanted teeth in the cat. *Archives of Oral Biology* 28: 1139–1147.

Rodd, H.D., Morgan, C.R., Day, P.F. et al. (2007). Pulpal expression of TRPV1 in molar incisor hypomineralisation. *European Archives of Paediatric Dentistry* 8: 184–188.

Rohof, E.C.M., Kerdijk, W., Jansma, J. et al. (2018). Autotransplantation of teeth with incomplete root formation: A systematic review and meta-analysis. *Clinical Oral Investigations* 22: 1613–1624.

Romero, M.F., Babb, C.S., Brenes, C. et al. (2018). A multidisciplinary approach to the management of a maxillary midline diastema: A clinical report. *Journal of Prosthetic Dentistry* 119: 502–505.

Rosa, M. (2020). Essay I: Orthodontic edentulous space closure in all malocclusions. Outcome evaluation of facial and dental esthetics. *International Journal of Esthetic Dentistry* 15 (Suppl 1): S14–S31.

Rosa, M., and Zachrisson, B.U. (2007). Integrating space closure and esthetic dentistry in patients with missing maxillary lateral incisors. *Journal of Clinical Orthodontics* 41: 563–573.

Rosa, M., Zachrisson, B.U. (2010). The space-closure alternative for missing maxillary lateral incisors: An update. *Journal of Clinical Orthodontics* 44: 540–549; quiz 561.

Rosa, M., and Zachrisson, B.U. (2014). Missing maxillary lateral incisors: New procedures and indications for optimal space closure. In: R. Nanda (ed.), *Esthetics and Biomechanics in Orthodontics*, 2nd ed. St. Louis, MO: Elsevier Saunders, pp. 528–559.

Rosenberg, B., Murray, P.E., and Namerow, K. (2007). The effect of calcium hydroxide root filling on dentin fracture strength. *Dental Traumatology* 23: 26–29.

Rosenbloom, R.G., and Tinanoff, N. (1991). Salivary Streptococcus mutans levels in patients before, during, and after orthodontic treatment. *American Journal of Orthodontics and Dentofacial Orthopedics* 100: 35–37.

Ruschel, V.C., Stolf, S.C., Shibata, S. et al. (2017). A conservative technique for repairing class IV composite restorations. *Operative Dentistry* 42: E10–E15.

Rygh, P. (1977). Orthodontic root resorption studied by electron microscopy. *Angle Orthodontist* 44: 1–16.

Sæle, P., Østhus, E., Ådalen, S. et al. (2017). Pattern of clefts and dental anomalies in six-year-old children: A retrospective observational study in western Norway. *Acta Odontologica Scandinavica* 75: 100–105.

Sameshima, G.T., and Asgarifar, K.O. (2001). Assessment of root resorption and root shape: Periapical vs panoramic films. *Angle Orthodontist* 71: 185–189.

Sano, Y., Ikawa, M., Sugawara, J. et al. (2002). The effect of continuous intrusive force on human pulpal blood flow. *European Journal of Orthodontics* 24: 159–166.

Saoud, T.M., Zaazou, A., Nabil, A. et al. (2014). Clinical and radiographic outcomes of traumatized immature permanent necrotic teeth after revascularization/revitalization therapy. *Journal of Endodontics* 40: 1946–1952.

Sarıoğlu, I., Aras, S., and Oztaş, D. (2006). Effect of deproteinization on composite bond strength in hypocalcified amelogenesis imperfecta. *Oral Diseases* 12: 305–308.

Schlichting, L.H., and Magne, P. (2020). Double-milled CAD-CAM composite resin restorations: A proof-of-concept approach to producing histo-anatomic bilaminar restorations. *Journal of Prosthetic Dentistry* 124: 5–9.

Schopf, P. (2008). *Curriculum Kieferorthopädie: Werkstoffe. Festsitzende Apparaturen. Kieferorthopädische Therapie. Interdisziplinäre Aspekte. Anhang: Kieferorthopädische Abrechnung*, 4th ed. Berlin: Quintessenz-Verlag.

Schwartz, O., Bergmann, P., and Klausen, B. (1985). Resorption of autotransplanted human teeth: A retrospective study of 291

transplantations over a period of 25 years. *International Endodontic Journal* 18: 119–131.

Schwartz, O., and Rank, C.P. (1986). Autotransplantation of cryopreserved tooth in connection with orthodontic treatment. *American Journal of Orthodontics and Dentofacial Orthopedics* 90: 67–72.

Schwendicke, F., Frencken, J.E., Bjørndal, L. et al. (2016). Managing carious lesions: Consensus recommendations on carious tissue removal. *Advances in Dental Research* 28: 58–67.

Sedghizadeh, P.P., Sun, S., Jones, A.C. et al. (2021). Bisphosphonates in dentistry: Historical perspectives, adverse effects, and novel applications. *Bone* 147: 115933.

Seifo, N., Robertson, M., MacLean, J. et al. (2020). The use of silver diamine fluoride (SDF) in dental practice. *British Dental Journal* 228: 75–81.

Sękowska, A., Chałas, R., and Dunin-Wilczyńska, I. (2018). Width of dental arches in patients with maxillary midline diastema. *Folia Morphologica* 77: 340–344.

Sen, N., and Iselr, S. (2019). Multidisciplinary management of a severe maxillary midline diastema: A clinical report. *Journal of Prosthodontics* 28: 239–243.

Shah, M.P., Gujjari, S.K., and Chandrasekhar, V.S. (2013). Evaluation of the effect of probiotic (inersan®) alone, combination of probiotic with doxycycline and doxycycline alone on aggressive periodontitis – a clinical and microbiological study. *Journal of Clinical and Diagnostic Research* 7: 595–600.

Shah, S. (2020). Traumatic dental injuries in the primary dentition – a review. *Journal of the Pakistan Medical Association* 70: 76–82.

Shaik, I., Dasari, B., Kolichala, R. et al. (2021). Comparison of the success rate of mineral trioxide aggregate, endosequence bioceramic root repair material, and calcium hydroxide for apexification of immature permanent teeth: Systematic review

and meta-analysis. *Journal of Pharmacy & Bioallied Science* 13(Suppl 1): 43–47.

Shaw, W.C., O'Brien, K.D., Richmond, S. et al. (1991). Quality control in orthodontics: Risk/benefit considerations. *British Dental Journal* 170: 33–37.

Sheerah, H., Othman, B., Jaafar, A. et al. (2019). Alveolar bone plate measurements of maxillary anterior teeth: A retrospective cone beam computed tomography study, AlMadianh, Saudi Arabia. *Saudi Dental Journal* 31: 437–444.

Shen, P., Fernando, J.R., Walker, G.D. et al. (2020). Addition of CPP-ACP to yogurt inhibits enamel subsurface demineralization. *Journal of Dentistry* 103: 103506.

Sifakakis, I., Papaioannou, W., Papadimitriou, A. et al. (2018). Salivary levels of cariogenic bacterial species during orthodontic treatment with thermoplastic aligners or fixed appliances: A prospective cohort study. *Progress in Orthodontics* 19: 25.

Signore, A., Kaitsas, V., Tonoloni, A. et al. (2013). Sectional porcelain veneers for a maxillary midline diastema closure: A case report. *Quintessence International* 44: 201–206.

Silveira, G.S., de Almeida, N.V., Pereira, D.M. et al. (2016). Prosthetic replacement vs space closure for maxillary lateral incisor agenesis: A systematic review. *American Journal of Orthodontics and Dentofacial Orthopedics* 150: 228–237.

Silverstone, L.M. (1983). Remineralization and enamel caries: Significance of fluoride and effect on crystal diameters. In: I. Leach and W.M. Edgar (eds.), *Demineralization and Remineralization of the Teeth*. Oxford: IRL Press, pp. 185–205.

Simon, S., Perard, M., Zanini, M. et al. (2013). Should pulp chamber pulpotomy be seen as a permanent treatment? Some preliminary thoughts. *International Endodontic Journal* 46: 79–87.

Simon, S., Rilliard, F., Berdal, A. et al. (2007). The use of mineral trioxide aggregate in one-visit apexification treatment: A

prospective study. *International Endodontic Journal* 40: 186–197.

Sinclair, P.M., Cannito, M.F., Goates, L.J. et al. (1986). Patient responses to lingual appliance. *Journal of Clinical Orthodontics* 20: 396–404.

Singh, A., Singh, R.P., and Pawar, A. (2018). *A Multifactorial Risk Assessment Model for Dental Caries*. Mauritius: LAP Lambert Academic Publishing.

Skaare, A.B., and Jacobsen, I. (2003). Dental injuries in Norwegians aged 7–18 years. *Dental Traumatology* 19: 67–71.

Skoglund, A., Hasselgren, G., and Tronstad, L. (1981). Oxidoreductase activity in the pulp of replanted and autotransplanted teeth in young dogs. *Oral Surgery, Oral Medicine, and Oral Pathology* 52: 205–209.

Skoglund, A., Tronstad, L., and Wallenius, K. (1978). A microangiographic study of vascular changes in replanted and autotransplanted teeth of young dogs. *Oral Surgery, Oral Medicine, and Oral Pathology* 45: 17–28.

Smidt, A., Nuni, E., and Keinan, D. (2007). Invasive cervical resorption: Treatment rationale with an interdisciplinary approach. *Journal of Endodontics* 33: 1383–1387.

Smith, A.J. (2002). Pulp responses to caries and dental repair. *Caries Research* 36: 223–232.

Sondeijker, C.F.W., Lamberts, A.A., Beckmann, S.H. et al. (2020). Development of a clinical practice guideline for orthodontically induced external apical root resorption. *European Journal of Orthodontics* 42: 115–124.

Spurrier, S.W., Hall, S.H., Joondeph, D.R. et al. (1990). A comparison of apical root resorption during orthodontic treatment in endodontically treated and vital teeth. *American Journal of Orthodontics and Dentofacial Orthopedics* 97: 130–134.

Stamm, T., Hohoff, A., and Ehmer, U. (2005). A subjective comparison of two lingual bracket systems. *European Journal of Orthodontics* 27: 420–426.

Steiner, D.R., and West, J.D. (1997). Orthodontic-endodontic treatment planning of traumatized teeth. *Seminars in Orthodontics* 3: 39–44.

Stenvik, A., and Mjör, A. (1970). Pulp and dentine reactions to experimental tooth intrusion. A histological study of the initial changes. *American Journal of Orthodontics* 57: 370–385.

Stewart, C.J., Elledge, R.O., Kinirons, M.J. et al. (2008). Factors affecting the timing of pulp extirpation in a sample of 66 replanted avulsed teeth in children and adolescents. *Dental Traumatology* 24: 625–627.

Sudjalim, T.R., Woods, M.G., and Manton, D.J. (2006). Prevention of white spot lesions in orthodontic practice; a contemporary review. *Australian Dental Journal* 51: 284–289.

Sukontapatipark, W., El-Agroudi, M.A., Selliseth, N.J. et al. (2001). Bacterial colonization associated with fixed orthodontic appliances: A scanning electron microscopy study. *European Journal of Orthodontics* 23: 475–484.

Sun, H.B., Zhang, W., and Zhou, X.B. (2017). Risk factors associated with early childhood caries. *Chinese Journal of Dental Research* 20: 97–104.

Susami, T., Matsuzaki, M., Ogihara, Y. et al. (2006). Segmental alveolar distraction for the correction of unilateral open-bite caused by multiple ankylosed teeth: A case report. *Journal of Orthodontics* 33: 153–159.

Suter, V.G., Heinzmann, A.E., Grossen, J. et al. (2014). Does the maxillary midline diastema close after frenectomy? *Quintessence International* 45: 57–66.

Swedish Council on Technology Assessment in Health Care (2008). Caries – diagnosis, risk assessment and non-invasive treatment: A

systematic review. https://www.ncbi.nlm.nih.gov/books/NBK447984/pdf/Bookshelf_NBK447984.pdf.

Swift, E.J., Jr. (1989). Effects of glass ionomers on recurrent caries. *Operative Dentistry* 14: 40–43.

Taha, N.A., Ahmad, M.B., and Ghanim, A. (2017). Assessment of mineral trioxide aggregate pulpotomy in mature permanent teeth with carious exposures. *International Endodontic Journal* 50: 117–125.

Taipale, T., Pienihäkkinen, K., Salminen, S. et al. (2012). Bifidobacterium animalis subsp. lactis BB-12 administration in early childhood: A randomized clinical trial of effects on oral colonization by mutans streptococci and the probiotic. *Caries Research* 46: 69–77.

Talic, N.F., Evans, C., and Zaki, A.M. (2006). Inhibition of orthodontically induced root resorption with echistatin, an RGD containing peptide. *American Journal of Orthodontics and Dentofacial Orthopedics* 129: 252–260.

Tallón-Walton, V., Manzanares-Céspedes, M.C., Carvalho-Lobato, P. et al. (2014). Exclusion of PAX9 and MSX1 mutation in six families affected by tooth agenesis. A genetic study and literature review. *Medicina Oral, Patología Oral y Cirugía Bucal* 19: e248–e254.

Tarnow, D.P., Magner, A.W., and Fletcher, P. (1992). The effect of the distance from the contact point to the crest of bone on the presence or absence of the interproximal dental papilla. *Journal of Periodontology* 63: 995–996.

Temmerman, L., De Pauw, G.A., Beele, H. et al. (2006). Tooth transplantation and cryopreservation: State of the art. *American Journal of Orthodontics and Dentofacial Orthopedics* 129: 691–695.

Ten Cate, J.M., and van Loveren, C. (1999). Fluoride mechanisms. *Dental Clinics of North America* 43: 713–742.

Tester, R.F., and Al-Ghazzewi, F.H. (2011). A preliminary study of the synbiotic effects of konjac glucomannan hydrolysates (GMH) and lactobacilli on the growth of oral bacterium Streptococcus mutans. *Nutrition & Food Science* 41: 234–237.

Teughels, W., Loozen, G., and Quirynen, M. (2011). Do probiotics offer opportunities to manipulate the periodontal oral microbiota? *Journal of Clinical Periodontology* 38(Suppl 11): 159–177.

Thilander, B., and Skagius, S. (1970). Orthodontic sequelae of extraction of permanent first molars. A longitudinal study. *Report of the Congress of the European Orthodontic Society* 1970: 429–442.

Thoma, D.S., Sailer, I., Ioannidis, A. et al. (2017). A systematic review of the survival and complication rates of resin-bonded fixed dental prostheses after a mean observation period of at least 5 years. *Clin Oral Implants Research* 28: 1421–1432.

Thomas, S., Turner, S.R., and Sandy, J.R. (1998). Autotransplantation of teeth: Is there a role? *British Journal of Orthodontics* 25: 275–282.

Thong, Y.L., Messer, H.H., Siar, C.H. et al. (2001). Periodontal response to two intracanal medicaments in replanted monkey incisors. *Dental Traumatology* 17: 254–259.

Thönen, A., Peltomaki, T., Patcas, R. et al. (2013). Occurrence of cervical invasive root resorption in first and second molar teeth of orthodontic patients eight years after bracket removal. *Journal of Endodontics* 39: 27–30.

Torabinejad, M., Anderson, P., Bader, J. et al. (2007). Outcomes of root canal treatment and restoration, implant-supported single crowns, fixed partial dentures, and extraction without replacement: A systematic review. *Journal of Prosthetic Dentistry* 98: 285–311.

Torres, F.C., de Freitas, C.F., Pereira, D.V. et al. (2018). Agenesis of all permanent maxillary incisors: A rare clinical case with an

interdisciplinary solution. *Journal of Clinical and Experimental Dentistry* 10: e402–e407.

Travassos, R.M., Caldas, A. de F., and de Albuquerque, D.S. (2003). Cohort study of endodontic therapy success. *Brazilian Dental Journal* 14: 109–113.

Trope, M. (2002). Root resorption due to dental trauma. *Endodontic Topics* 1: 79–100.

Tsukiboshi, M. (2002). Autotransplantation of teeth: Requirements for predictable success. *Dental Traumatology* 18: 157–180.

Tuby, H., Maltz, L., and Oron, U. (2007). Low-level laser irradiation (LLLI) promotes proliferation of mesenchymal and cardiac stem cells in culture. *Lasers in Surgery and Medicine* 39: 373–378.

Tuncer, D., Arhun, N., Halacoğlu, D.M. et al. (2015). A clinical complication of fiber reinforced ribbon-composite provisional fixed partial denture of an adolescent patient. *Journal of Dentists* 3: 41–43.

Türköz, C., Canigür Bavbek, N., Varlik, S.K. et al. (2012). Influence of thermoplastic retainers on Streptococcus mutans and Lactobacillus adhesion. *American Journal of Orthodontics and Dentofacial Orthopedics* 141: 598–603.

Turley, P.K., Crawford, L.B., and Carrington, K.W. (1987). Traumatically intruded teeth. *Angle Orthodontist* 57: 234–244.

Twetman, S. (2016). Caries risk assessment in children: How accurate are we? *European Archives of Paediatric Dentistry* 17: 27–32.

Twetman, S. (2018). Prevention of dental caries as a non-communicable disease. *European Journal of Oral Sciences* 126(Suppl 1): 19–25.

Twetman, S., and Fontana, M. (2009). Patient caries risk assessment. *Monograms in Oral Science* 21: 91–101.

Unsterseher, R., Nieberg, L., Weimar, A. et al. (1987). The response of human pulp tissue after orthodontic force application. *American Journal of Orthodontics and Dentofacial Orthopedics* 92: 220–224.

Uribe, F., Padala, S., Allareddy, V. et al. (2013). Cone-beam computed tomography evaluation of alveolar ridge width and height changes after orthodontic space opening in patients with congenitally missing maxillary lateral incisors. *American Journal of Orthodontics and Dentofacial Orthopedics* 144: 848–859.

Uysal, T., Eldeniz, A.U., Usumez, S. et al. (2005). Thermal changes in the pulp chamber during different adhesive clean-up procedures. *Angle Orthodontist* 75: 220–225.

Vandevska-Radunovic, V., Kristiansen, A.B., Heyeraas, K.J. et al. (1994). Changes in blood circulation in teeth supporting tissues incident to experimental tooth movement. *European Journal of Orthodontics* 16: 361–369.

Van Meerbeek, B., De Munck, J., Yoshida, Y. et al. (2003). Buonocore memorial lecture. Adhesion to enamel and dentin: Current status and future challenges. *Operative Dentistry* 28: 215–235.

Van Meerbeek, B., Peumans, M., Poitevin, A. et al. (2010). Relationship between bond-strength tests and clinical outcomes. *Dental Materials* 26: e100–e121.

Veberiene, R., Smailiene, D., Danielyte, J. et al. (2009). Effects of intrusive force on selected determinants of pulp vitality. *Angle Orthodontist* 79: 1114–1118.

Venezie, R.D., Vadiakas, G., Christensen, J.R. et al. (1994). Enamel pretreatment with sodium hypochlorite to enhance bonding in hypocalcified amelogenesis imperfecta: Case report and SEM analysis. *Pediatric Dentistry* 16: 433–436.

Vilhjálmsson, V.H., Knudsen, G.C., Grung, B. et al. (2011). Dental autotransplantation to anterior maxillary sites. *Dental Traumatology* 27: 23–29.

Villa-Chávez, C.E., Patiño-Marín, N., Loyola-Rodríguez, J.P. et al. (2013). Predictive values of thermal and electrical dental pulp tests: A clinical study. *Journal of Endodontics* 39: 365–369.

Villavicencio, J., Villegas, L.M., Arango, M.C. et al. (2018). Effects of a food enriched with probiotics on Streptococcus mutans and Lactobacillus spp. salivary counts in preschool children: A cluster randomized trial. *Journal of Applied Oral Science* 26: e20170318.

Viswambaran, M., Londhe, S.M., and Kumar, V. (2015). Conservative and esthetic management of diastema closure using porcelain laminate veneers. *Medical Journal Armed Forces India* 71: S581–S585.

Vitale, M.C., Caprioglio, C., Martignone, A. et al. (2004). Combined technique with polyethylene fibers and composite resins in restoration of traumatized anterior teeth. *Dental Traumatology* 20: 172–177.

Vivaldi-Rodrigues, G., Demito, C.F., Bowman, S.J. et al. (2006). The effectiveness of a fluoride varnish in preventing the development of white spot lesions. *World Journal of Orthodontics* 7: 138–144.

von Böhl, M., Ren, Y., Fudalej, P.S. et al. (2012). Pulpal reactions to orthodontic force application in humans: A systematic review. *Journal of Endodontics* 38: 1463–1469.

Vucic, S., Dhamo, B., Kuijpers, M.A. et al. (2016). Craniofacial characteristics of children with mild hypodontia. *American Journal of Orthodontics and Dentofacial Orthopedics* 150: 611–619.

Wade, W.G. (2013). The oral microbiome in health and disease. *Pharmacological Research* 69: 137–143.

Waggoner, W.F., Johnston, W.M., Schumann, S. et al. (1989). Microabrasion of human enamel in vitro using hydrochloric acid and pumice. *Pediatric Dentistry* 11: 319–323.

Walshaw, E.G., Noble, F., Conville, R. et al. (2020). Molar incisor hypomineralisation and dental anomalies: A random or real

association? *International Journal of Paediatric Dentistry* 30: 342–348.

Watanabe, Y., Mohri, T., Takeyama, M. et al. (2010). Long-term observation of autotransplanted teeth with complete root formation in orthodontic patients. *American Journal of Orthodontics and Dentofacial Orthopedics* 138: 720–726.

Weerheijm, K.L. (2004). Molar incisor hypomineralization (MIH): Clinical presentation, aetiology and management. *Dental Update* 31: 9–12.

Weerheijm, K.L., Duggal, M., Mejàre, I. et al. (2003). Judgement criteria for molar incisor hypomineralisation (MIH) in epidemiologic studies: A summary of the European meeting on MIH held in Athens, 2003. *European Journal of Pediatric Dentistry* 4: 110–113.

Weissheimer, T., Silva, E.J.N.L., Pinto, K.P. et al. (2021). Do orthodontic tooth movements induce pulp necrosis? A systematic review. *International Endodontic Journal* 54: 1246–1262.

Wheeler, B., Carrico, C.K., Shroff, B. et al. (2018). Management of the maxillary diastema by various dental specialties. *Journal of Oral and Maxillofacial Surgery* 76: 709–715.

White, C., Jr., and Bryant, N. (2002). Combined therapy of mineral trioxide aggregate and guided tissue regeneration in the treatment of external root resorption and an associated osseous defect. *Journal of Periodontology* 73: 1517–1521.

Wickwire, N.A., McNeil, M.H., Norton, L.A. et al. (1974). The effects of tooth movement upon endodontically treated teeth. *Angle Orthodontist* 44: 235–242.

Wiechmann, D., Klang, E., Helms, H.J. et al. (2015). Lingual appliances reduce the incidence of white spot lesions during orthodontic multibracket treatment. *American Journal of Orthodontics and Dentofacial Orthopedics* 148: 414–422.

Willmot, D.R. (2004). White lesions after orthodontic treatment: Does low fluoride make a difference? *Journal of Orthodontics* 31:

235–242.

Willmot, D.R. (2008). White spot lesions after orthodontic treatment. *Seminars in Orthodontics* 14: 209–219.

Wilmes, B., Nienkemper, M., Renger, S. et al. (2014). Mini-implant-supported temporary pontics. *Journal of Clinical Orthodontics* 48: 422–429.

Wiltshire, W.A., and Noble, J. (2010). Clinical and laboratory perspectives of improved orthodontic bonding to normal, hypoplastic, and fluorosed enamel. *Seminars in Orthodontics* 16: 55–65.

Witherspoon, D.E., Small, J.C., Regan, J.D. et al. (2008). Retrospective analysis of open apex teeth obturated with mineral trioxide aggregate. *Journal of Endodontics* 34: 1171–1176.

Witkop, C.J., Jr. (1988). Amelogenesis imperfecta, dentinogenesis imperfecta and dentin dysplasia revisited: Problems in classification. *Journal of Oral Pathology* 17: 547–553.

Witt, M., and Flores-Mir, C. (2011). Laypeople's preferences regarding frontal dentofacial esthetics: Periodontal factors. *Journal of American Dental Association* 142: 925–937.

Wolff, D., Kraus, T., Schach, C. et al. (2010). Recontouring teeth and closing diastemas with direct composite buildups: A clinical evaluation of survival and quality parameters. *Journal of Dentistry* 38: 1001–1009.

Wolters, W.J., Duncan, H.F., Tomson, P.L. et al. (2017). Minimally invasive endodontics: A new diagnostic system for assessing pulpitis and subsequent treatment needs. *International Endodontic Journal* 50: 825–829.

Wright, J., Bosio, J.A., Chou, J.C. et al. (2016). Maxillary lateral incisor agenesis and its relationship to overall tooth size. *Journal of Prosthetic Dentistry* 115: 209–224.

Yagi, M., Ohno, H., and Takada, K. (2009). Computational formulation of orthodontic tooth extraction decisions. Part II:

Which tooth should be extracted? *Angle Orthodontist* 79: 892–898.

Yassir, Y.A., McIntyre, G.T., and Bearn, D.R. (2021). Orthodontic treatment and root resorption: An overview of systematic reviews. *European Journal of Orthodontics* 43: 442–456.

Yates, J.A. (1992). Root fractures in permanent teeth: A clinical review. *International Endodontic Journal* 25: 150–157.

Yetkiner, E., Gürlek, Ö., Işık, A. et al. (2019). Do adhesive flash-free brackets affect bacterial plaque in patients with adequate oral hygiene? A randomised controlled clinical and microbiological assessment. *Oral Health & Preventive Dentistry* 17: 533–539.

Yilmaz, H.G., Kalender, A., and Cengiz, E. (2010). Use of mineral trioxide aggregade in the treatment of invasive cervical resorption. *Journal of Endodontics* 36: 160–163.

Yüzügüllü, B., Polat, O., and Ungör, M. (2008). Multidisciplinary approach to traumatized teeth: A case report. *Dental Traumatology* 24: e27–e30.

Zaccara, I.M., Ginani, F., Mota-Filho, H.G. et al. (2015). Effect of low-level laser irradiation on proliferation and viability of human dental pulp stem cells. *Lasers in Medical Science* 30: 2259–2264.

Zach, L., and Cohen, C. (1965). Pulp response to externally applied heat. *Oral Surgery, Oral Medicine, and Oral Pathology* 19: 515–530.

Zachrisson, B.U., Rosa, M., and Toreskog, S. (2011). Congenitally missing maxillary lateral incisors: Canine substitution. *American Journal of Orthodontics* 139: 434–438.

Zachrisson, B.U., Stenvik, A., and Haanaes, H.R. (2004). Management of missing maxillary anterior teeth with emphasis on autotransplantation. *American Journal of Orthodontics and Dentofacial Orthopedics* 126: 284–288.

Zakizade, M., Davoudi, A., Akhavan, A. et al. (2020). Effect of resin infiltration technique on improving surface hardness of enamel

lesions: A systematic review and meta-analysis. *Journal of Evidence-Based Dental Practice* 20: 101405.

Zero, D.T. (1999). Dental caries process. *Dental Clinics of North America* 43: 635–664.

Zhang, Y., Wang, X., Li, H. et al. (2018). Human oral microbiota and its modulation for oral health. *Biomedicine & Pharmacotherapy* 99: 883–893.

Zitzmann, N.U., Arnold, D., Ball, J. et al. (2015). Treatment strategies for infraoccluded dental implants. *Journal of Prosthetic Dentistry* 113: 169–174.

18

Orthodontics and Pediatric Dentistry: Two Specialties, One Goal

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Summary

The pediatric dentist and orthodontist share many professional interests by virtue of the fact that they both are treating the same patient, often on a regular and sustained basis. Furthermore, the treatment delivered by both specialties often has profound overall effects on the function and esthetics of these young patients as they approach adulthood. Each clinician has the opportunity to support the other's therapeutic efforts; however, there appears to be a significant "disconnect" in treatment focus and interspecialty communication and overall interactivity. Individual patient care suffers as the potential synergistic collaboration of the pediatric dentist and orthodontist is never fully realized. The ongoing sharing of new information between specialties is critical, as is coordination of pediatric dental and orthodontic treatment. This chapter explores some of the existing problems of communication and interspecialty interactivity. Several commonly encountered clinical scenarios are presented to illustrate these problems as well as to suggest changes in future pediatric dental and orthodontic education, clinical practice, and ongoing assessments of respective specialty guidelines.

The pediatric dentist is a unique dental clinician, as he or she is both a primary care dental health provider and a specialist. As such, the pediatric dentist has an extraordinary responsibility in treating, triaging, and coordinating dental healthcare for infants, children, and adolescents. The pediatric dentist will most likely interface with the orthodontist on a daily basis far more than any other dental clinician, for the obvious reason that many pediatric dental patients will be under the care of both clinicians during the same and often extended time period. Both the orthodontist and the pediatric dentist will be applying therapies to their mutual patient, and in many instances these therapeutic decisions will have impacts on the immediate and long-term esthetic and functional status of their patient. It is the authors' belief that new and more profoundly effective avenues of communication and interaction between the orthodontist and pediatric dentist need to be established and maintained if individual patients and the public at large are to benefit from modern orthodontic and pediatric dental care. Additionally, achieving meaningful and consequential interactivity and communication between these specialties will require a re-examination of orthodontic and pediatric dental postgraduate curricula, as well as existing guidelines that have been established by each specialty.

Both specialties need to inculcate core information that crosses traditionally defined borders of academic and clinical interest. Some of these areas might include caries management, enamel decalcification, fluoride use, ectopic and impacted teeth, timing of orthodontic treatment, overall benefit of extraction strategies in orthodontic treatment, management of third molars, dental trauma, patient management, root resorption, and treatment options in cases of missing permanent teeth. Additionally, the pediatric dentist needs more core information on both evidence-based and evidence-"bolstered" information about a number of initial orthodontic strategies and midcourse orthodontic treatment changes that might become necessary as a result of adverse dentofacial growth and development and/or poor patient compliance. Similarly, the orthodontist should appreciate the incontrovertible value of faithful routine pediatric dental recall visits for patients undergoing active orthodontic treatment. Both clinicians require new thinking

that integrates “best evidence” with clinical experience and individual patient or parental values. Finally, the orthodontist and pediatric dentist must establish mutually acceptable and practical communication protocols to ensure that any or all of these clinical insights will ultimately result in a consistently higher level of patient care for each individual patient. While it would be impossible for the authors to cover all of the clinical situations that the orthodontist and pediatric dentist will encounter in the mixed dentition stage of dental development in one chapter, several commonly encountered clinical entities will be included in an effort to emphasize the importance of clinician interactivity between these two specialties.

Coordinating orthodontic and pediatric dental appointments in a group or solo practitioner setting

In order for the pediatric dentist and orthodontist to be optimally supportive of each other’s efforts, several conditions need to be met. An understanding of the overall emphasis of comprehensive care for the pediatric dental and orthodontic patient must be appreciated by both clinicians. Most important are the development and maintenance of ongoing communication paths, so that each clinician is maximally apprised of the treatment that might already be in progress and/or will be contemplated for the immediate or long-term future. There is a growing trend all over the world for the formation of consequential ethical professional partnerships or group types of practice that include the participation of pediatric dentists and orthodontists. One would think that such a consortium or association would facilitate the streamlining of communication efforts between the orthodontist and pediatric dentist. However, unless such group practices develop new and unprecedented communication avenues, the net result would be no better than what is observed in other types of traditional treatment settings in which the orthodontist and pediatric dentist frequently are virtually working independently in their own milieu, unaware of each other’s treatment plan and its progress.

A glaring but rather basic example of this point is the pediatric dental recall visit schedule for patients undergoing orthodontic treatment. It is a frequent complaint of the pediatric dentist that some patients undergoing orthodontic treatment do not faithfully keep their regular pediatric dental recall appointments during the often extended period of orthodontic treatment. The reason for this occurrence might be a misunderstanding by parents who mistakenly confuse monthly visits to the orthodontist as being substitutes for semi-annual or annual visits to the pediatric dentist while their child is undergoing orthodontic treatment. The pediatric dentist might therefore be denied an opportunity to observe important developmental changes in the dentition and beyond during orthodontic treatment. It is the authors' belief that the orthodontist should bear responsibility for assisting the pediatric dentist in ensuring that all patients are receiving regularly scheduled pediatric dental appointments during orthodontic treatment.

Figure 18.1 shows a typical orthodontic appointment schedule in a group orthodontic/pediatric dental practice. At the bottom of the page are several columns that were derived from scheduling information supplied to the orthodontist from the pediatric dental section of the practice. The first column at the bottom is a list of patients who will be seen by the orthodontist and already have pediatric dental appointments scheduled. This section is helpful in coordinating orthodontic treatment and pediatric dental treatment in the near future. For example, timely prescriptions (removal of primary or permanent teeth, oral hygiene recommendations and/or concerns, etc.) can be prepared in advance of the individual patient's pediatric dental appointment. The second column is a list of patients who will also be seen by the pediatric dentist that particular day. This information may help overall pediatric dental concerns, as posterior orthodontic bands can be removed, a thorough caries check can be performed, and the bands can be replaced that very same day. Additionally, oral hygiene concerns or any unusual in-treatment findings can be discussed directly with the pediatric dentist and dental hygienist. The third column shows patients who the orthodontist will be seeing, but who are overdue for their pediatric dental appointments. It is perhaps this particular column that is most important, as it identifies patients who are undergoing

orthodontic treatment and who are not being seen by the pediatric dentist during the course of that orthodontic treatment. Identifying these potentially “high-risk” patients gives the orthodontist an opportunity to have frank conversations with the parents of these patients about the importance of regular pediatric dental appointments during the course of orthodontic treatment, and encourage them to make pediatric dental appointments while they are being seen that day for their child’s orthodontic appointment. This protocol has greatly improved oral hygiene efforts and decreased the incidence of white spot lesions and any associated liability in our practice during orthodontic treatment, as the orthodontist, pediatric dentist, patient, and parent are optimally apprised of any adverse conditions during orthodontic treatment, and appropriate strategies (bolstered oral hygiene instruction, use of fluoride varnishes, etc.) can be administered on a regular and thoroughly coordinated basis.

For those solo orthodontic practitioners who might be interested in a more proactive method of encouraging their patients to keep routine pediatric dental appointments during orthodontic treatment, a similar strategy can be employed. Figure 18.2 is a chart that the orthodontist sends to the pediatric dentist along with a note that the listed patients are under the care of the orthodontist, and Figure 18.3 is the returned chart with any of the patients listed who are overdue for their pediatric dental appointments. The orthodontist can now speak to the parents at their child’s next orthodontic appointment and inform them that one of the requirements of quality orthodontic treatment is to ensure that patient’s overall pediatric oral health needs are met during the course of orthodontic treatment. This single measure is well appreciated by the referring pediatric dentist and represents the orthodontist’s “team” participation in the overall care of the orthodontic/pediatric dental patient.

APPOINTMENT BOOK VIEW (06/10/2022)

East Side Orthodontic Dental Group

Date: (06/10/2022)								**Page:** 1
	Thursday, 06/10/2022							
					OP 1	OP 2	OP 3	OP 4
9:00 am								
:15								
:30								
:45								
10:00 am					Clinton, Chelsea	Fields, Mrs.	Shepard, Sam	Do Not Book
:15					Marley, Bob	Fields, Sarah	Jones, Allan	Do Not Book
:30					Thomas, Dylan	VanGogh, Vincent	Marley, Marie	Do Not Book
:45					Tutu, Desmond	Monet, Claude	Lady Gaga	Whelan, Jenny
11:00 am					Jones, Sarah	Dylan, Robert	Ferguson, Sarah	Smith, Jada P.
:15					Bennett, Anthony	Tutu, Desmond	Griffin, Merv	Smith, Johnny
:30					Whelan, Cathy	Jones, Sarah	Povich, Maurie	Presley, Elvis
:45					Jones, Spike	Bennett, Anthony	Cooper, Peter	Jackson, Michael
12:00 pm					Smith, Johnny	Kahn, Genghis	Bernhardt, Sarah	Cardinale, Claudia
:15					Sing, Li	Jones, Catherine Z.	Lama, Dahli	King, Peggy
:30					Cary, Harry	Zimmerman, Bob	Buffett, Warren	Welsch, Racquel
:45					Leno, J.	Pearl, Minnie	Trump, Don	Smith, Adam
1:00 pm								
:15								
:30								
:45								
2:00 pm					Noth, Christooher	Woods, Tiger	Jennings, Whelan	Do Not Book
:15					Parker, S. J.	Smits, Jimmy	Orbach, Jerry	Do Not Book
:30					Monk, Thelonius	Smith, Johnny	Winfrey, Oprah	Martin, Dean
:45					Mariner, Silas	Foster, P.	McGhee, Bobby	Lewis, Jerry
3:00 pm					Paige, Pattie	Simmons, Jean	Jones, Tom	Crosby, Bing
:15					Rose, S.	Garbo, Greta	Jones, Star	Sirrus, Miley
:30					Combs, Sean	May, Pearlie	Latitah, Queen	Lauren, Sophia
:45					Thomas, Danny	Kadiddlehoffer, C.	Kimmel, James	Lauder, Estee
4:00 pm					Heinz, B.	Bond, James	Cooper James F.	Ono, Yoko
:15					Wall, Jon	Veneer, Fred	Zuckerberg, Mark	Yip, John
:30					Black, Jack	Diver, Pearl	Gates, Bill	Donovan, James
:45					Hanks, Thomas	Upton, Sinclair	Gates, Melinda	Crow, Russ
5:00 pm					Stein, Sally	Bundy, George	Bloomberg, Mike	Armstrong, Louis
:15					Shaw, Dinah	Whitiger, Forrest	Sandler. Adam	Phelps, Mike
:30					Streisand, B.	Harden, Marcia G.	Turner. Ted	Letterman, Dave
:45					Brecht, Berthold	Lewis, Sinclair	Seinfeld, Jerry	Christopherson, C.
6:00 pm								
:15								
:30								
:45								

Scheduled Pedo Appt

Chris Noth 6/9
J. Leno 5/5
Tom Dylan 5/28
Minnie Pearl 6/8
Bob Marley 6/10

Scheduled for Pedo Today

George Bundy 6/9
Spike Jones @ 11.45 am
Sarah Jones @ 11 am

Overdue for Pedo

Sammy Kahn 1/18
John Leeds 3/9
Ilya Kazan 5/1
Jason Bateman 4/30
Sidney Ceasar 3/30
Chris Lee 5/9

Figure 18.1 Appointment schedule of an orthodontic/pediatric dental group, which faithfully tracks the individual orthodontic patient's pediatric dental appointments during orthodontic treatment.

Figure 18.2 A list of orthodontic patients (and their commencement date of active orthodontic treatment) who are also being treated by the pediatric dentist, Dr. John Doe.

Dr. Jon Doe – Pediatric dentist
Mary Smith – August 2022
Jim Cohen – June 2022 (Overdue 2 months)
William Burk – September 2021 (Overdue 12 months)
Andrea Wilks – February 2021 (Overdue 1 year and 8 months)
Simon Grove – May 2022 (Overdue 3 months)

Figure 18.3 The returned list indicating which patients are overdue for their pediatric dental appointments.

Identifying orthodontic and pediatric dental problems earlier rather than later

The pediatric dentist is often the first clinician to recognize malocclusions in the mixed dentition. Figure 18.4 is a chart that should assist the pediatric dentist and dental hygienist in quickly assessing any deviations from the ideal or norm, and serves as a useful adjunct to the routine overall pediatric dental examination as well as an important vehicle of communication to the orthodontist. The orthodontist, similarly, can utilize this check-off assessment chart to further augment his or her traditional orthodontic examination and study of current orthodontic diagnostic records. The pediatric dentist should obtain a panoramic radiograph as an integral part of any initial orthodontic examination in the mixed dentition. Without the use of such a screening image, missing, supernumerary, or ectopic teeth and a number of other salient underlying deviations and/or frank pathology will go unnoticed. Radiographs obtained by the pediatric dentist or orthodontist need to be shared so that each clinician is maximally informed at each juncture of patient assessment efforts. Routine yearly panoramic images obtained by the treating orthodontist should also be sent to the pediatric dentist. The modern age of digital or electronic

capabilities makes this a seamless routine for both clinicians and it should be faithfully included in their basic communication protocols.

Figure 18.5 is a panoramic radiograph of a patient undergoing orthodontic treatment in the mixed dentition. Despite the less than average quality of this panoramic radiograph, the pediatric dentist viewing this radiograph noticed possible developmental caries in the mandibular second molars. Further specific periapical radiographs were then taken, the parents were apprised of this finding early on, and the matter was reassessed and managed after the eruption of the mandibular second molars. After confirmation of caries, the teeth were appropriately and conservatively restored (Figure 18.6). Figure 18.7 is an intraoral view of HW, a patient in the mixed dentition, who, after examination by the pediatric dentist, was considered to have seemingly unremarkable orthodontic issues that would require later rather than earlier orthodontic treatment (i.e. orthodontic treatment in the permanent rather than mixed dentition stage). The screening panoramic radiograph (Figure 18.8), however, suggested otherwise. The path of eruption of the canines and several other teeth was notably altered. There is considerable evidence, not only from the authors' clinical observations but from other investigators as well, to support the supposition that the majority of observed ectopically developing maxillary canines that are predisposed to becoming frank impactions can be conservatively managed by appropriate orthodontic intervention if such treatment is commenced earlier rather than later (Leonardi et al., 2004; Baccetti et al., 2009). HW was comprehensively treated utilizing maxillary expansion, removal of the maxillary primary canines, and fixed edgewise orthodontic appliances. Figure 18.9 is an in-treatment panoramic radiographic view and Figure 18.10 is an intraoral view of the maxillary canines mid-treatment and already well positioned into the dental arch. The overall pediatric dental and orthodontic management of this patient was considerably helped by recognition of the benefits of panoramic "screening" radiographs obtained in the mixed dentition for pediatric dental patients.

It is the authors' belief that the pediatric dentist should serve as the most important screening clinician for orthodontic problems for children in his or her practice. The clinical examination (utilizing the aforementioned orthodontic examination checklist) during a routine

pediatric dental appointment and a panoramic radiograph should be sufficient for identifying many early developing orthodontic problems. The panoramic radiograph should be considered indispensable to any clinical examination and should be obtained by the age of 7–8 years. Prompt treatment (when appropriate) and/or referral to an orthodontic colleague for an assessment of the need for and timing of earlier (mixed dentition) rather than later orthodontic intervention (in the adult permanent dentition) can be more proactively managed in many instances prior to the onset of more serious and sometimes irreversible adverse developmental problems. While it is generally accepted that many malocclusions can benefit from earlier rather than later orthodontic treatment, some other clinicians think that this might not result in an overall benefit to individual patients. And while controversy in some instances might exist with respect to both timing and specific treatment strategy, suffice to say that the early recognition of any developing orthodontic deviation can and should serve as the beginning of an important dialog between the pediatric dentist and orthodontic clinician.

OCCLUSAL AND FUNCTIONAL ASSESSMENT

EXTRA ORAL EVALUATION

Frontal: [ ] dolichofacial [ ] mesofacial [ ] brachyfacial

[ ] symmetrical [ ] asymmetrical

[ ] skeletal [ ] functional

Profile: [ ] convex [ ] Mx prognathic [ ] Md retrognathic [ ] BiMax prognathic

[ ] straight

[ ] concave [ ] Mx retrognathic [ ] Md prognathic [ ] BiMax retrognath

Anterior display: Dental: [ ] excessive @ rest [ ]wnl [ ] minimal @ rest

Gingival: [ ] excessive @ rest [ ]wnl [ ] minimal @ rest

INTRA ORAL EVALUATION

Dental Development: [ ] ahead for age [ ] WNL [ ] behind for age

[ ] aplasias [ ] ectopias [ ] supernumeraries

Occlusion:					
	Left Molar:	[ ] Class II	[ ] End on	[ ] Class I	[ ] Class III
	Right Molar:	[ ] Class II	[ ] End on	[ ] Class I	[ ] Class III
	Left Canine:	[ ] Class II	[ ] End on	[ ] Class I	[ ] Class III
	Right Canine:	[ ] Class II	[ ] End on	[ ] Class I	[ ] Class III

Overbite: [ ] Deep [ ] WNL [ ] Open

Overjet: [ ] Excessive [ ] WNL [ ] Negative

Transverse: [ ] Anterior X-bite [ ] Posterior X-bite

[ ] w/ shift [ ] w/o shift [ ] w/shift [ ] w/o shift

[ ] bilateral [ ] unilateral

Midlines: [ ] Mx & Md Coincident w/ face

[ ] Mx off

[ ] Md off If yes: [ ] skeletal asymm [ ] funct asymm [ ] dental asymm

Crowding:					
	Mx:	[ ] none	[ ] mild	[ ] moderate	[ ] severe
	Md:	[ ] none	[ ] mild	[ ] moderate	[ ] severe

Spacing:					
	Mx:	[ ] none	[ ] mild	[ ] moderate	[ ] severe
	Md:	[ ] none	[ ] mild	[ ] moderate	[ ] severe

Frenal concern:: [ ] no [ ] yes

[ ] max [ ] mand [ ] lingual

FUNCTIONAL EVALUATION

TMJ / MPD [ ] yes [ ] no

Habits [ ] yes [ ] no

Figure 18.4 Orthodontic status assessment chart that can be incorporated into the examination protocol of a pediatric dental practice.

Figure 18.5 Panoramic radiograph obtained during the course of orthodontic treatment suggests developmental caries in the unerupted mandibular second molars.

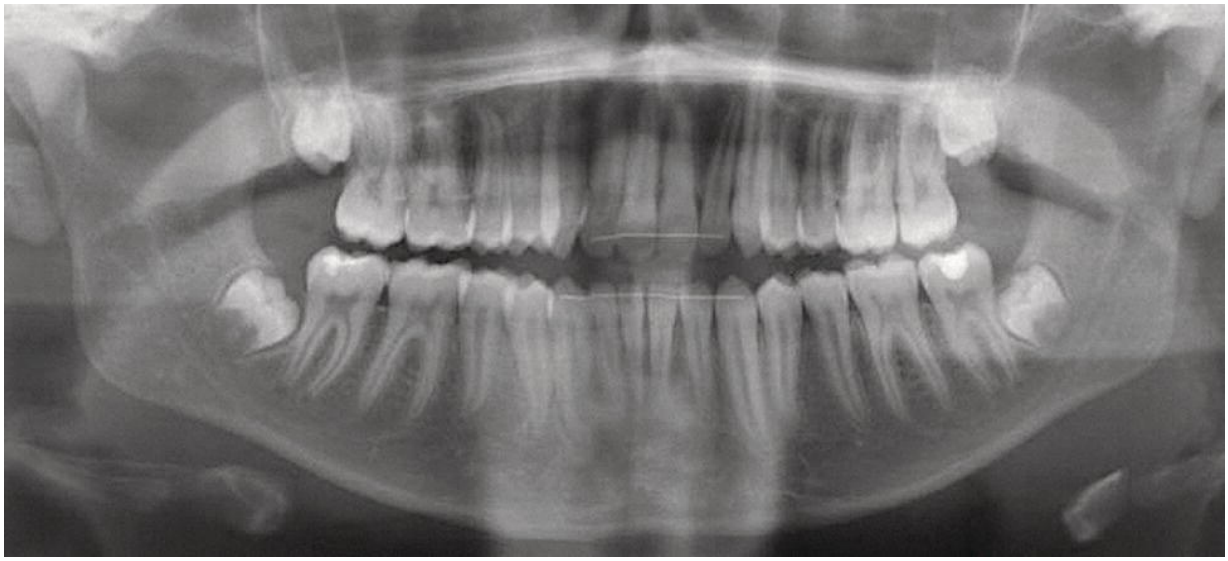


Figure 18.6 Removal of caries and restoration of the mandibular second molars.

Figure 18.7 Intraoral view of a young patient (HW) undergoing a clinical examination, with what appear to be minor deviations from the expected norms.

Figure 18.8 Panoramic radiograph of HW revealed altered path of eruption of canine and other teeth.

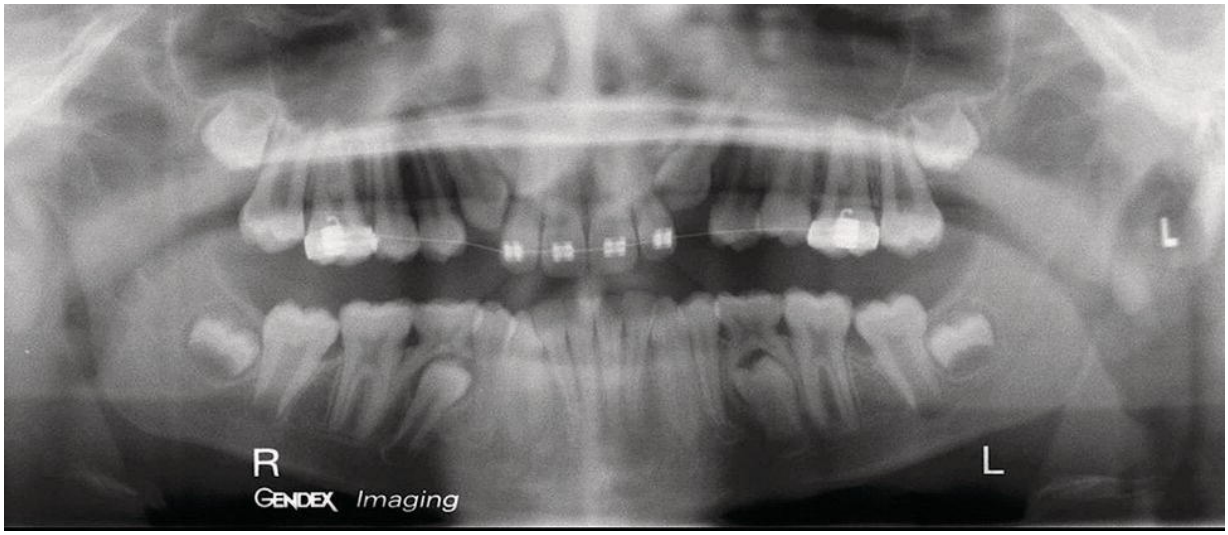


Figure 18.9 In-treatment radiograph of HW with initial orthodontic objectives of redirecting the ectopic path of eruption of the maxillary permanent canines.

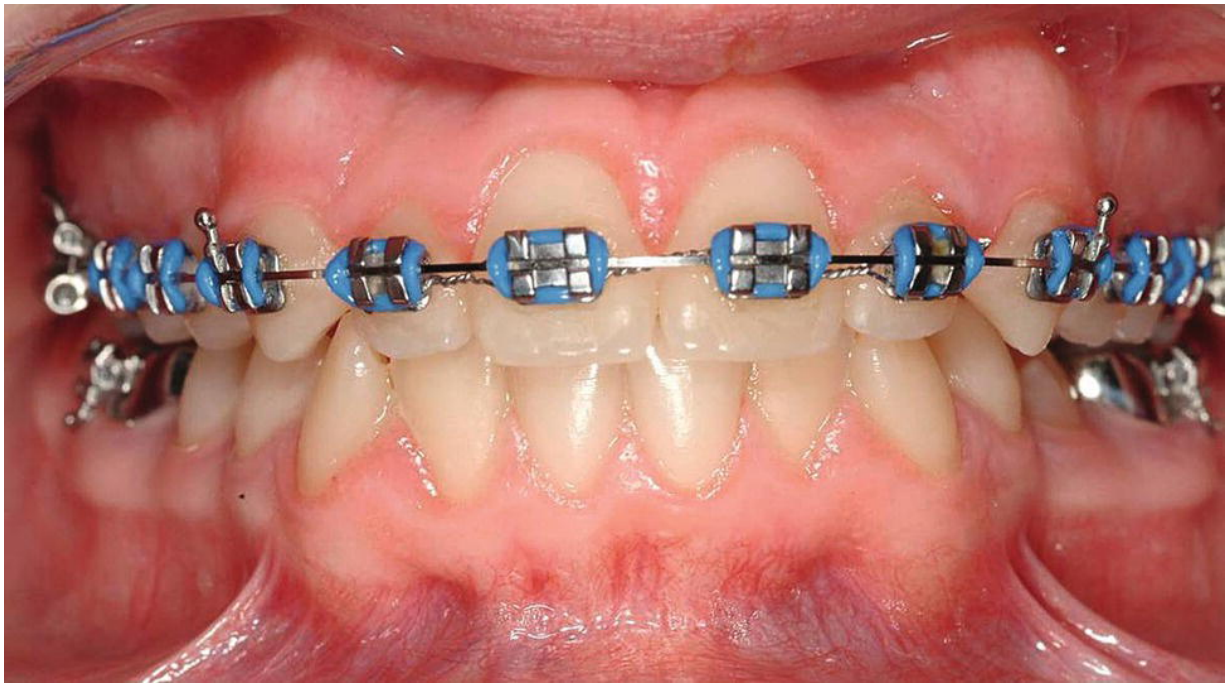


Figure 18.10 In-treatment intraoral view of the maxillary permanent canines successfully and conservatively redirected into the dental arch.

Restoring form and function: Revisiting the unilateral posterior crossbite with a functional mandibular shift

The unilateral posterior crossbite is a commonly observed clinical finding in the mixed dentition. Posterior crossbites in the mixed or permanent dentition represent deviations from the normal buccolingual occlusal relationships. Posterior crossbites can be caused by malpositions of individual or groups of posterior teeth (dental crossbites), malpositions of posterior teeth accompanied by a functional shift of the mandible (functional crossbites), or transverse disharmonies of the maxilla and mandible (skeletal crossbites; Moskowitz, 2005). Posterior crossbites are frequently observed as palatal crossbites (Figure 18.11), but may occur in a buccal crossbite relationship as well. There is a wide range of reported prevalence of unilateral posterior crossbites in the primary and mixed dentition, from 7% to 23% (Kutin and Hawes, 1969; Day and Foster, 1971; Infante, 1976; Kurol and Bergland, 1982; De Vis et al., 1984; Thilander et al., 1984; Heikinheimo and Salmi, 1987; Hannuksela et al., 1988). They have been reported to develop at between 19 months and 5 years of age, with approximately 80% being accompanied by functional shifts of the mandible (Gottlieb et al., 2006).

Figure 18.11 Lingual crossbite of several teeth in a patient in the mixed dentition.

Unilateral posterior crossbites with functional shifts of the mandible should be differentiated from unilateral posterior crossbites without shifts of the mandible. Figure 18.12 is a posterior dental crossbite caused by an individual tooth malposition of the maxillary left molar. Note that the maxillary and mandibular dental midlines coincide. This type of crossbite can be treated by moving the tooth (or teeth) in crossbite into the normal position. However, the situation in Figure 18.13 is quite different. The observed crossbite relationship in the maximum intercuspation position appears to be identical to the dental crossbite anomaly. A closer look, however, reveals a notable disparity between the maxillary and mandibular dental midlines. The mandible has shifted (to the side of the observed crossbite) as it encountered prematurities on closure. If we were to place the mandible in its normal transverse position (lining up the true maxillary and mandibular dental midlines), we would observe the

actual transverse relationship between the maxillary and mandibular posterior teeth (Figure 18.14). It becomes apparent that both the right and left sides of the maxillary posterior segments are lingually displaced. Consequently, the functional crossbite (even though it resembles the dental posterior crossbite in the maximum intercuspation position) is a result of a bilateral constriction or narrowness of the maxillary dental arch, and therefore requires bilateral expansion.

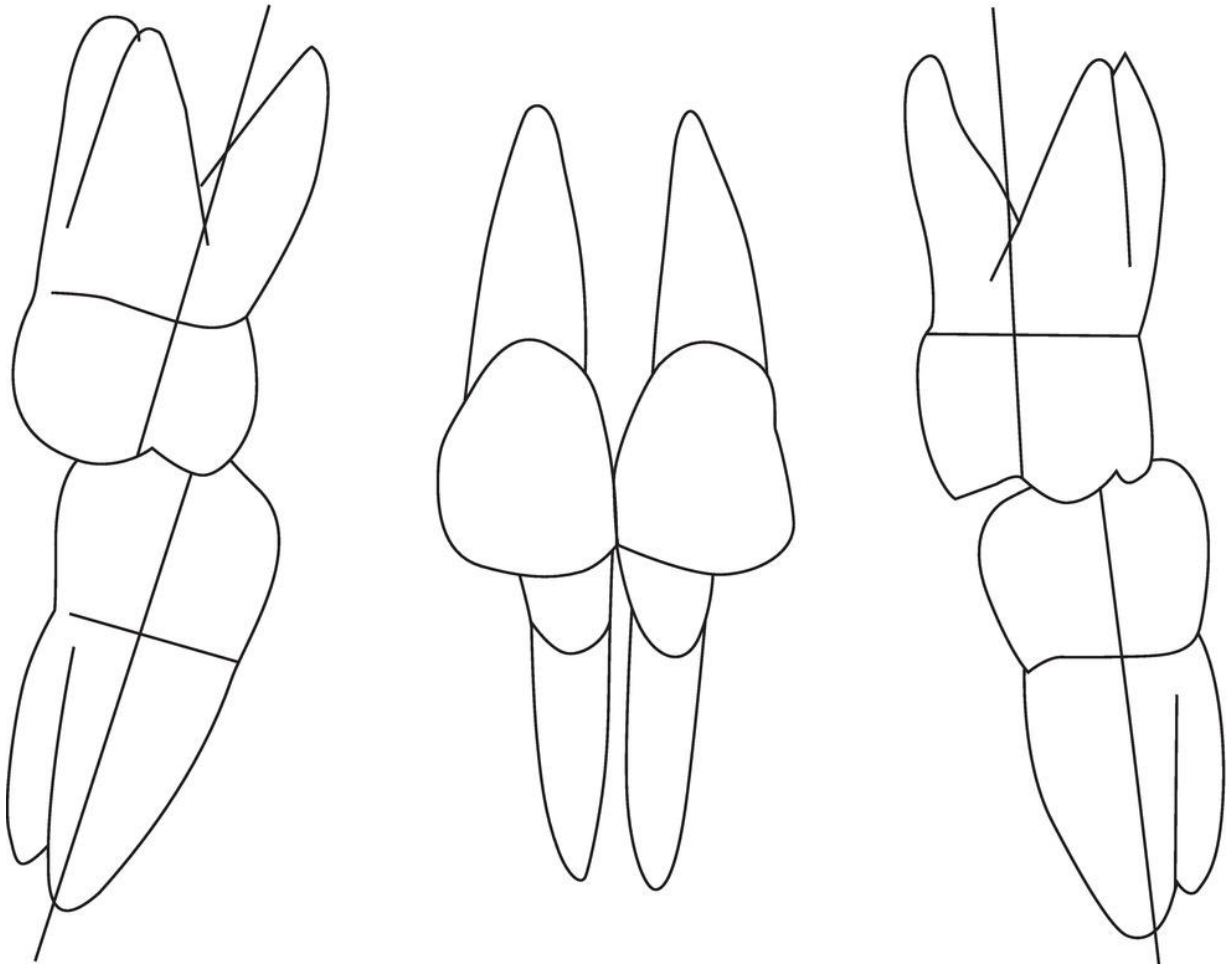


Figure 18.12 Dental lingual crossbite caused by malpositions of individual teeth. The maxillary and mandibular dental midlines are coincident.

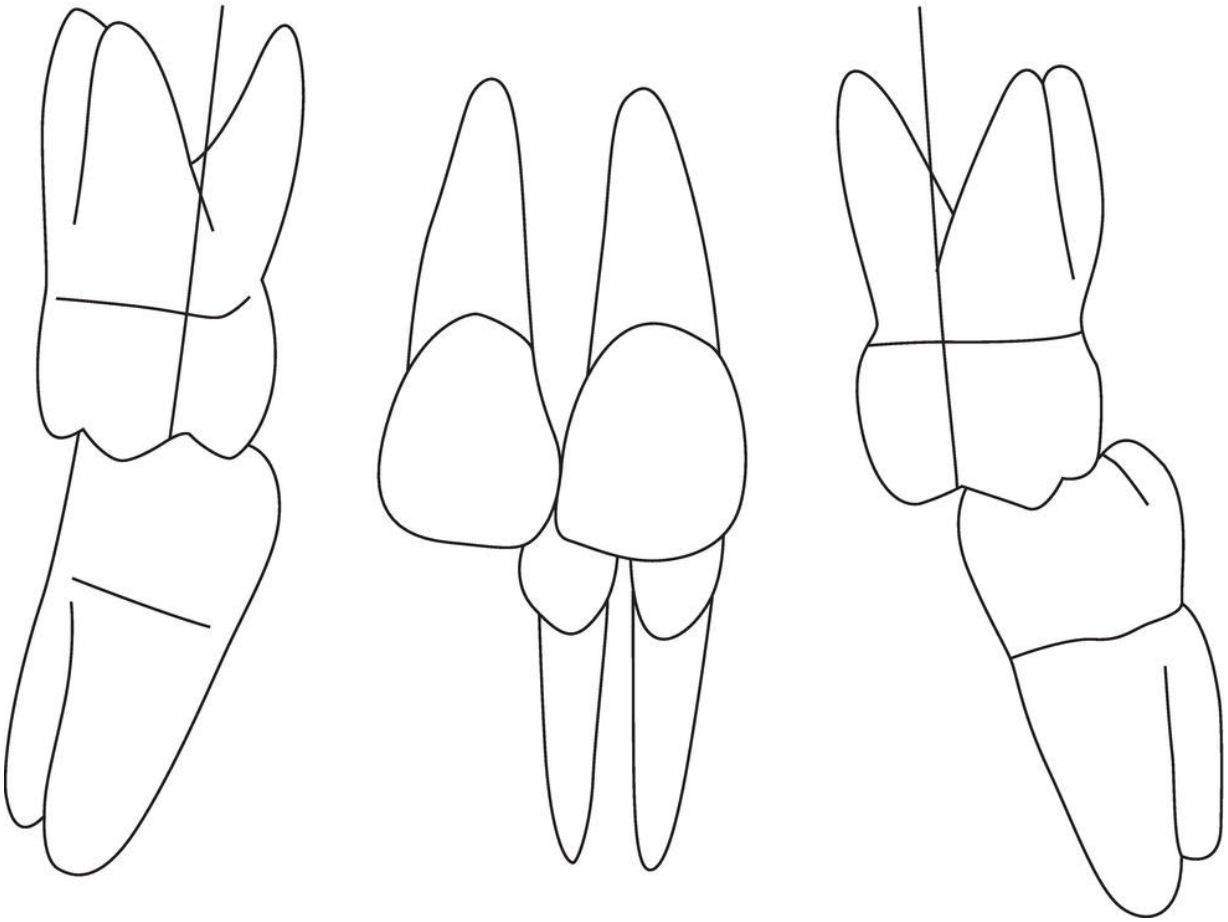


Figure 18.13 Functional crossbite resembling a dental lingual crossbite; however, the maxillary and mandibular dental midlines are not coincident. This situation represents a functional shift of the mandible on closure to the patient's left side.

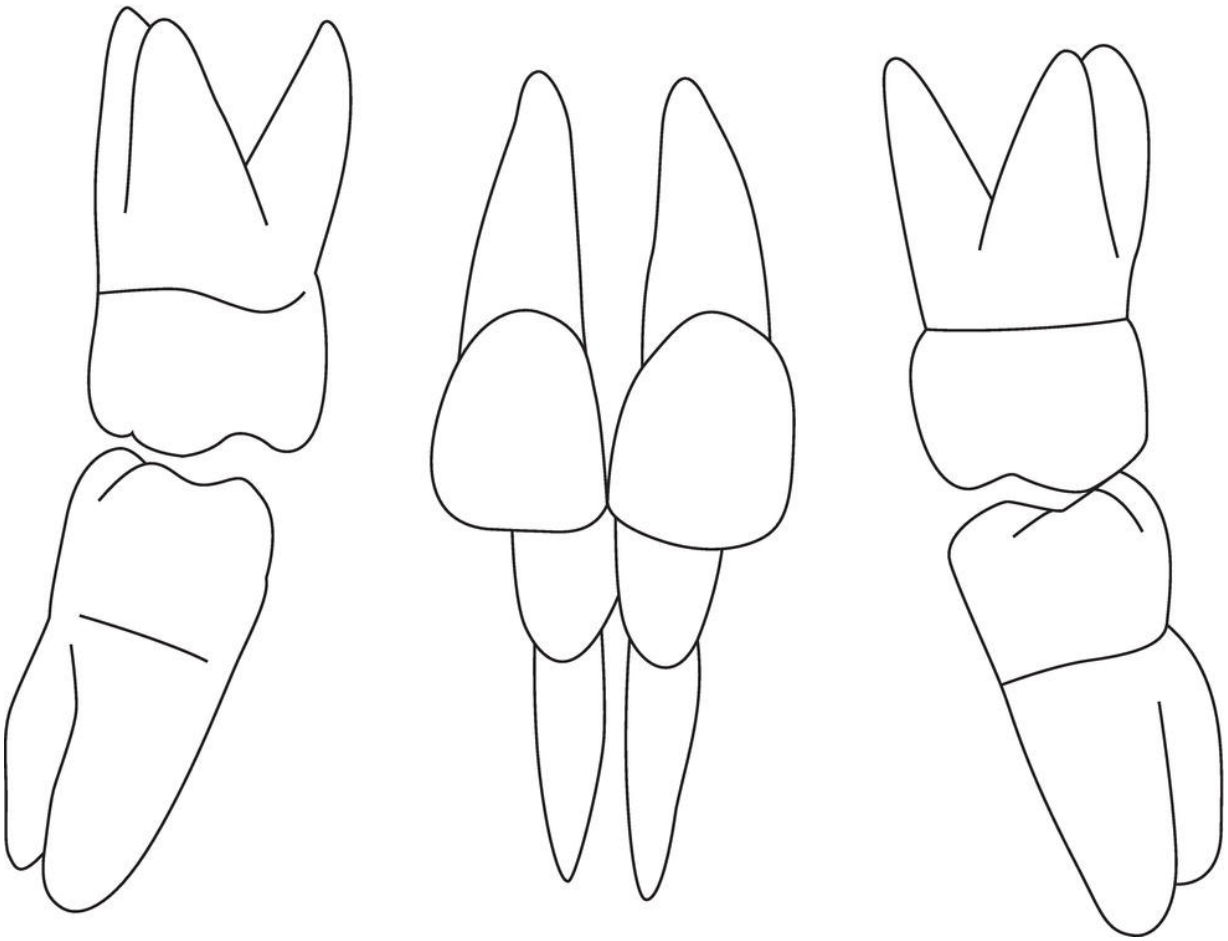


Figure 18.14 As a diagnostic aid, placing the midlines in their correct coincident positions will reveal the bilateral constriction of the maxilla and suggest the need for bilateral expansion of the maxillary dental arch.

EH was a young female patient in the mixed dentition with a unilateral posterior crossbite (Figure 18.15). Note the disparity between the maxillary and mandibular dental midlines, which is reflective of the mandibular shift to the right side on closure and resultant facial asymmetry (Figure 18.16). Maxillary expansion (Hyrax palatal expander) as part of a 'Phase I' type of treatment in the mixed dentition was used to accomplish the goal of bilateral maxillary posterior expansion (Figure 18.17). Phase I treatment resulted in a normal transverse relationship of the mandible in relation to the maxilla and improvement in facial symmetry, and extended for approximately 12 months (Figure 18.18).

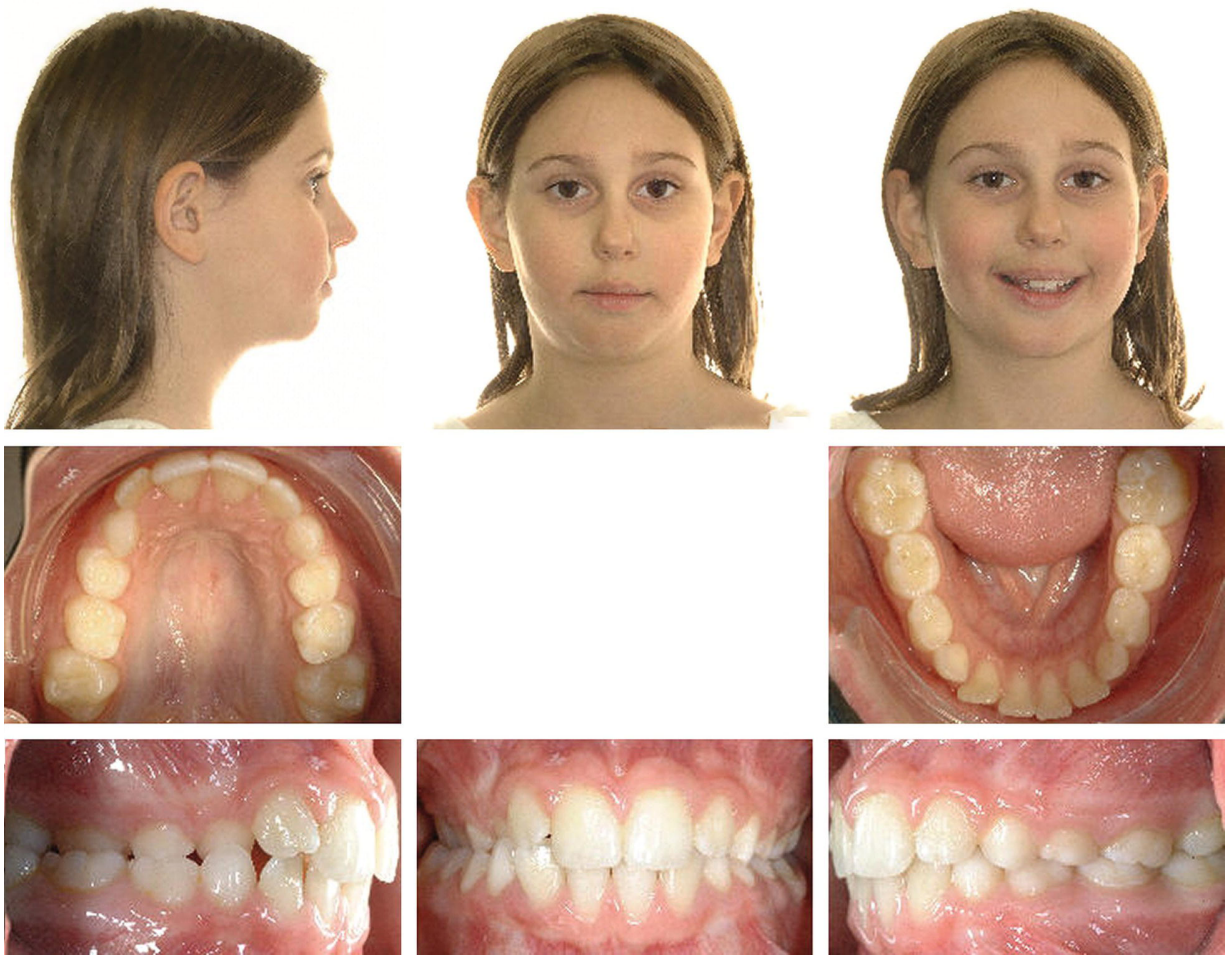


Figure 18.15 Patient EH has a unilateral posterior crossbite with a functional shift of the mandible to the right side on closure and dental midline disharmony.

Undoubtedly, orthodontic treatment can often significantly improve both dental and facial esthetics. Quantifying functional benefits of orthodontic treatment outcomes has been a difficult task for the orthodontic specialty for specific types of orthodontic problems. However, the unilateral posterior crossbite with a functional shift is one opportunity for the orthodontist and pediatric dentist to restore function and balance within the dentofacial complex. There is evidence that untreated unilateral posterior crossbite accompanied by transverse functional shifts of the mandible in still-growing patients may result in morphological asymmetries in addition to translational disharmonies (Pinto et al., 2001). Such transverse translational and morphological disparities may further result in notable facial asymmetries as well as predispositions to

temporomandibular joint-related pathology (Sonnesen et al., 2001; Moskowitz, 2003). Figure 18.19 shows an adult patient, GL, with an obvious facial asymmetry as a result of a longstanding and untreated unilateral crossbite. Figure 18.20 shows the crossbites on the left side and mandibular shift on closure to the patient's left side. Note that the maxillary and mandibular dental midlines do not coincide. This longstanding interdental arch occlusal condition has contributed to profound morphological differences on the left and right sides, as evidenced in both the frontal facial photograph and the anteroposterior cephalometric radiograph (Figure 18.21). The distance from the condylar to antegonial areas (ramal length) is remarkably different on the two sides. Although orthodontic treatment at this juncture for this patient could improve some of the translation or positional issues associated with a deviated mandible as a result of prematurities of the occlusion, it is obvious that establishing a fully symmetrical mandible with equal ramal length would involve a coordinated orthodontic and orthognathic surgical procedure.

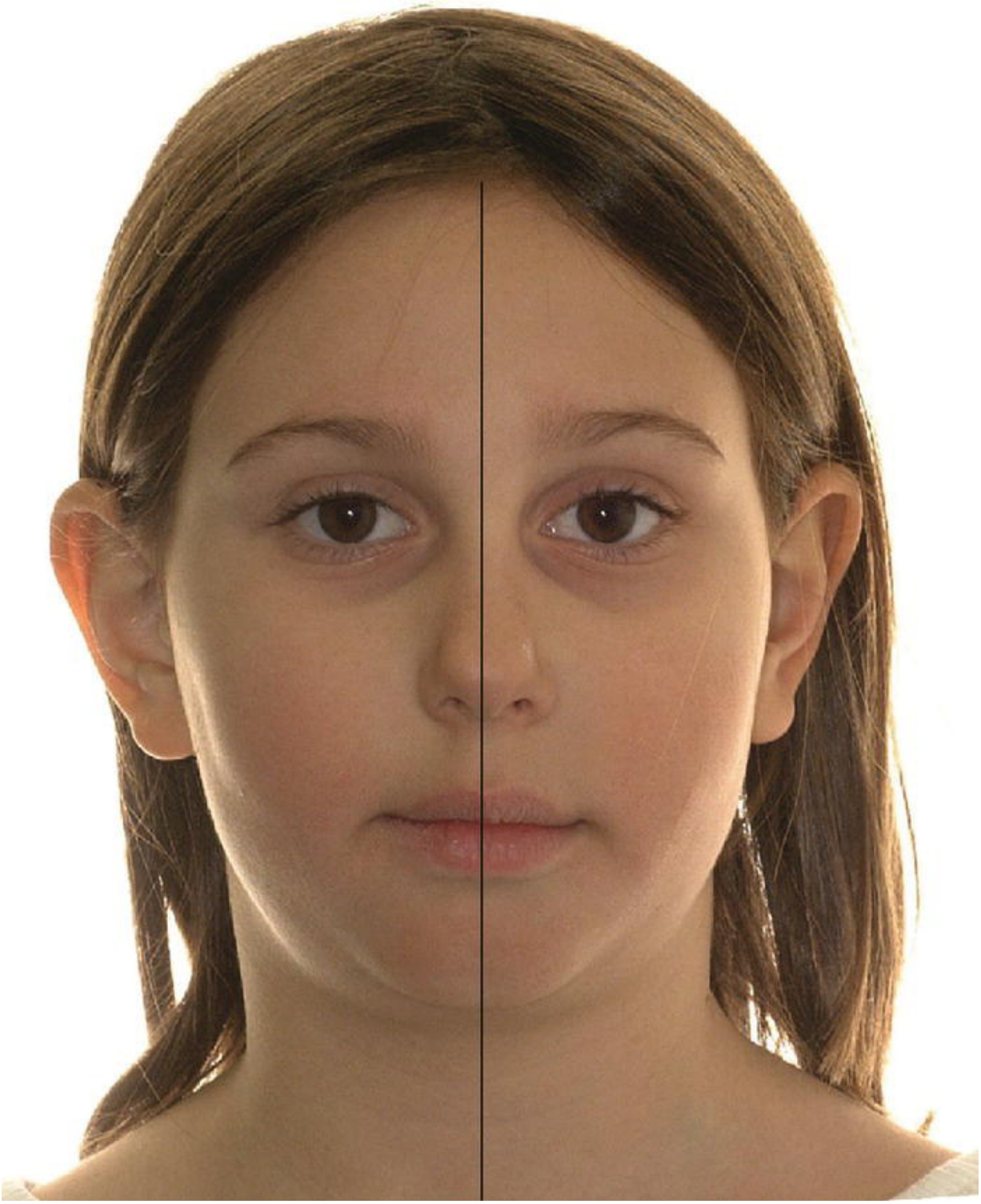


Figure 18.16 Patient EH displays a facial asymmetry from the frontal view as a result of the imposed improper position of the mandible in centric occlusion.

The earlier dentofacial orthopedic possibilities rather than those employed in later stages for patients exhibiting unilateral posterior crossbites with functional shifts might be analogous to our orthopedic medical colleagues who choose to treat scoliosis (Figure 18.22) in a growing child quite differently from patients who have already completed their growth. In the former situation, patients are treated with an orthopedic brace for the spine, and in the latter situation surgery is often performed. Pinto et al. (2001) have demonstrated that orthodontic patients exhibiting morphological differences in cases of unilateral posterior crossbite with functional shifts have a remarkable capacity to rebound to normal as a result of treatment during the active growth years. It would be interesting and beneficial for future investigations to determine whether there is an identifiable timeline threshold beyond which individual patients are incapable of such a dramatic reversal in condylar and ramal asymmetry corrections via conventional orthodontic/dentofacial treatment.

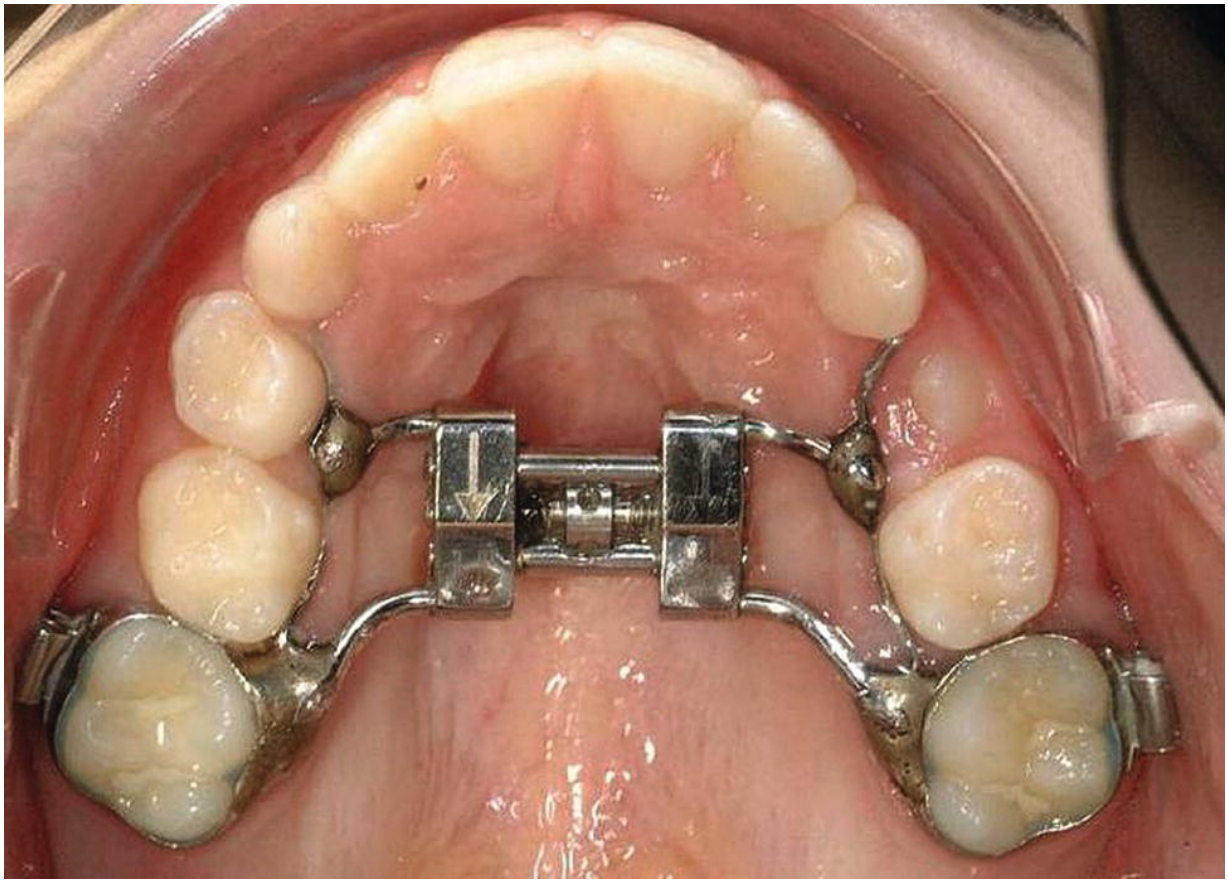


Figure 18.17 Maxillary bilateral posterior expansion achieved with a fixed palatal expanding appliance.

Congenitally missing maxillary lateral incisors: Who does what, when, and how?

The congenitally missing lateral incisor either unilaterally or bilaterally presents a unique challenge to the orthodontic clinician in many respects. First, a decision needs to be made as to whether or not the maxillary permanent canines will be used as a substitute for the missing lateral incisors, or whether the treatment plan will dictate creating adequate space for an implant and subsequent implant-supported restoration. It should be appreciated that decisions made with respect to the appropriate treatment plan for individual patients with missing maxillary lateral incisors will indeed have an impact on the esthetics and function of the young patient as he or she matures into and beyond the adult permanent dentition. Second, utilizing the modern implant modality requires exquisite

coordination between several clinicians other than the pediatric dentist.

Figure 18.23 is representative of a typical young patient who may be referred to the orthodontist by the pediatric or general dentist. The patient has a malocclusion caused in great measure by a congenitally missing maxillary left lateral incisor, undersized maxillary right lateral incisor, and resulting shifting of the maxillary central incisors. This seemingly routine and frequently encountered type of malocclusion requires a considerable degree of treatment planning prior to orthodontic treatment, during orthodontic treatment, and following orthodontic treatment, in order to provide comprehensive care consistent with modern orthodontic, pediatric dental, periodontal, prosthodontic, and restorative requirements. The specific needs of this young patient at each juncture of his or her chronological and developmental age should dictate which clinician makes the appropriate decision affecting the immediate and long-term needs of the patient. The orthodontist will need to coordinate orthodontic treatment, as some of the salient considerations beyond the usual orthodontic requirements include the precise amount of space to be left between the maxillary permanent left central incisor and permanent maxillary canine at the coronal, gingival, and apical levels; the amount of space to be created in the area of the existing undersized maxillary right lateral incisor; the selection of the most effective type of esthetic and functional retentive device; the timing of the implant placement in the area of the missing maxillary left lateral incisor; and the choice of implant and implant-supported restoration, which are all important details to satisfy modern requirements of esthetics, function, and stability.

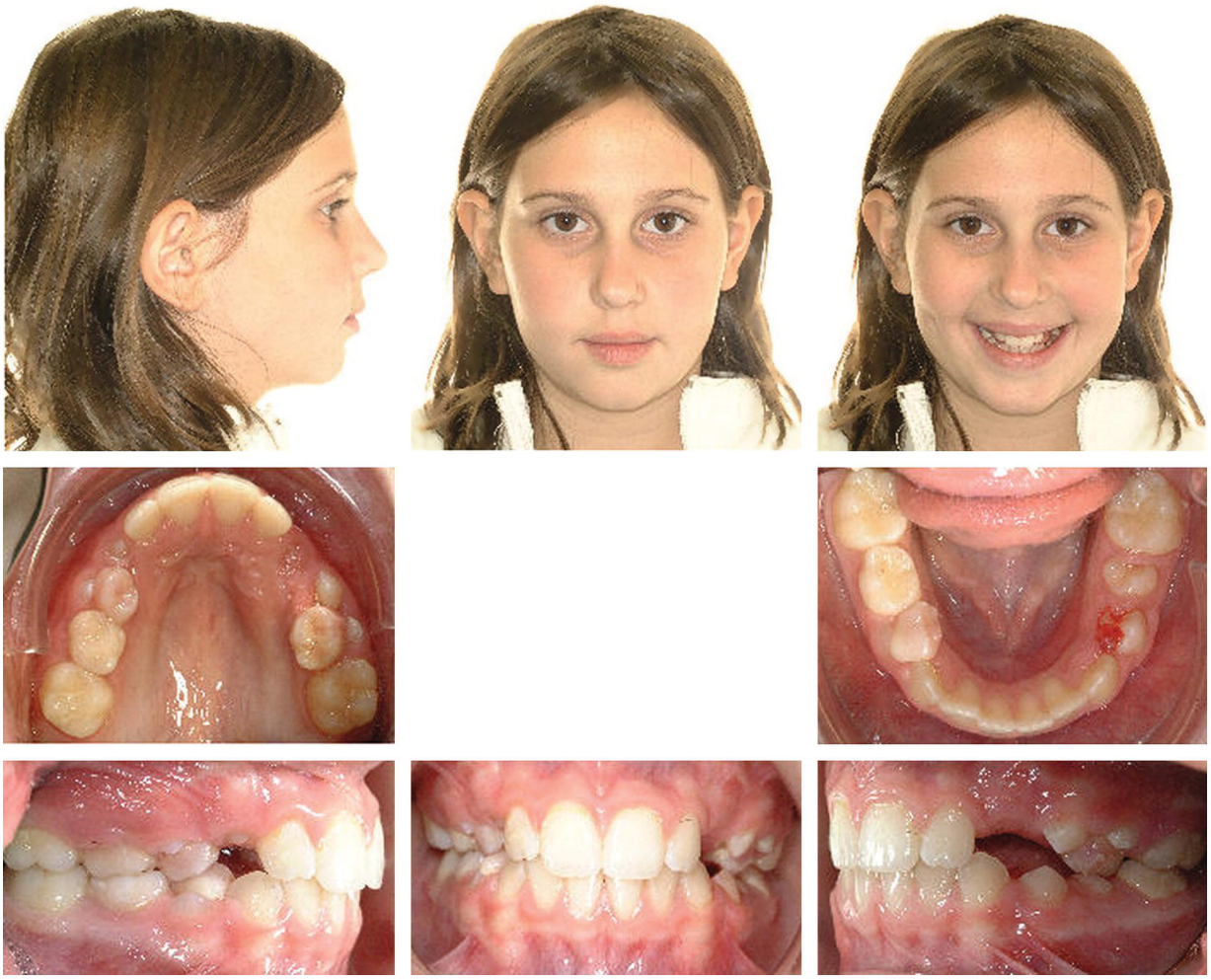


Figure 18.18 Phase I orthodontic treatment completed with the elimination of the functional crossbite and restoration of normal mandibular position.

Figure 18.19 Patient GL has a significant facial asymmetry due to a long-standing and untreated unilateral crossbite with a functional shift.

Figure 18.20 Intraoral views of the malocclusion of patient GL. Note the definite lingual crossbite of the maxillary left canine and first premolar as well as the dental midline discrepancy.

Figure 18.21 The disparity in ramal lengths in patient GL as a result of a long-standing imposed mandibular malposition during the many growth cycles of development.

Figure 18.22 Scoliosis of the spine, representing an orthopedic developmental anomaly.

Figure 18.23 Pediatric dental patient with a congenitally missing maxillary left lateral incisor and undersized maxillary right lateral incisor, who will be undergoing orthodontic treatment.

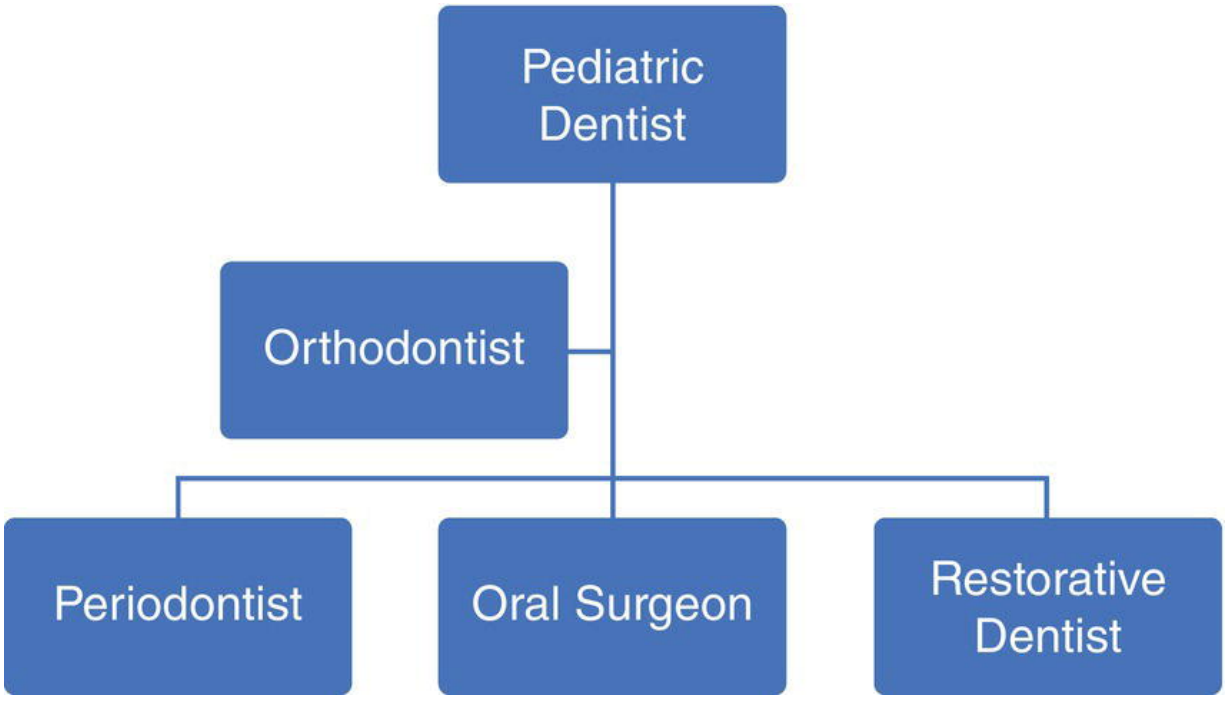


Figure 18.24 Interaction between different specialties is needed when long-term treatment plans are formulated for pediatric dental patients.

Figure 18.25 Orthodontics completed in the patient in Figure 18.23, with appropriate space created for the future implant-supported restoration.

Figure 18.24 depicts the interaction sequence that might follow an initial referral of a young patient with a congenital missing maxillary lateral incisor to an orthodontist and several other clinicians who might be consulted during the orthodontic treatment period. Figure 18.25 shows the same patient as in Figure 18.23 immediately following fixed appliance removal, and Figures 18.26 and 18.27 illustrate the consequences of a lack of such coordination. The patient had received orthodontic treatment in which little to no consideration was given to the size of the resulting space requiring future replacement, as well as the lack of divergence of the roots of teeth adjacent to the missing maxillary left lateral incisor. A cantilever bridge intended to replace the missing maxillary left lateral incisor was deemed to be the only long-term solution to this clinical dilemma. As an alternative to the existing situation, further orthodontic treatment was planned to recreate the appropriate space needed, respecting the caveats of modern implant placement and

implant-supported restorations (Figure 18.28). The orthodontic objectives included diverging the roots of the maxillary left central incisor and maxillary left canine to accommodate an appropriate implant and implant-supported restoration. The implant placement (Figure 18.28d) and final restorations (Figure 18.29) were coordinated with the orthodontic treatment to ensure that implant and prosthodontic needs were properly met. This type of coordination, once again, should have taken place during the earlier pediatric/orthodontic treatment experience of this patient, thereby avoiding orthodontic retreatment in adulthood.

Figure 18.26 The missing maxillary left lateral incisor was replaced by a cantilever bridge due to the lack of space for a conventional implant.

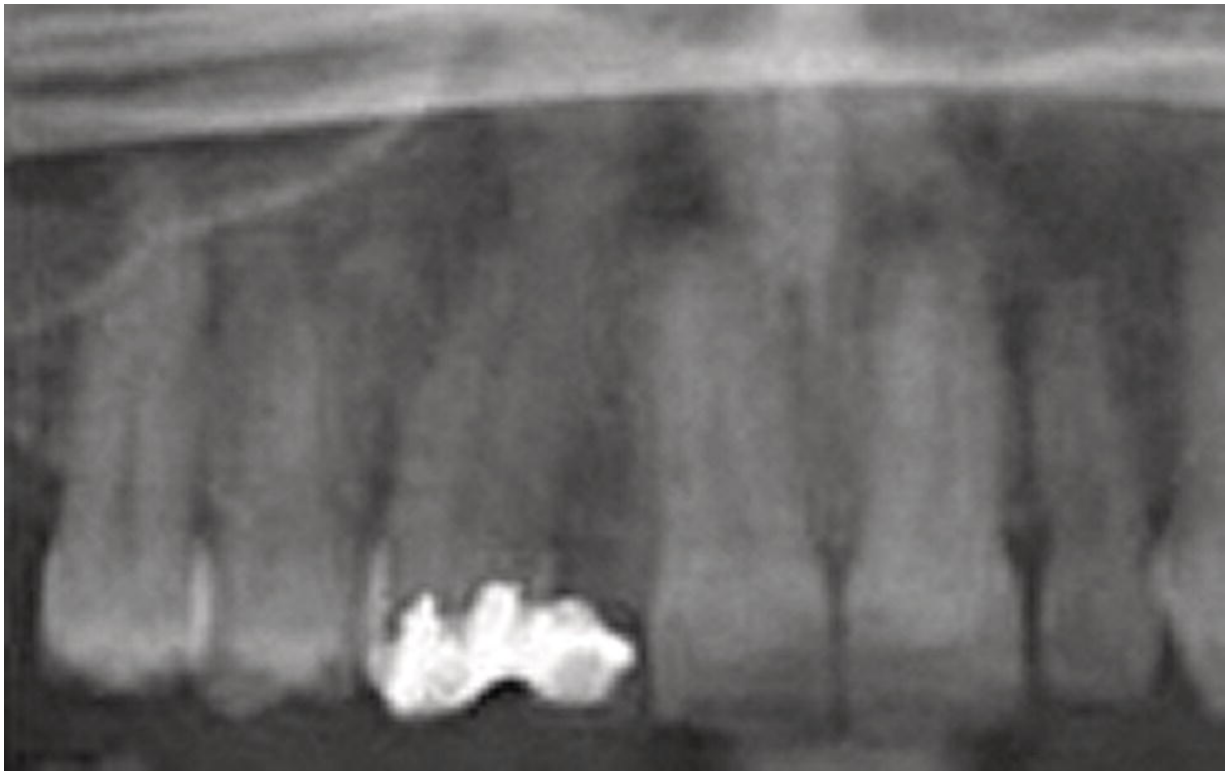
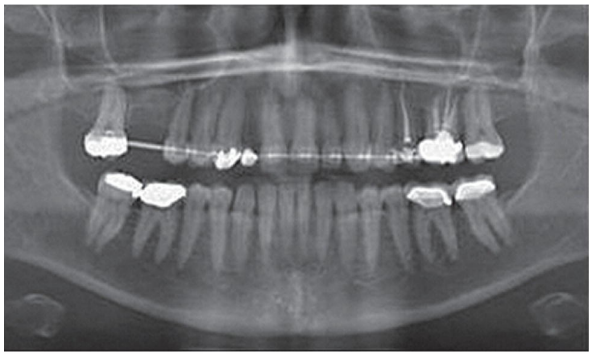


Figure 18.27 Radiograph showing the inadequate space for an appropriate implant due to the convergence of the roots of the adjacent teeth.



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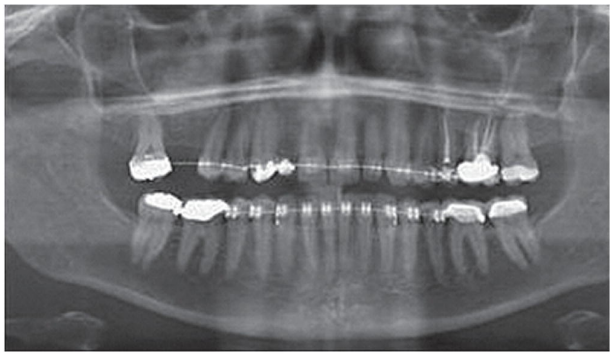

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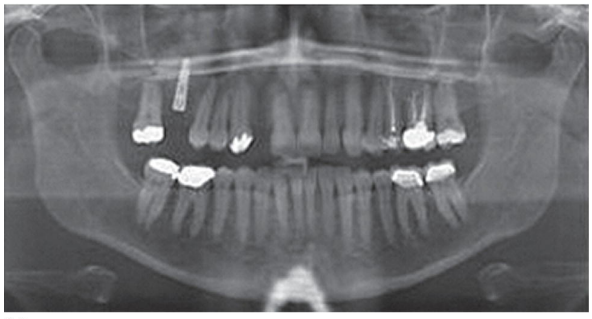

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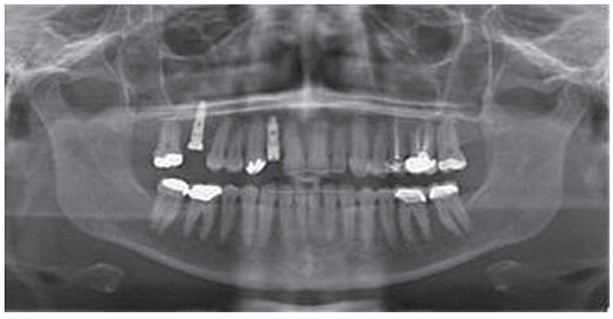

(d)

Figure 18.28 (a–d) Sequential radiographs of a patient requiring orthodontic treatment to accommodate future implants.

Figure 18.29 Final implant-supported restorations and veneers placed after orthodontic treatment.

Figure 18.30 Postorthodontic patient requiring implants to replace congenitally missing maxillary lateral incisors.

Retention considerations and beyond

Retention of the corrected malocclusions of individual patients who will be receiving implants for missing anterior teeth needs to be coordinated as well. Patients receiving implants immediately following orthodontic treatment, such as the patient depicted in Figure 18.30, might fare well with either a conventional Hawley type of retainer (Figure 18.31) or a typical "flipper" type of removable appliance that provides for the maintenance of beneficial tooth movements achieved during orthodontic treatment, pontic replacement of the missing maxillary lateral incisors, and some function. However, removable appliances with traditional labial bows are not esthetic and present long-term issues such as interference with settling of the occlusion and tissue irritation (Figure 18.32), hygiene issues, and, when used, simple "flipper" types cannot prevent reconvergence of the adjacent roots in the implant site. Short-term esthetic retention alternatives include the use of thermoplastic (Essix-type) removable devices with a pontic replacement in the area of the missing teeth (Figure 18.33). Long-term retention in postorthodontic patients who will not be receiving implants until clinicians are reasonably assured of the cessation of

any significant dentofacial growth, however, requires a more sophisticated type of retentive device.

Patient ID (Figure 18.34) underwent orthodontic treatment for a malocclusion complicated by the absence of the maxillary right lateral incisor and peg-shaped maxillary left lateral incisor. Figure 18.35 shows the completed treatment, with appropriate space left for the implant and subsequent implant-supported restoration, as well as the needed space for the peg-shaped maxillary left lateral incisor restoration. However, this patient will not be receiving an implant for approximately 2–3 years. Once again, the orthodontist and pediatric dentist need to interact on behalf of this patient so that the most appropriate retentive device can be planned. Such interaction might very well ultimately direct this patient to a general dentist or prosthodontist who is capable of fabricating a bonded resin type of bridge. A bonded resin bridge was used to replace the maxillary right lateral incisor, with some esthetic bonding with composite of the maxillary left peg-shaped lateral incisor (Figure 18.36). This more sophisticated type of prosthesis/retainer will serve this patient well until an implant-supported restoration can be placed for the missing maxillary right lateral incisor and a veneer placed on the maxillary left lateral incisor. As can be appreciated, these seemingly “routine” types of cases do indeed require a considerable degree of coordination and interactivity among the orthodontist, referring pediatric dentist, and several other specialists.

Figure 18.31 Removable retainer with a labial bow to maintain space for future implants in the maxillary lateral incisor area.

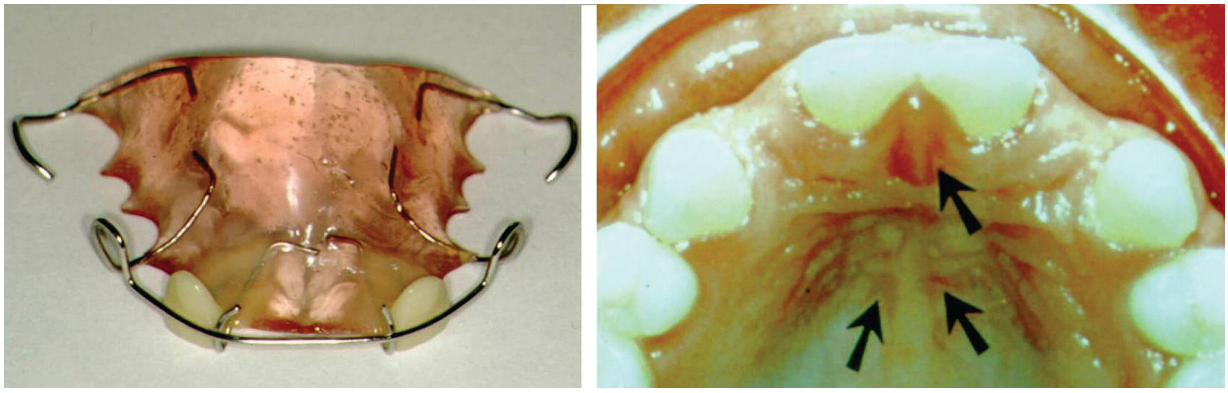

Figure 18.32 Long-term removable appliance wear for postorthodontic/preimplant patients poses hygienic issues as well potential areas of palatal tissue irritations (arrows).

Figure 18.33 Essix-type thermoplastic retainers are excellent short-term retentive devices for patients missing maxillary lateral incisors.

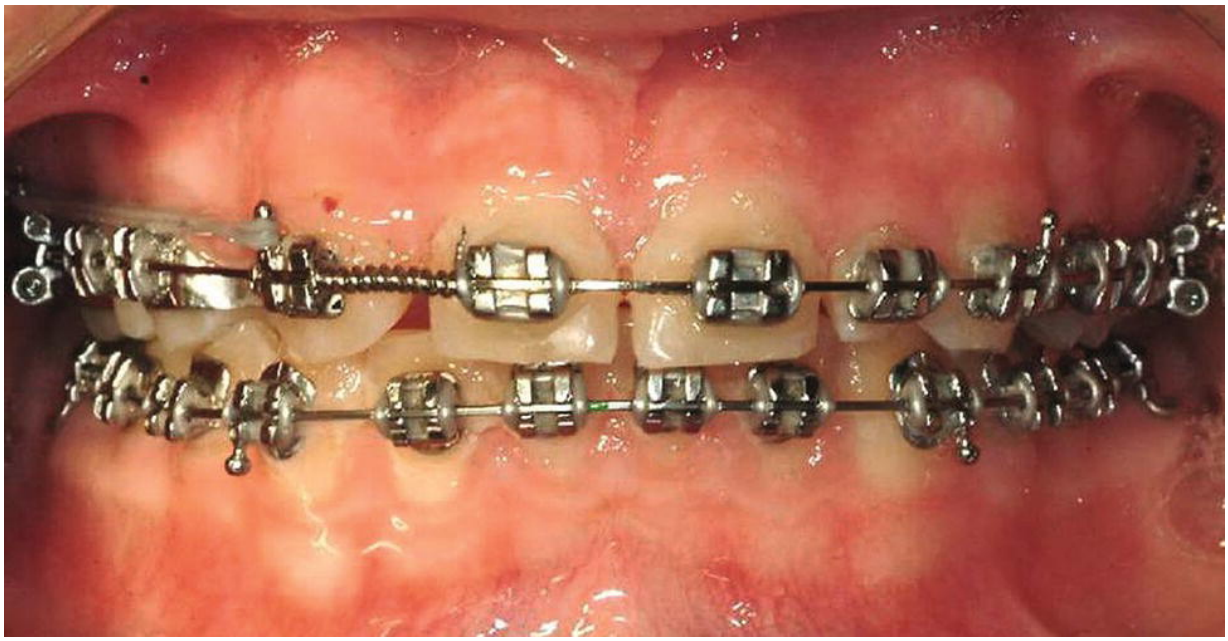

Figure 18.34 Patient ID: appropriate space being created for an implant-supported restoration of the maxillary right lateral incisor and a veneer for the peg-shaped maxillary left lateral incisor.

Figure 18.35 Patient ID, post orthodontic treatment, requiring planning for an appropriate retainer prior to implant placement.

(a)

(b)

Figure 18.36 (a, b) The bonded resin bridge replacing the maxillary right lateral incisor and bonded composite resin restoration on the maxillary left lateral incisor will serve as excellent long-term (2–3 years) transitional retentive devices until the patient is ready for an implant and veneer.

Enamel demineralization during orthodontic treatment: Who takes responsibility for prevention?

Orthodontic treatment with fixed appliances offers many distinct advantages to the patient and the orthodontic clinician. These

advantages include broad capability in the management of inter- and intraarch tooth movements during orthodontic treatment. Regrettably, however, one disadvantage is that fixed orthodontic appliances can present significant oral hygiene challenges to the young orthodontic patient. Consequently, increased plaque retention around orthodontic brackets can contribute to enamel demineralization, resulting in unsightly white spot lesions with or without cavitation. Figure 18.37 depicts a teenage patient with notably poor oral hygiene during orthodontic treatment and resulting enamel demineralization with both noncavitated and cavitated white spot lesions. The patient had missed his monthly orthodontic visits for six months and failed to keep his regular pediatric dental examination appointments. Such adverse occurrences seriously question any perceived benefit (esthetic or otherwise) of the orthodontic service itself. Clinician-prescribed fluoride rinses and gels, although remarkably effective for orthodontic patients with scrupulous oral hygiene, are predictably ineffective for patients who demonstrate poor oral hygiene compliance.

Geiger et al. (1988, 1992) found that poor compliance with a preventive fluoride rinse program occurred in 50% of patients. Along with other orthodontic and pediatric dental colleagues, the authors have utilized fluoride varnishes for patients undergoing active orthodontic treatment with fixed orthodontic appliances in an effort to either completely prevent or at least minimize the occurrence of white spot lesions during orthodontic treatment. Duraflor (Pharmascience Inc., Montreal, Canada) is a fluoride varnish that contains 5% sodium fluoride by weight in a natural colophony base. An *ex vivo* study by Todd et al. (1999) as well as the *in vivo* investigation by Farhadian et al. (2008) have reported a measurable benefit of fluoride varnish in significantly minimizing white spot lesions in the orthodontic population with fixed orthodontic appliances. Coordinating the use of these new varnishes between the pediatric dentist and orthodontist remains a notable challenge to attain the maximum benefit and avoid any possible overdosing of fluoride. This is yet another example of the need for a smooth and continual interaction between the pediatric dentist and orthodontist so that therapeutic compounds can be judiciously prescribed at

optimal efficacy levels. Our orthodontic group has been using such varnishes at three-monthly intervals and this protocol needs to be transmitted to the pediatric dentist to avoid unnecessary overlapping and duplication of effort.

(a) (b)

Figure 18.37 (a, b) A teenage patient with notably poor oral hygiene during orthodontic treatment and resulting enamel demineralization with both noncavitated and cavitated white spot lesions.

While the pediatric dentistry specialty has vast experience with fluoride compounds and their uses, this area is relatively new to the orthodontic specialty. In the absence of acceptable bond strength associated with fluoride-releasing orthodontic bonding resins, orthodontists should consider routinely incorporating fluoride varnishes in their clinical protocols. Finally, both the orthodontist and pediatric dentist need to take responsibility for recognizing orthodontic patients at risk for developing white spot lesions, and take appropriate and coordinated proactive measures to minimize such occurrences.

Conclusions

We conclude this chapter by revisiting our original intention – that is, to emphasize the profound need for greater interactivity and communication between the orthodontist and the pediatric dentist in order to optimize the treatment of individual patients. Each specialist must be educated to appreciate each other's goals and objectives, and, when necessary, be prepared to call on the expertise of other medical and dental specialists, as required for the specific needs of each individual patient. We recommend a reassessment of respective postgraduate curricula, re-examination of each specialty's clinical "guidelines," and increased effort on the part of each

specialty association to encourage ongoing interdisciplinary forums, so that orthodontists and pediatric dentists will continue to travel along parallel and intersecting paths together in harmony, with the singular purpose of providing the most modern, evidence-based, and high-quality oral healthcare to our mutual patients.

References

Baccetti, T., Mucedero, M., Leonardi, M. et al. (2009). Interceptive treatment of palatal impaction of maxillary canines with rapid palatal expansion: A randomized clinical trial. *American Journal of Orthodontics and Dentofacial Orthopedics* 136: 657–661.

Day, A.J., and Foster, T.D. (1971). An investigation into the prevalence of molar crossbite and some associated etiological conditions. *Dental Practice* 21: 402–410.

De Vis, H., de Boever, J.A., and van Cauwenberge, P. (1984). Epidemiologic survey of functional conditions of the masticatory system in Belgian children aged 3–6 years. *Community Dentistry and Oral Epidemiology* 12: 203–207.

Farhadian, N., Miresmaeili, A., Eslami, B. et al. (2008). Effect of fluoride varnish on enamel demineralization around brackets: An in-vivo study. *American Journal of Orthodontics and Dentofacial Orthopedics* 133: S95–S98.

Geiger, A.M., Gorelick, L., Gwinnett, A.J. et al. (1988). The effect of a fluoride program on white spot formation during orthodontic treatment. *American Journal of Orthodontics and Dentofacial Orthopedics* 93: 929–938.

Geiger, A.M., Gorelick, L., Gwinnett, A.J. et al. (1992). Reducing white spot lesions in orthodontic populations with fluoride rinsing. *American Journal of Orthodontics and Dentofacial Orthopedics* 101: 403–407.

Gottlieb, E., Cozzani, M., de Harfin, J.F. et al. (2006). JCO roundtable: Stability of orthodontic treatment, part 2. *Journal of Clinical Orthodontics* 40(2): 83–94.

Hannuksela, A., Laurin, A., Lehmus, V. et al. (1988). Treatment of crossbite in early mixed dentition. *Proceedings of Finnish Dental Society* 84: 175–182.

Heikinheimo, K., and Salmi, K. (1987). Need for orthodontic intervention in five-year-old Finnish children. *Proceedings of the Finnish Dental Society* 83: 165–169.

Infante, P.F. (1976). An epidemiologic study of finger habits in preschool children as related to malocclusion, socioeconomic status, race, sex, and size of community. *Journal of Dentistry for Children* 1: 33–38.

Kurol, J., and Bergland, L. (1982). Longitudinal study and cost-benefit analysis of the effect of early treatment of posterior crossbites in the primary dentition. *European Journal of Orthodontics* 14: 173–179.

Kutin, G., and Hawes, R.R. (1969). Posterior crossbites in the deciduous and mixed dentition. *American Journal of Orthodontics* 56: 491–504.

Leonardi, M., Armi, P., Franchi, L. et al. (2004). Two interceptive approaches to palatally displaced canine: A prospective longitudinal study. *Angle Orthodontist* 74: 581–586.

Moskowitz, E. (2003). Orthodontics in the progressive dental practice. In: R. Edwab (ed.), *Essential Dental Handbook*. Tulsa, OK: PennWell, pp. 387–430.

Moskowitz, E. (2005). The unilateral posterior functional crossbite, an opportunity to restore form and function. *New York State Dental Journal Aug/Sept*: 36–39.

Pinto, A.S., Buschang, P.H., Throckmorton, G.S. et al. (2001). Morphological and positional asymmetries of young children with functional unilateral posterior crossbite. *American Journal of Orthodontics and Dentofacial Orthopedics* 20: 513–520.

Sonnesen, L., Bakke, M., and Solow, B. (2001). Bite force in pre-orthodontic children and unilateral crossbite. *European Journal of Orthodontics* 23: 741–749.

Thilander, B., Wahlund, S., and Lennartsson, B. (1984). The effect of early interceptive treatment in children with posterior posterior crossbite. *European Journal of Orthodontics* 6: 25–34.

Todd, M., Staley, R., Kanellis, M. et al. (1999). Effect of a fluoride varnish on demineralization adjacent to orthodontic brackets. *American Journal of Orthodontics and Dentofacial Orthopedics* 116: 159–167.

19

Optimizing Prosthodontic Care with Orthodontic Mechanotherapeutics

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Summary

Orthodontic treatment for adult patients is often accompanied by restorative treatment to achieve the desired functional and esthetic outcomes. The treatment plan must be articulated through joint efforts between the restorative dentist, the orthodontist, and the lab technician. Also, the patient must be aware of the end goal of the treatment and all possible complications that may arise during and after treatment. Therefore, effective communication between the treating dental team and the patient is crucial to reach a satisfactory result for the patient and all healthcare personnel involved. Prior to restorative treatment, management of excessive or limited spaces is fundamental for creating biologically, esthetically, and functionally adequate dental restorations. The restorative dentist, in collaboration with the dental laboratory, must provide a roadmap to guide the orthodontic treatment and achieve a proper final tooth position in accordance with the future restorative plan. Additionally, orthodontic treatment may be needed to supplement missing tooth structures in preparation for a final dental restoration. Occlusal plane discrepancy management is another aspect of orthodontic treatment that must precede restorative treatment. Thus, in such cases orthodontic treatment should not be initiated without a full treatment plan involving all related dental specialties and all alternative options must be carefully evaluated to choose the most beneficial option for each case. In this chapter we describe joint treatment planning and execution between the restorative and orthodontic branches of dentistry, as well as different conditions requiring multidisciplinary cooperation.

Integrating orthodontic treatment into comprehensive treatment planning for adult patients can enhance both esthetic and functional results (Alfallaj, 2020; Kokich and Spear, 1997). However, unlike conventional orthodontics performed in young or adolescent patients, where patients present with a healthy periodontium and minimally restored dentition, it is common for adult patients to have

multiple missing teeth and a periodontally and structurally compromised dentition that will require considerable reconstructive dental treatment, all of which would make orthodontic treatment more challenging (Kokich and Spear, 1997). Furthermore, one of the objectives of restorative treatment is to achieve a stable occlusal relationship on completion of the treatment, which is challenging in severe malocclusion cases if not treated orthodontically prior to restorative treatment. Therefore, the objectives of orthodontic treatment must be planned in a team setting in conjunction with a restorative dentist and other specialists to establish a proper tooth position and stable occlusal relationship that will simplify future restorations. All the specialists involved should communicate and plan the case before implementing any treatment. Also, each of them should know the specific stage at which they should intervene, the time required to accomplish the objectives of their intervention, and the costs associated with it (Alfallaj, 2020; Kokich, 2008).

For effective and more reliable management of pre-prosthetic orthodontic cases, a diagnostic set-up and wax-up for future restorations are needed at the planning stage (Kokich and Spear, 1997). The orthodontist should confirm that changes in tooth position on a physical or digital diagnostic cast are achievable in the patient's mouth, and the restorative dentists should ensure that the tooth position is suitable for future restorations that are both esthetically and functionally acceptable (Figure 19.1). Furthermore, advances in digital technology and its applications in dentistry can be used to facilitate and integrate both restorative and orthodontic treatments. Intraoral scanners and desktop scanners can be reliably and accurately used to transform the dentition to a three-dimensional (3D) model that can be used for planning orthodontic and restorative aspects of the treatment (Cho et al., 2015; Wesemann et al., 2017). Teeth can be moved virtually, restorations designed, and then the desired treatment can be visualized on a monitor or physically through 3D printing (Figure 19.2). This application of digital technology allows for better communication between the treating dentists, an easier and faster workflow, and good estimation of the needed treatment and its intended outcomes.

Indeed, as with any conventional orthodontic treatment, patients should undergo the disease control phase before starting any

orthodontic teeth movement, which includes extraction of hopeless teeth, complete removal of all factors causing gingival inflammation, correction of defective restorations, and restoration of carious lesions to achieve long-term therapeutic goals of comfort and predictability.

Pre-prosthodontic orthodontic treatment can be summarized as the management of excessive or limited inter- and intraarch restorative spaces and correction of malocclusion in order to achieve the desired functional and esthetic outcomes. While simple malocclusion cases might benefit from simple orthodontic intervention using removable orthodontic appliances prior to or during prosthodontic treatment, advanced cases of malocclusion will require more comprehensive orthodontic treatment before initiating any restorative treatment in order to provide the restorative dentist with ideal occlusion and teeth positions. On the other hand, prosthodontic treatment could precede the orthodontic treatment in order to provisionalize structurally compromised teeth and provide means for orthodontic tooth movement.

The focus of this chapter will be to discuss the rationale and procedures performed as part of pre-prosthodontic orthodontic treatment. In brief, the following topics will be discussed in this chapter:

- Pre-prosthetic management of intraarch spaces.
- Pre-prosthetic management of interach spaces.
- Correction of ridge deformity though orthodontic tooth movement.
- Pre-orthodontic prosthodontic treatment.

Pre-prosthodontic management of intraarch spaces

Intraarch space discrepancy, either due to space deficiency such as crowding and teeth migration or due to excessive spaces such as diastema, microdontia, and missing teeth through congenital or environmental factors, is a major area of interaction between restorative dentistry and orthodontics. These patients present with

compromised esthetics, difficulties in pronunciation, bone loss, reduced chewing efficiency, malocclusion problems, and negative psychosocial impact (Behr et al., 2011; Johal et al., 2022; Kokich, 2005; Polder et al., 2004; Rakhshan, 2015). The future restorative plan must be taken into consideration prior to initiating orthodontic treatment and each clinical situation must be managed accordingly. Therefore, a multidisciplinary approach is essential for a successful treatment outcome (Figures 19.3 and 19.4). It must be emphasized that moderate to severe malocclusion cases will require comprehensive orthodontic treatment before initiating the final restorative treatment in order to provide the restorative dentist with ideal tooth position and occlusion to facilitate fabrication of biologically, functionally, and esthetically satisfactory restorations (Figure 19.5). However, simple crowding cases could be managed with straightforward orthodontic intervention, such as removable orthodontic appliances with minor interproximal reduction to provide the needed space for tooth movement prior to or during prosthodontic treatment to achieve the desired esthetic, functional, and occlusal outcomes (Figure 19.6).

Congenitally missing teeth

Management of dental agenesis should be planned and initiated during adolescence while the patient is growing, which usually requires an interim treatment at around 7–9 years of age (Behr et al., 2011). Early orthodontic intervention in these cases preserves more treatment options in the future that are more predictable, and have better esthetic and functional outcomes (Kokich, 2005). Different treatment options are possible, ranging from space closure to space creation with prosthetic replacement or transplantation, depending on several occlusion factors.

Missing lower second premolar

Patients with congenitally missing second premolars can present with either a retained or an exfoliated primary second molar. Three treatment options are possible: (i) maintaining the primary second molar; (ii) extraction of the primary second molar and space closure; and (iii) extraction of the primary second molar and prosthetic

replacement or auto-transplantation. The treatment decision depends on several factors, including the patient's age and growth potential, primary second molar condition, eruption pattern, and general space conditions (Kokich, 2005).

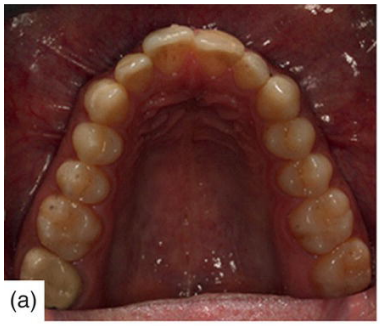
When the primary second molar tooth is in good condition, the patient has no arch length deficiency, and he or she does not need the extraction to treat the malocclusion, maintaining the primary second molar is the treatment of choice in order to maintain the bone vertically and buccolingually (Kokich, 2005). However, the size of the primary molar must be modified to achieve the proper occlusal relationship. A reduction of the mesiodistal width of the primary second molar to 7.5–8 mm to approximate the average width of the permanent second premolar with careful consideration of root divergence is recommended (Biggerstaff, 1992; Kokich, 2001; Sabri, 2004; Spear et al., 1997). In addition, the occlusal surface can be restored with a direct or indirect restoration to achieve proper occlusal contact (Kokich, 2005).

When the primary second molar is compromised or ankylosed, extraction is recommended. As ankylosis becomes worse with time, early extraction is recommended to avoid significant vertical bone loss and periodontal complications that could affect future implant placement (Bjerklin and Bennett, 2000; Kokich, 2005; Kokich, 2002; Kurol and Thilander, 1984). In these cases, the decision to maintain the space for future replacement or to close it depends on the overall malocclusion of the patient. If space closure is indicated, the anchorage requirements should be considered, and the use of temporary anchorage devices (TAD) might be needed (Figure 19.7).

Missing upper lateral incisor

Treatment options in cases of missing lateral incisors are either space closure with canine substitution or space opening with prosthetic replacement. Several factors must be considered in order to select the appropriate treatment option, such as the patient's malocclusion and canine condition (Kokich, 2002). Space closure is the treatment of choice in cases that have a balanced facial profile, maxillary crowding or protrusion, Class II molar relationship with no mandibular crowding or protrusion, Class I molar relationship with

mandibular crowding that requires extraction, a premolar that is suitable to substitute for a canine, or a canine that has acceptable size, shape, and color to substitute for a lateral incisor (Figure 19.8; Rosa and Zachrisson, 2001, 2007). However, communication and planning with the restorative dentist and periodontist before orthodontic treatment are vital to achieve the desired outcomes. Canines and premolars used for substitution will require modification in their height, width, thickness, rotation, gingival height, torque, and color (Table 19.1; Kokich and Spear, 1997; Kokich et al., 2011; Rosa and Zachrisson, 2007; Sharma and Sharma, 2015; Zachrisson et al., 2011). This approach, if carefully planned and executed, will result in conservative, stable, and long-lasting esthetic results (Sharma and Sharma, 2015; Zachrisson et al., 2011).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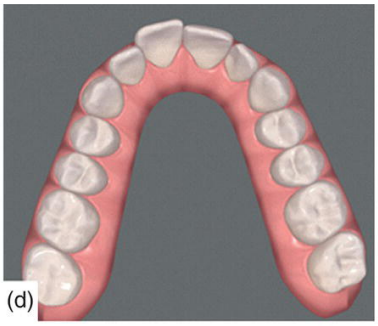
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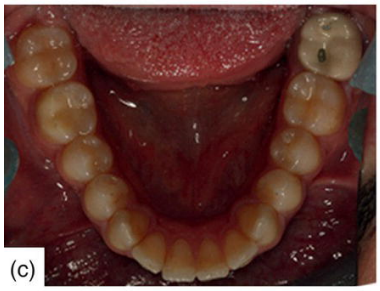
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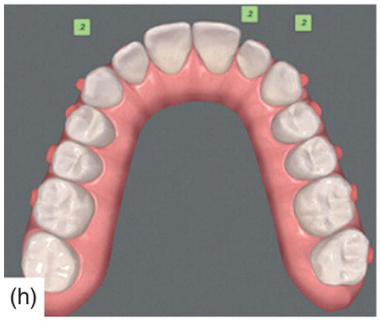
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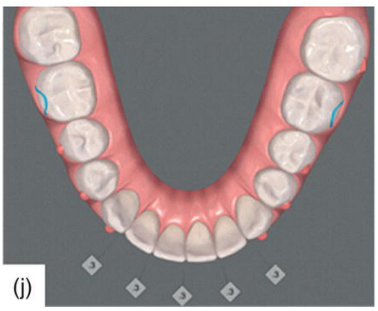

(j)

(m)

(g)

Figure 19.1 A case of small upper lateral incisors and Bolton discrepancy treated with clear aligners. (a–c) Pretreatment intraoral photographs with mild upper and lower crowding and small lateral incisors, especially #22. (d–f) Pretreatment digital model (ClinCheck, Align Technology, Tempe, AZ, USA). (g) Bolton analysis showing anterior Bolton discrepancy of 2.11 mm. The case was discussed by the treating orthodontist and restorative dentist and the plan was to restore the size of the upper lateral incisors and to reduce the mesio-distal dimensions of lower anterior teeth to address the Bolton discrepancy. (h–j) Digital planning includes clear aligners with restoration of the upper lateral incisors width through space opening distal to #12 (0.2 mm) and mesial and distal to #22 (0.2 mm mesial and 0.2 mm distal) in addition to lower incisor interproximal reduction (IPR) of 1.5 mm distributed between the lower anterior teeth. (k–m) Posttreatment intraoral photographs with crowding resolved and planned spaces opened for restorative build-up. The patient was referred to the restorative dentist at this stage.

Courtesy of Dr. Samah Alfuriji.

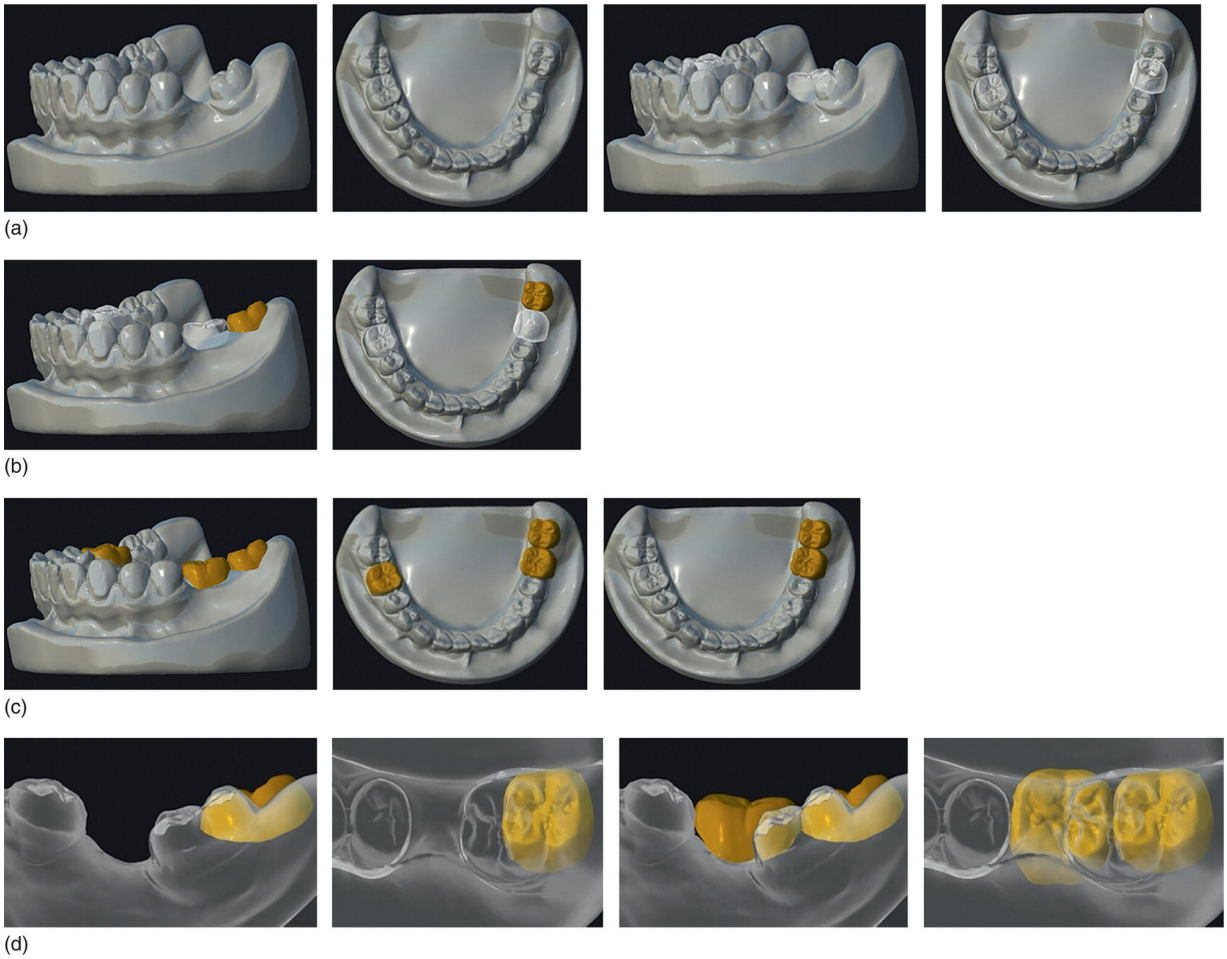


Figure 19.2 Example of combined restorative and orthodontic virtual planning. (a) Mesially tipped #37 invading the restorative space of missing #36. The contralateral tooth #46 was mirrored virtually and used to assess the space needed to be created through orthodontic uprighting. (b) #37 uprighted virtually. (c) #36 future restoration was created virtually through mirroring the contralateral tooth. (d) The amount of orthodontic movement needed to achieve the desired treatment outcome can be estimated digitally.

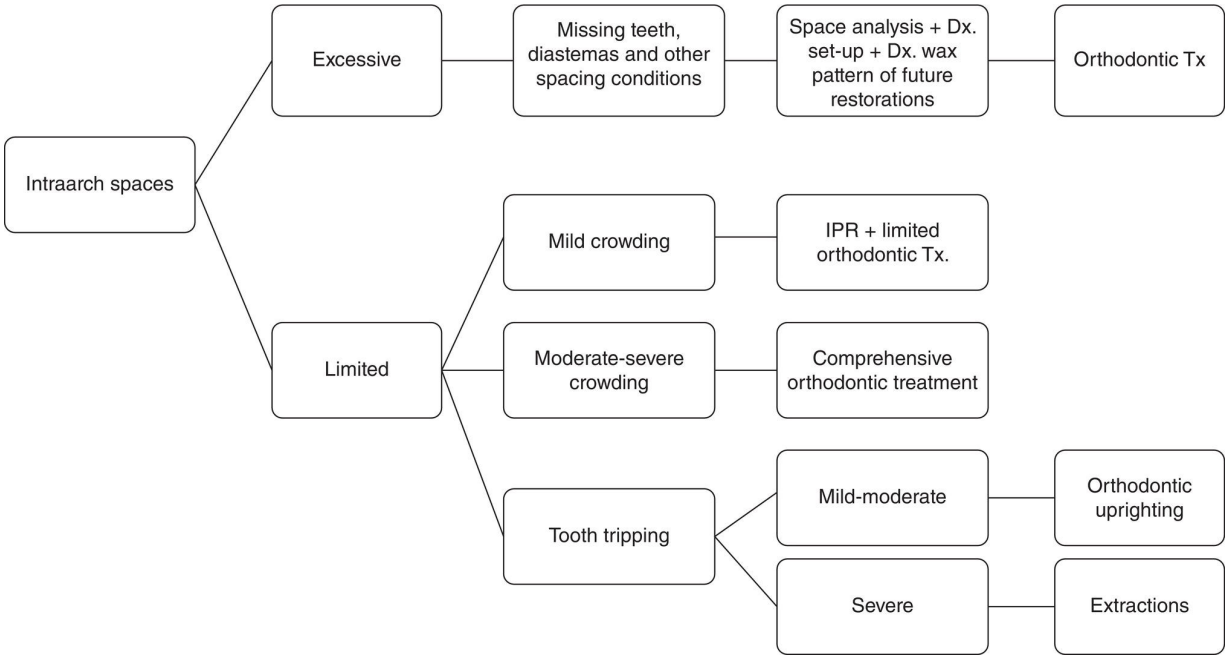


Figure 19.3 Schematic diagram summarizing various conditions associated with intraarch spaces and their management. Dx, diagnosis; IPR, interproximal reduction; Tx, treatment.

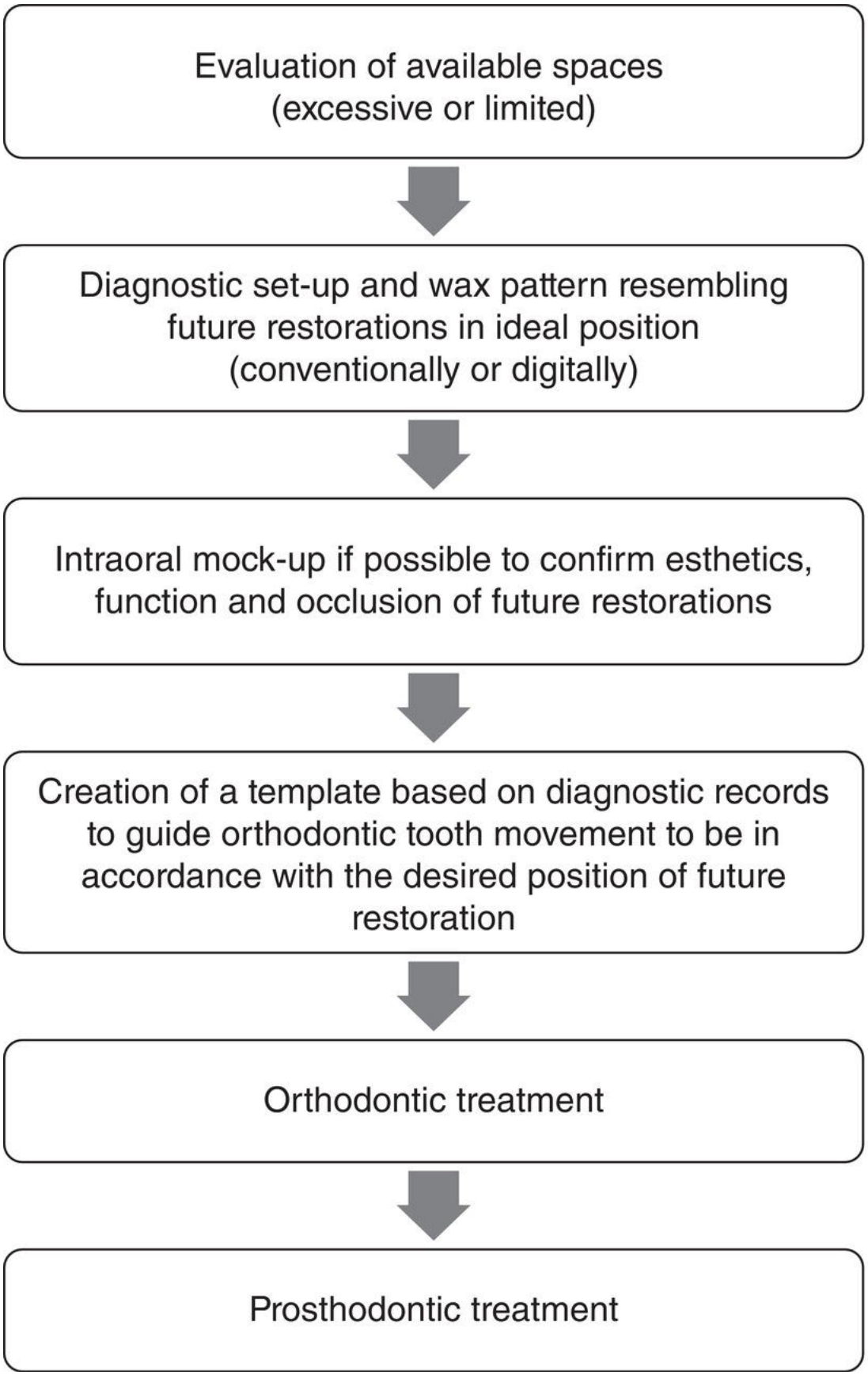

Evaluation of available spaces
(excessive or limited)
Diagnostic set-up and wax pattern resembling
future restorations in ideal position
(conventionally or digitally)
Intraoral mock-up if possible to confirm esthetics,
function and occlusion of future restorations
Creation of a template based on diagnostic records
to guide orthodontic tooth movement to be in
accordance with the desired position of future
restoration
Orthodontic treatment
Prosthodontic treatment

Figure 19.4 Schematic diagram summarizing rationale and staging in the management of intraarch spaces.

On the other hand, if the patient does not meet the criteria for space closure, space opening and prosthetic replacement with either implant or tooth-supported prosthesis is the alternative option (Figures 19.9 and 19.10; Sharma and Sharma, 2015). For space opening, early management during the mixed dentition is required to preserve the ridge height and width through guided permanent canine eruption into the lateral incisor space (Kokich, 2005; Kokich, 2002). When facial growth is completed and the patient is ready for prosthetic replacement, the permanent canine can be moved distally to develop an adequate buccolingual alveolar bone width for implant placement (Kokich, 2001; Kokich and Spear, 1997). Adequate implant space both coronally and apically must be determined before space opening through arrangement with the restorative dentist. Several methods are available to determine the required coronal space, like measuring the contralateral tooth size assuming it has normal morphology and size (Spear et al., 1997), Bolton analysis (Bolton, 1962), and diagnostic wax-up, with the latter being the most predictable method (Kokich, 2005). Adequate apical space must be available between the roots of the incisor and the canine to allow for safe implant placement (Figure 19.10; Sharma and Sharma, 2015). A single tooth implant is the most conservative option for replacement, but since the implant cannot be placed until growth is completed, other options like a retainer with a pontic tooth, resin-bonded bridge, and canine cantilever can be used temporarily to maintain the space (Kokich, 2005; Sharma and Sharma, 2015). An implant can be placed only after confirmation of facial growth cessation to avoid infraocclusion, esthetic, and periodontal issues. Several methods are available to check the vertical growth, with serial lateral cephalometric superimposition being the most accurate (Sharma and Sharma, 2015). The appropriate age varies and is estimated to be after 17 years in girl and 21 years in boys (Fudalej et al., 2007; Sharma and Sharma, 2015; Thilander et al., 1992).

(a)

(b)

Figure 19.5 A 33-year-old male patient with missing upper right second premolar. (a) The patient presented with Class I malocclusion, generalized spacing, edge-to-edge bite, and shifted lower midline to the left side. The case was referred from the restorative dentist to close the spaces and achieve adequate overjet and overbite before proceeding with restorative treatment. (b) The patient was treated with clear aligners. Posttreatment photographs show molars and canines in Class I occlusion, positive overjet and overbite, and coincident midlines with implant placed at the area of the upper right second premolar.

Courtesy of Dr. Samah Alfuriji.

Figure 19.6 A case of mild crowding. (a) The patient presented with mild mandibular anterior crowding requesting esthetic restorations for the maxillary anterior teeth. (b) The patient was treated using a lower removable orthodontic appliance with interproximal reduction, following an orthodontic diagnostic tooth set-up to avoid occlusal overloading of individual teeth and achieve the desired esthetic outcome. The diagnostic set-up was used for estimating the space needed for orthodontic tooth movement and fabricating the removable appliance. (c) Esthetic prosthodontic treatment of the maxillary anterior segment was performed following completion of orthodontic treatment.

Courtesy of Dr. Sara Bukhari.

Tooth migration

Even though tooth migration usually presents with both vertical and horizontal components affecting interarch and intraarch spaces simultaneously and causing occlusal plane discrepancy, this section will mainly discuss the mesio-distal component to simplify approaching the required space management prior to the restorative treatment. On loss of interproximal contact, due to loss or extensive cavitation of the adjacent tooth, mesial tipping, tilting, or drifting of posterior teeth will occur and the available space for the future restoration will be reduced. The severity of tooth movement is both time and patient dependent; however, correction of the resulting altered space should be prosthetically driven. While simple enameloplasty could be performed to regain the reduced space and create the desired distal contact of a future implant restoration replacing the missing tooth in minor cases, more advanced situations will require greater space correction (Figure 19.2 and 19.11). Ideally, a diagnostic set-up and diagnostic wax pattern should be made to evaluate the amount of space needed to create a restoration with favorable contours. Then, orthodontic uprighting is performed to correct the migration and create sufficient restorative mesio-distal space for the future restoration. If this space is not corrected orthodontically, the resulting future restoration will have poor anatomical contours and the distal contact with the mesially tilted tooth will act as a food trap, creating a triangular space that is extremely difficult to clean. Also, when a fixed partial denture is the treatment of choice to replace the missing tooth, orthodontic uprighting is beneficial in correcting the angulation of a tilted abutment tooth and reducing the amount of tooth preparation needed to create a passive path of insertion between both abutments for the future prosthesis. When compared to other restorative treatment modalities to correct tilted abutments, such as locked attachments or telescopic crowns, orthodontic uprighting is less invasive, therefore it should be considered as the first treatment choice (Becker et al., 1982; Revah et al., 1985; Simon, 1984).

(a)

(b)

(c)

(d)

(e)

(f)

Figure 19.7 A case of congenitally missing lower second premolars. (a, b) Pretreatment photographs and panoramic radiograph showing congenitally missing lower second premolars and retained primary second molars. (c, d) After extraction of primary second molars, temporary anchorage devices were placed distal to the first premolars to help with space closure through molar protraction. (e, f) Posttreatment photographs and panoramic radiograph after complete space closure.

Courtesy of Dr. Samah Alfuriji.

Pre-prosthodontic management of interarch spaces

A short clinical crown is an often encountered problem in combined restorative and orthodontic treatments. Treatment is usually dictated by the etiological factor. Since this chapter focuses on pre-prosthetic orthodontics, the discussion will be mainly on the management of localized worn-down anterior teeth and management of a short clinical crown for restorative purposes.

Management of localized worn-down anterior teeth

Localized worn-down anterior dentition is a situation that involves short anterior clinical crowns, with posterior teeth of normal height maintaining the vertical dimension of occlusion. The reason for significant anterior teeth wear is typically a parafunctional habit of anterior bruxism. The worn tooth continues to erupt with the surrounding bone and periodontal tissues (dentoalveolar extrusion) to maintain contact with the opposing dentition. This results in short clinical crowns of anterior teeth and a disproportionate marginal gingiva (Kokich, 2008; Turner and Missirlian, 1984; Figure 19.12). Options for restoring worn anterior dentition include orthodontic intrusion; surgical crown lengthening; enhancing the vertical dimension by restoring the occlusal surfaces of posterior teeth, thereby gaining more restorative space to restore anterior teeth; and lastly application of the Dahl concept (relative axial tooth movement that is observed when a localized appliance or localized restorations are placed in supraocclusion and the occlusion re-establishes full arch contacts over a period of time; Dahl et al., 1975).

Compared to surgical crown lengthening, orthodontic intrusion of worn anterior teeth is the preferred option because it is less invasive, and it aids in correction of the gingival margin. Moreover, it can provide adequate interocclusal space for final restorations, thereby eliminating the need for incisal reduction during teeth preparation. However, orthodontic intrusion is a lengthy treatment, requires patient compliance, and has a potential risk of apical root resorption. Therefore, intrusion movement requires low forces with close monitoring. In addition, the restorative dentist should carefully evaluate the future crown-to-root ratio of the teeth that are considered for intrusion (Bellamy et al., 2008; Table 19.2).

When considering orthodontic treatment to correct the dentoalveolar extrusion, careful examination of the gingival margin must be performed to exclude an altered passive eruption condition, which is defined as failure of the gingival margin to migrate cervically after tooth eruption (Goldman and Cohen, 1968: 302). Therefore, when the gingival margin is located coronal to the cemento-enamel

junction, surgical crown lengthening with or without bone reduction is necessary to achieve a correct gingival position before orthodontic treatment.

(a)

(b)

Figure 19.8 A case of congenitally missing upper lateral incisors and lower left second premolar. (a) Pretreatment photographs showing Class I malocclusion with Class II canines, anterior crossbite in upper left canine, retained lower left primary second molar, lower anterior crowding, and lower dental midline shifted to the right of the upper midline. The patient was treated with canine substitution of upper lateral incisors, with extraction of lower right second premolar and lower left primary second molar. (b) Posttreatment photographs showing Class I molar occlusion maintained and Class I canine relationship achieved, lower crowding and lower midline corrected, and upper canines reshaped to substitute for lateral incisors.

Courtesy of Dr. Fahad Aljamal.

In planning orthodontic intrusion, the amount of tooth intrusion needed is determined by the amount of teeth display at rest and when smiling. Also, the gingival margin level of adjacent teeth could be used as a reference during intrusion. For example, when intruding central and lateral incisors that are worn down and overerupted, the central incisor should be intruded until its gingival margin is at the same level as the gingival margin of the nonworn canine, while the gingival margin of the lateral incisor should be placed 0.5–1 mm coronally (Kokich and Spear, 2007). Orthodontic intrusion of the worn teeth will provide the restorative dentist with adequate incisal space to restore the proper clinical crown height without the need for incisal reduction.

Table 19.1 Canine and premolar modifications for canine substitution cases.

Aspect	Canine	Premolar
Height	Round off the cusp tip to a straighter incisal edge Build-up of mesial and distal corners by composite resin	Restore the cusp tip to the proper height by either direct or indirect restorations Modify the palatal cusp to avoid interferences
Width	Reduction of the convex mesial and distal sides to a straighter surface prior to space closure	Premolar width might need modification/ addition to match the contralateral canine
Thickness	Recontouring of the canine bulbous labial and palatal surfaces while maintaining the enamel integrity	
Rotation		Mesial rotation of the premolar to simulate the canine prominence by either distal offset of the rectangular stainless steel archwire or distal bracket positioning
Gingival height	Gingival harmony with adjacent and contralateral teeth can be achieved with orthodontic extrusion (bracket placement, wire bending) or periodontal surgery (additive/resective)	Gingival harmony with adjacent and contralateral teeth can be achieved with orthodontic intrusion (bracket placement, wire bending) or periodontal surgery (additive/ resective)
Torque	Reduction of the labial root torque and increasing the palatal root torque by third-	

Aspect	Canine	Premolar
	order wire bending, use of torquing auxiliary, or use of different bracket variation	
Color	External bleaching to match the dark canine with adjacent teeth	

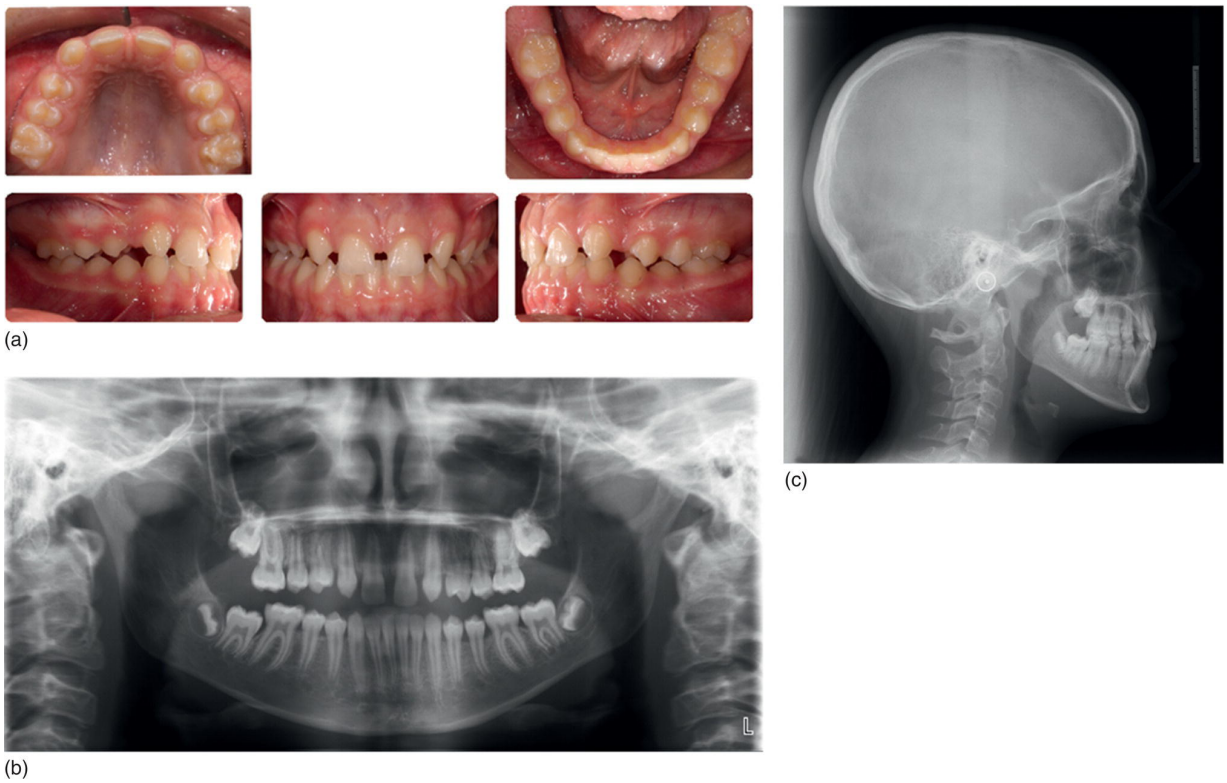


Figure 19.9 A case of congenitally missing upper lateral incisors. (a) Pretreatment photographs showing Class I malocclusion with Class II canines and moderate upper spacing. (b) Pretreatment panoramic radiograph. (c) Pretreatment lateral cephalometric radiograph showing orthognathic maxilla and mandible, and retroclined upper incisors. The case was treated with space opening and prosthetic replacement for the missing upper lateral incisors.

Courtesy of Dr. Samah Alfuriji.

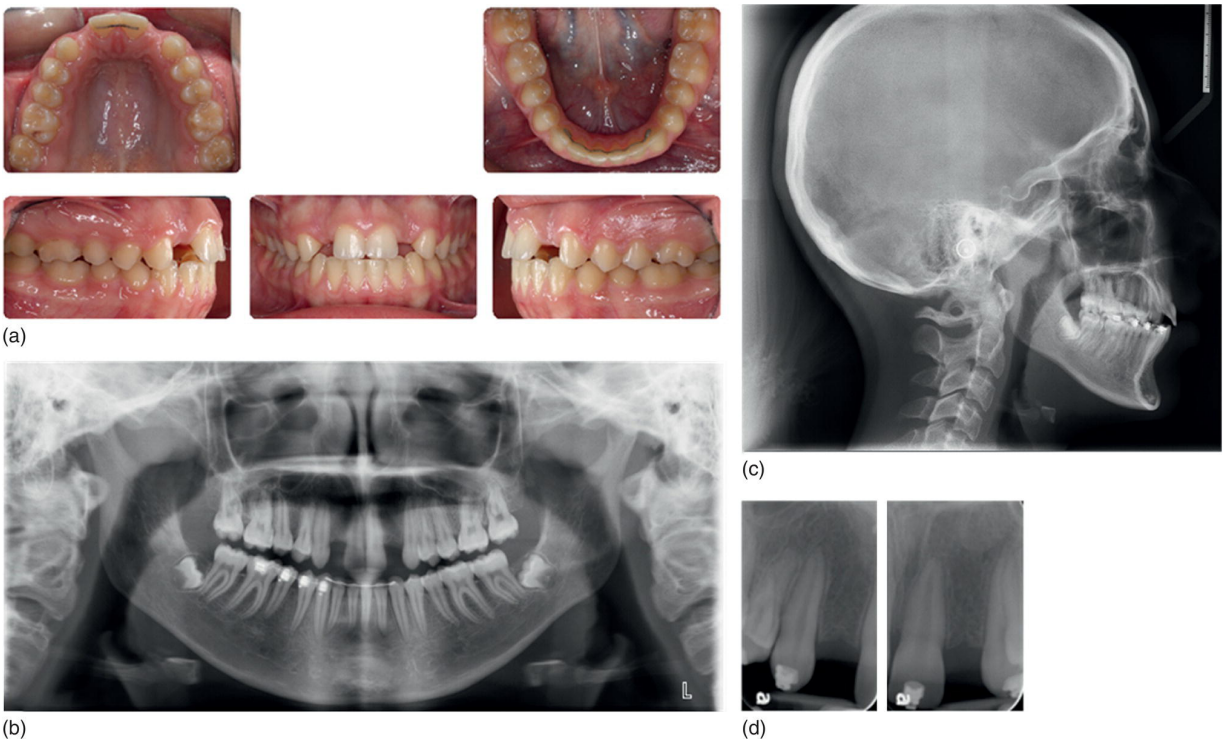


Figure 19.10 Posttreatment record of the patient in Figure 19.9. (a) Photographs after space opening for upper lateral incisor replacement with adequate coronal space created, Class I molar occlusion was maintained and Class I canine relationship was achieved. (b) Panoramic radiograph with adequate space created between central incisors and canines. (c) Lateral cephalometric radiograph with normal upper incisor inclination. (d) Periapical radiographs with adequate apical space created between central incisors and canines.

Courtesy of Dr. Samah Alfuriji.

Following orthodontic intrusion, the position of the teeth should be stabilized for at least six months to aid in reorganization of periodontal and gingival fibers into a more stable position, thus preventing re-extrusion of the teeth. After the retention period, teeth will receive final crowns, and an occlusal splint should be delivered for night-time wear, to stabilize the occlusion and to help protect the final restorations (Kokich and Spear, 2007).

Management of short dental crown due to lost tooth structure

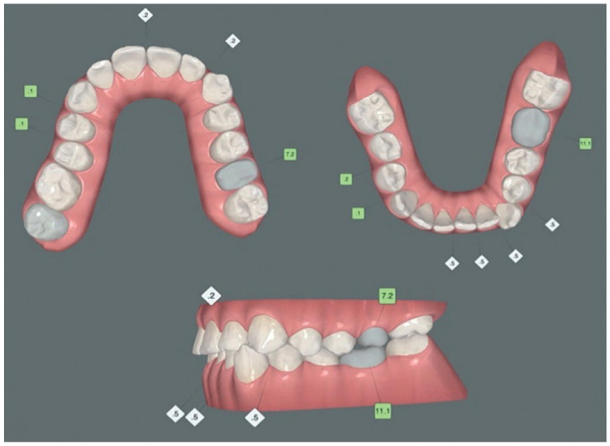
In prosthetic rehabilitation of severely damaged endodontically treated teeth, it is crucial to create a sufficient ferrule effect for favorable biomechanical behavior of the restored tooth. An adequate amount of sound supragingival tooth structure (1.5–2 mm) significantly increases the fracture resistance of endodontically treated teeth (Juloski et al., 2012). Furthermore, an adequate distance of at least 3 mm between the restorative margin and the alveolar crest must be ensured to preserve the supracrestal tissue attachment commonly known as biological width (Baba et al., 2014; Juloski et al., 2012). Additionally, generalized wear of the dentition with loss of vertical dimension will cause teeth to have short clinical crowns (less than 2 mm) that will not offer the necessary retention for the future restorations required to restore the vertical dimension (Figure 19.13). It has been recommended that a minimum of 3 mm and 4 mm of preparation height is a prerequisite for the success of anterior and posterior crowns, respectively (Goodacre et al., 2001). Therefore, when the clinical crown is short or severely compromised yet maintainable, exposure of sound tooth structure through crown lengthening procedures is indicated for better retention and resistant form and for maintenance of periodontal health. In such cases, the available treatment options are surgical crown lengthening and orthodontic extrusion (Table 19.3).

Surgical crown lengthening

The prevailing option for crown lengthening to restore teeth with inadequate clinical crown height has been osseous surgery that involves bone resection around the tooth. While this procedure is predictable in increasing the clinical crown height, it carries the risk of compromising the periodontal support of adjacent teeth. The bone is resected not only around the tooth to be restored, but from the adjacent teeth as well. Consequently, soft tissue recession, teeth sensitivity, uneven gingival margin, and poor esthetic of long crowns might compromise the final restorative results (Huang et al., 2021; Ingber, 1976). To avoid the undesirable consequences of surgical

crown lengthening, orthodontic extrusion should be considered, particularly in esthetic areas.

(a)



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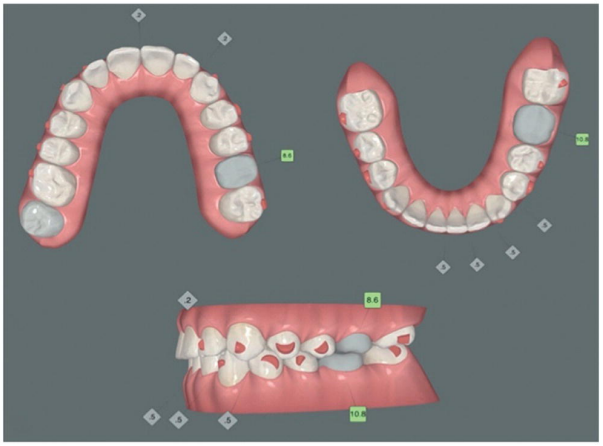


(c)

Figure 19.11 Patient with missing upper and lower first molars treated with clear aligners prior to prosthodontic treatment. (a) Pretreatment photographs showing Class I molar occlusion at the right side and Class I canine relationship bilaterally, with localized lower anterior crowding and anterior crossbite at tooth #33. (b) Pretreatment digital model (ClinCheck) showing 7.2 mm space available in the area of tooth #26, and 11.1 mm space available in the area of tooth #36. The case was collaboratively planned by the orthodontist and restorative dentist to open enough space for a small molar implant replacing tooth #26 and to correct the lower left canine crowding and crossbite with interproximal reduction and slight distalization of teeth #34 and #35 into the area of missing tooth #36. (c) Digital planning with ClinCheck software showing the predictive posttreatment model with maintained Class I molar and canine relationship, improved arch forms and coordination, correction of anterior crossbite and crowding in #33, increased space for replacing #26 by 1.4 mm (from 7.2 mm to 8.6 mm), and slight reduction in the space of missing #36 by 0.3 mm (from 11.1 mm to 10.8 mm).

Courtesy of Dr. Ruba Alkadhi.

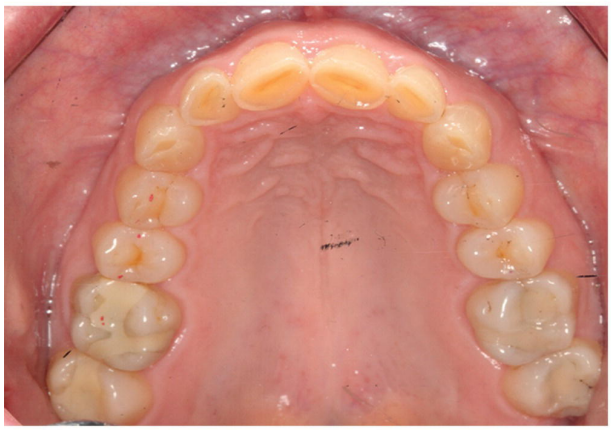
Orthodontic extrusion for crown-lengthening purposes

Orthodontic extrusion, also known as forced eruption, is defined as tooth movement by application of coronally directed traction forces (Bach et al., 2004). It was first described by Heithersay (1973) as a new method for management of teeth with subgingival transverse root fracture. A few years later, Ingber (1976) published an article proposing the use of forced eruption as a less invasive alternative to surgical crown lengthening for management of otherwise nonrestorable teeth.

When applying continuous extrusion force to the teeth, vertical coronal migration of bone and gingiva is an inevitable consequence. This is considered favorable if orthodontic extrusion is performed to correct infrabony defects or for implant site preparation. However, it is undesirable if orthodontic extrusion is carried out to expose subgingival tooth structure for restoration purposes. The extent of migration of tissues around the extruded tooth depends on how rapid the extrusion is and how much force is used.

Orthodontic extrusion can be performed with various orthodontic techniques: fixed appliances, removable appliances, and temporary anchorage devices. Even the use of attractive magnets for orthodontic extrusion has been proposed (Bondemark et al., 1997). Typically, the tooth is treated endodontically before extrusion begins to prevent pulpal irritation and necrosis, particularly with rapid extrusion. Also, occlusal reduction is required during the active extrusion to avoid interference with the opposing teeth, which could cause sensitivity or pulp exposure if a significant amount of extrusion is planned. Generally, the recommended extrusion rate is 1–2 mm per month. The extrusion force varies according to the type of extrusion that is desired. For slow extrusion the accepted forces are 15–30 cN, while for rapid extrusion the forces are 50–70 cN, depending on the type of tooth to be extruded (single- or multirooted teeth; Bondemark et al., 1997). Rapid extrusion with relatively high force (Table 19.4) could prevent the migration of attachment apparatus with the extruded tooth, because the rapid movement exceeds the tissue capacity for physiological adaptation (Alsahhaf and Att, 2016; Potashnick and Rosenberg, 1982; Figure 19.14).

(a)



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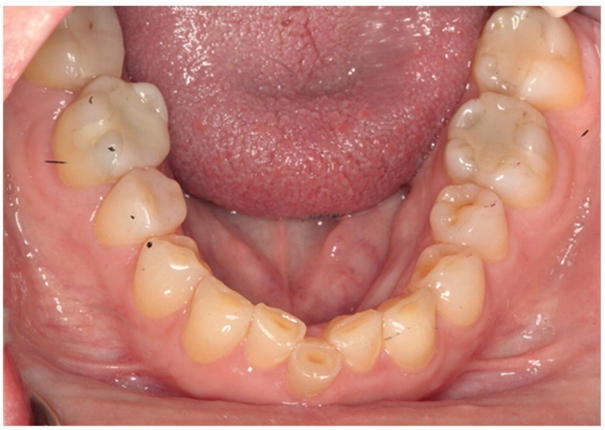

(c)

Figure 19.12 Localized anterior worn-down dentition due to protrusive bruxism habit. (a) Short anterior clinical crowns with posterior teeth of normal height maintaining the vertical dimension of occlusion. (b, c) Maxillary and mandibular occlusal views show moderate to severe tooth wear on anterior teeth.

Table 19.2 Main differences between surgical crown lengthening and orthodontic intrusion for localized worn-down anterior dentition.

Aspect	Surgical crown lengthening	Orthodontic intrusion
Incisal reduction	Required to create restorative space	Not required: restorative space is created through intruding the affected teeth
Crown : root ratio	Reduced periodontal support, therefore less	Crown : root ratio might be compromised by apical root resorption

Aspect	Surgical crown lengthening	Orthodontic intrusion
	favorable crown : root ratio.	
Invasiveness	Invasive treatment with more biological morbidity	Conservative treatment with no to minimal biological morbidity
Effect on adjacent teeth	Adjacent teeth are affected by the surgical procedure and sensitivity is expected from vital teeth exposed root surfaces	Adjacent teeth are not affected by orthodontic treatment
Esthetic consideration	Black triangles are expected between teeth, due to placement of preparation margins on the narrower root surface, which compromises the esthetic outcome	Esthetic outcome is not compromised as the preparation margins are kept on more coronal tooth surface
Treatment duration	One appointment procedure with healing period of 8–12 weeks	Extremely long treatment time
Retention	Retention and resistance forms are superior as the preparation height is improved through exposing more tooth structure	Retention and resistance forms are less favorable as the preparation height is not improved, especially for extremely short teeth

Figure 19.13 An example of generalized worn-down dentition with loss of vertical dimension. A combined treatment of orthodontic extrusion or surgical crown lengthening is required in such cases, to increase the height of short clinical crowns and provide adequate retention and resistance forms, along with full-mouth restorative rehabilitation.

Table 19.3 Main differences between surgical crown lengthening and orthodontic extrusion for structurally compromised teeth.

Aspect	Surgical crown lengthening	Orthodontic extrusion
Crown : root ratio	Reduced periodontal support therefore less favorable crown : root ratio	Maintained periodontal support therefore more favorable crown : root ratio
Interarch space	Interocclusal space not affected following treatment	Interocclusal space reduced following treatment
Effect on adjacent teeth	Adjacent teeth are affected by the surgical procedure, therefore more biological morbidity	Adjacent teeth are not affected by the orthodontic treatment, therefore less biological morbidity
Esthetic consideration	Gingival esthetics is compromised therefore it	Gingival esthetics is not affected therefore it is

Aspect	Surgical crown lengthening	Orthodontic extrusion
	must involve adjacent teeth in the esthetic zone	advantageous in the esthetic zone
Treatment duration	One appointment procedure	Multiple appointments needed over a period of 1–2 months
Retention	Healing period of 8–12 weeks is required	Retention period of 8 weeks–6 months

When the goal of orthodontic extrusion is to lengthen the clinical crown for restoration, fiberotomy is usually performed. The aim of fiberotomy is to sever the supracrestal gingival fibers to prevent coronal migration of the periodontal attachment apparatus. This could be explained by preventing the transmission of tensile forces generated by supracrestal fibers to the bone, thus eliminating bone formation coronal to the remaining fiber attachment (Pontoriero et al., 1987; Schwimer et al., 1990). However, some authors have reported that corrective periodontal surgery is still needed following orthodontic extrusion to correct the position of the marginal gingiva (Ingber, 1976). A randomized clinical trial reported that teeth that received weekly fiberotomy and root planing during the active extrusion needed significantly fewer corrective surgical procedures after orthodontic treatment compared to teeth that did not receive fiberotomy treatment (Carvalho et al., 2006).

Following orthodontic extrusion, an adequate period of retention to stabilize the root in its new position and to allow remodeling and adaptation of the periodontium is mandatory in all cases. A rigid stainless steel wire can be used for this purpose. The minimum recommended retention duration is eight weeks; however, longer stabilization times, up to six months, are recommended for implant site development, especially in the esthetic zone to maximize remodeling of the alveolar ridge (Carvalho et al., 2006; Ingber, 1976; Mantzikos and Shamus, 1998; Schwimer et al., 1990). After completion of the orthodontic extrusion, the restorative dentist is faced with the challenge of a reduced mesio-distal diameter of the root (especially in single-rooted teeth with conical roots), which results in larger interproximal gingival embrasures. In this situation,

the restorative dentist must balance between an overcontoured crown that might adversely affect gingival health and a tapered crown that will reveal unesthetic black triangles between teeth (Ingber, 1976).

Table 19.4 Main differences between slow and rapid orthodontic extrusion.

Aspect	Slow orthodontic extrusion	Rapid orthodontic extrusion
Force level	Light force (15–30 cN)	Relatively higher force (50–70 cN)
Bone and soft tissue level	Bone and soft tissue migration is expected	Bone and soft tissue migration is minimized
Adjunctive procedure	No adjunctive procedures performed during active extrusion	Fiberotomy usually performed as adjunctive procedure during active extrusion to minimize coronal migration of periodontal tissues
Corrective surgery	Corrective periodontal surgery might be needed after extrusion	Periodontal surgical procedures less likely to be needed following extrusion when fiberotomy performed
Treatment duration	Longer treatment duration; extrusion rate 1 mm per month	Shorter treatment duration; extrusion rate 1 mm per week
Retention	Longer retention period, especially in esthetic zones (up to 6 months' retention)	Shorter retention period (minimum of 8 weeks)

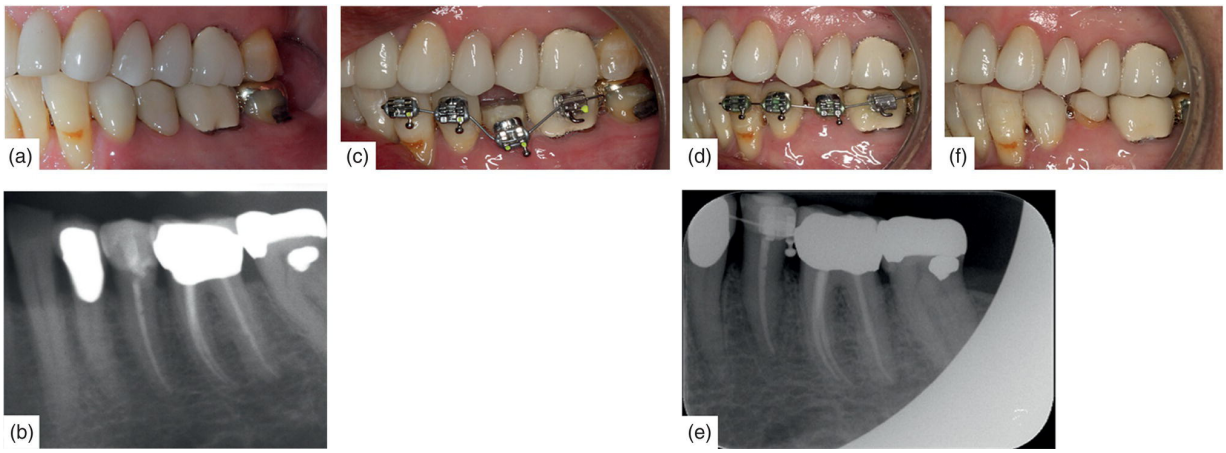

Figure 19.14 Short clinical crown of lower left second premolar (#35) referred by the restorative dentist to increase the crown length by rapid orthodontic extrusion. (a, b) Pretreatment photograph and radiograph – the periapical radiograph shows the short coronal tooth structure. (c) The restorative dentist did an occlusal reduction equal to the amount of extrusion needed (2 mm). A sectional edgewise appliance was used to extrude #35 using the adjacent teeth as an anchorage. (d) Two-month progress photograph. (e, f) Posttreatment photograph and radiograph (four months treatment time) after extrusion with increased crown length. Notice the difference in crown: root ratio.

Courtesy of Dr. Samah Alfuriji.

Orthodontic extrusion is a minimally invasive and predictable treatment. It has several advantages compared to surgical crown lengthening. With orthodontic extrusion, there is no risk of compromising bone support of adjacent teeth and there is a more favorable crown-to-root ratio (Bach et al., 2004). Also, performing surgical crown lengthening of a single tooth causes disharmony of the gingival counter of adjacent teeth, which could lead to unsatisfactory esthetic results. Conversely, orthodontic extrusion can enhance esthetics by maintaining harmonious gingival morphology. Last but not least, orthodontic extrusion can be performed with relatively simple tooth movement; it is the easiest among orthodontic movements because it stimulates physiological tooth eruption (Scholtes et al., 2018). The main disadvantage of orthodontic extrusion is the duration of treatment, with an average of 4–6 weeks of active extrusion and 8 weeks to 6 months of

retention potentially being required for some cases, depending on the treatment goal (Mantzikos and Shamus, 1998).

Correction of occlusal plane discrepancies

A careful assessment of occlusal planes, including the anterior–posterior occlusal plane (curve of Spee) and mediolateral occlusal plane (curve of Wilson), must be performed when treating cases comprehensively. Many patients with tooth loss or structurally compromised teeth will develop some form of occlusal plane discrepancies that would benefit from orthodontic treatment to eliminate occlusal interferences and simplify future restorative treatment (Wiens, 2015).

A commonly encountered clinical scenario is when the patient presents with supraeruption of an unopposed tooth. This could range from a minor supraeruption that would cause occlusal interference to a severe supraeruption that would obliterate the restorative space on the opposing arch. Determining the appropriate treatment modality to level the occlusal plane is usually dictated by the amount of the discrepancy (Wiens, 2015), and the available options are:

- Guided occlusal enameloplasty.
- Intentional endodontic treatment followed by indirect restoration at the desired occlusal plane.
- Orthodontic intrusion of the supraerupted teeth.
- Extraction of severely supraerupted teeth.

Another challenging clinical scenario to the restorative dentist is treating patients with deep anterior vertical overlap and excessive curve of Spee. If not corrected orthodontically, this situation will indirectly affect the anatomy of posterior restorations and in severe cases could cause occlusal trauma to the anterior and posterior dentition. Thus, including orthodontic treatment to correct the occlusal plane can be immensely beneficial when restoring anterior teeth in patients with deep anterior vertical overlap and excessive curve of Spee (Capp and Warren, 1991). In these cases, the available treatment options to level the excessive curve of Spee include:

- Increasing the vertical dimension utilizing direct or indirect restorations on the occlusal surfaces of posterior teeth, thus allowing enough space and less stress on the anterior teeth (Beddis et al., 2014; Ergun and Yucel, 2014; Torbjörner and Fransson, 2004).
- Orthodontically correcting the occlusal plane by intruding the anterior teeth, extruding the posterior teeth, or combining the two treatments based on the source of occlusal plane discrepancy (Kokich, 2008; Kokich and Spear, 2007).

While raising the vertical dimension using occlusal coverage restorations might be a faster-accomplished treatment, orthodontic treatment is more beneficial in conserving tooth structure and leveling anterior teeth gingival margins. Nevertheless, involving orthodontic treatment requires thorough occlusal assessment and excellent communication between the restorative dentist and the orthodontist to optimize the results.

Correction of ridge deformity though orthodontic tooth movement

It is known that alveolar bone is preserved as long as teeth are present. When teeth are lost, bone resorption both horizontally and vertically follows and increases over time. Adequate buccolingual bone width and vertical height are required for proper implant placement and for an ideal esthetic result. A deficient bony ridge necessitates deeper implant placement and results in unesthetic dark appearance of the implant through the gingival tissue (Sharma and Sharma, 2015). Restoration of the alveolar ridge height and width can be achieved through tooth movement to develop the site. Horizontal bone development can be achieved through guided tooth eruption followed by tooth movement, as explained earlier in cases of missing lateral incisors (Figures 19.9, 19.15, and 19.16). For vertical bone development, significant bone gain has been reported with orthodontic extrusion of hopeless teeth (Korayem et al., 2008). This could be a valuable alternative to traditional surgical bone augmentation.

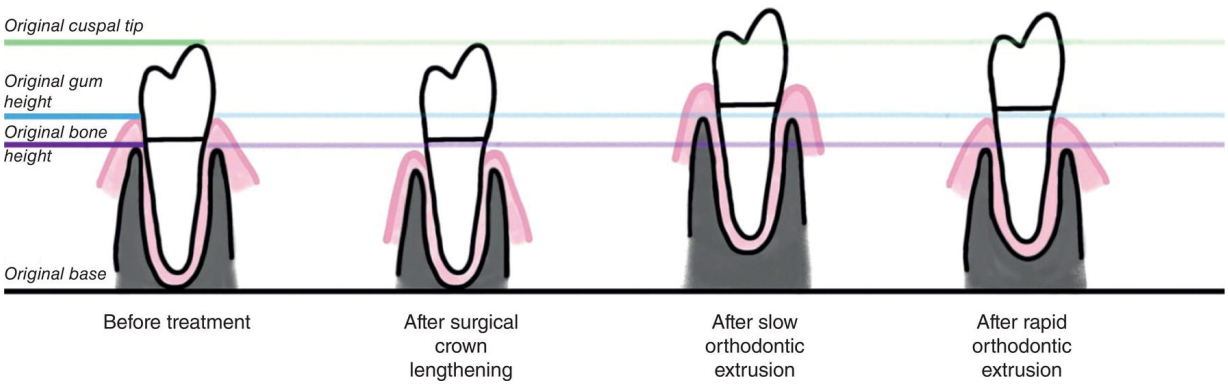

Figure 19.15 Gingival height and bone level following surgical crown lengthening and slow and rapid orthodontic extrusion.

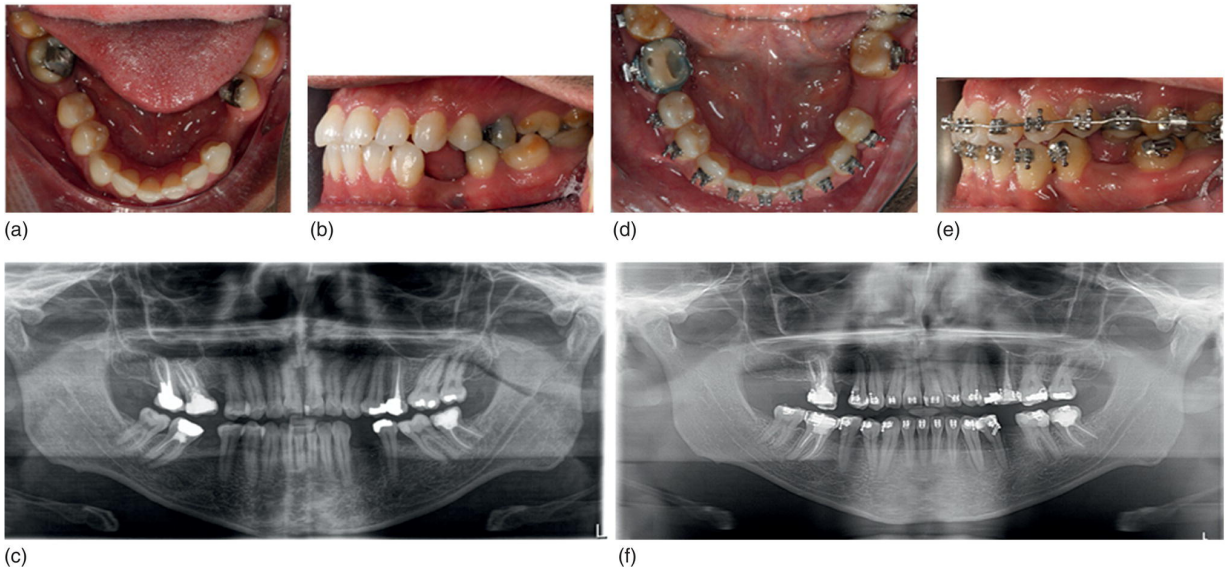

Figure 19.16 Patient with extracted lower left first premolar (#34) and right first molar (#46). (a) Pretreatment occlusal photograph showing the thin bony ridge at the area of #34, and mesially tilted #47. (b) Pretreatment left lateral photograph showing the vertical bone loss at the area of #34. (c) Pretreatment panoramic radiograph with mesially tilted #36 and 47. (d, e) Progress occlusal and left lateral photographs with the treatment planned to move #35 to the area of #34 to improve the bony ridge both horizontally and vertically. (f) Progress panoramic radiograph with space opened between #35 and #36 with increased vertical bone height and uprighted #36. The space of #46 was closed by protraction and uprighting of #47.

Courtesy of Dr. Samah Alfuriji.

Restorative treatment before orthodontics (means for tooth movement)

Pre-prosthetic orthodontic treatment aims to facilitate restoration of teeth by repositioning them into a more favorable position mesio-distally, bucco-lingually, and occluso-apically. Orthodontic treatment for structurally compromised teeth could be challenging, as they lack the structural integrity to be repositioned through fixed or removable orthodontic appliances. Therefore, temporary or definitive restorative treatment often is required prior to orthodontic treatment to replace the missing tooth structure and provide the orthodontist with the means for orthodontic tooth movement. Moreover, the bond between the orthodontic bracket and the tooth or the restorative material is essential for effective orthodontic tooth movement. It has been reported that the required shear bond strength of orthodontic brackets to withstand orthodontic force ranges from 5 to 10 MPa (Elekdag-Turk et al., 2007; Lopez, 1980).

For teeth with substantial loss of coronal tooth structure, a definitely cemented post and core are usually needed to facilitate orthodontic extrusion (Figure 19.17). Additionally, structurally compromised teeth, previously prepared teeth, and teeth undergoing restorative treatment will require coronal coverage with provisional crowns prior to orthodontic treatment. The provisional crown provides protection to the remaining tooth structure, occlusal stability, esthetics, and function. Also, it will serve as a means for tooth movement, as the orthodontic bracket will be bonded to the provisional crown material. Therefore, provisional crowns should have sufficient strength and durability to last through the duration of the orthodontic treatment.

Figure 19.17 A custom cast post and core fabricated with buccal and lingual extensions to facilitate orthodontic extrusion.

Several methods have been suggested to enhance the bond strength of orthodontic brackets, including mechanical, chemical, and laser surface treatment. Mechanical preparations aim to roughen the surface by sandblasting or grinding with carbide or diamond burs. Chemical methods include micro-etching with 9.6% hydrofluoric acid for 15 seconds followed by saline primer application (Hori et al., 2008; Maryanchik et al., 2010). This method significantly increases the bond strength of brackets to glass ceramics (Juntavee et al., 2020). However, 10-MDP (10-methacryloyloxydecyl dihydrogen phosphate) containing zirconia primer is more effective with polycrystalline ceramics (Kwak et al., 2016). For provisional materials, it has been reported that bonding of orthodontic brackets to composite provisional materials is superior to that of acrylic provisional materials (Pinho et al., 2017). Furthermore, sandblasting was found to be the most effective method of surface treatment of composite provisional materials (Shahin et al., 2021).

Conclusion

Integrating orthodontic tooth movement in the treatment of comprehensive restorative cases can enhance both esthetic and functional outcomes. However, this requires excellent communication between the orthodontist, the restorative dentist, and other specialists involved to achieve optimal treatment results.

References

Alfallaj, H. (2020). Pre-prosthetic orthodontics. *Saudi Dental Journal* 32(1): 7–14.

Alsahhaf, A., and Att, W. (2016). Orthodontic extrusion for pre-implant site enhancement: Principles and clinical guidelines. *Journal of Prosthodontic Research* 60(3): 145–155.

Baba, N.Z., Goodacre, C.J., Jekki, R. et al. (2014). Gingival displacement for impression making in fixed prosthodontics: Contemporary principles, materials, and techniques. *Dental Clinics* 58(1): 45–68.

Bach, N., Baylard, J.-F., and Voyer, R. (2004). Orthodontic extrusion: Periodontal considerations and applications. *Journal of the Canadian Dental Association* 70(11): 775–780.

Becker, A., Zalkind, M., and Stern, N. (1982). The tilted posterior tooth. Part II: Biomechanical therapy. *Journal of Prosthetic Dentistry* 48(2): 149–155.

Beddis, H., Durey, K., Alhilou, A. et al. (2014). The restorative management of the deep overbite. *British Dental Journal* 217(9): 509–515.

Behr, M., Proff, P., Leitzmann, M. et al. (2011). Survey of congenitally missing teeth in orthodontic patients in Eastern Bavaria. *European Journal of Orthodontics* 33(1): 32–36.

Bellamy, L.J., Kokich, V.G., and Weissman, J.A. (2008). Using orthodontic intrusion of abraded incisors to facilitate restoration:

The technique's effects on alveolar bone level and root length. *Journal of the American Dental Association* 139(6): 725–733.

Biggerstaff, R.H. (1992). The orthodontic management of congenitally absent maxillary lateral incisors and second premolars: A case report. *American Journal of Orthodontics and Dentofacial Orthopedics* 102(6): 537–545.

Bjerklin, K., and Bennett, J. (2000). The long-term survival of lower second primary molars in subjects with agenesis of the premolars. *European Journal of Orthodontics* 22(3): 245–255.

Bolton, W.A. (1962). The clinical application of a tooth-size analysis. *American Journal of Orthodontics* 48(7): 504–529.

Bondemark, L., Kurol, J., Hallonsten, A.-L. et al. (1997). Attractive magnets for orthodontic extrusion of crown-root fractured teeth. *American Journal of Orthodontics and Dentofacial Orthopedics* 112(2): 187–193.

Capp, N.J., and Warren, K. (1991). Restorative treatment for patients with excessive vertical overlap. *International Journal of Prosthodontics* 4(4): 353–360.

Carvalho, C.V., Bauer, F.P.F., Romito, G.A. et al. (2006). Orthodontic extrusion with or without circumferential supracrestal fiberotomy and root planing. *International Journal of Periodontics & Restorative Dentistry* 26(1): 87–93.

Cho, S.-H., Schaefer, O., Thompson, G.A. et al. (2015). Comparison of accuracy and reproducibility of casts made by digital and conventional methods. *Journal of Prosthetic Dentistry* 113(4): 310–315.

Dahl, B.L., Krogstad, O., and Karlsen, K. (1975). An alternative treatment in cases with advanced localized attrition. *Journal of Oral Rehabilitation* 2(3): 209–214.

Elekdag-Turk, S., Sarac, Y.S., Turk, T. et al. (2007). The effect of a light-emitting diode on shear bond strength of ceramic brackets

bonded to feldspathic porcelain with different curing times. *European Journal of Orthodontics* 29(3): 299–303.

Ergun, G., and Yucel, A.S. (2014). Full-mouth rehabilitation of a patient with severe deep bite: A clinical report. *Journal of Prosthodontics* 23(5): 406–411.

Fudalej, P., Kokich, V.G., and Leroux, B. (2007). Determining the cessation of vertical growth of the craniofacial structures to facilitate placement of single-tooth implants. *American Journal of Orthodontics and Dentofacial Orthopedics* 131(4): S59–S67.

Goldman, H., and Cohen, D. (1968). *Periodontal Therapy*, 4th ed. St. Louis, MO: Mosby.

Goodacre, C.J., Campagni, W.V., and Aquilino, S.A. (2001). Tooth preparations for complete crowns: An art form based on scientific principles. *Journal of Prosthetic Dentistry* 85(4): 363–376.

Heithersay, G.S. (1973). Combined endodontic-orthodontic treatment of transverse root fractures in the region of the alveolar crest. *Oral Surgery, Oral Medicine, and Oral Pathology* 36(3): 404–415. 10.1016/0030-4220(73)90220-x.

Hori, S., Minami, H., Minesaki, Y. et al. (2008). Effect of hydrofluoric acid etching on shear bond strength of an indirect resin composite to an adhesive cement. *Dental Materials Journal* 27(4): 515–522.

Huang, G., Yang, M., Qali, M. et al. (2021). Clinical considerations in orthodontically forced eruption for restorative purposes. *Journal of Clinical Medicine* 10(24): 5950.

Ingber, J.S. (1976). Forced eruption: Part II. A method of treating nonrestorable teeth—periodontal and restorative considerations. *Journal of Periodontology* 47(4): 203–216.

Johal, A., Huang, Y., and Toledano, S. (2022). Hypodontia and its impact on a young person's quality of life, esthetics, and self-esteem. *American Journal of Orthodontics and Dentofacial Orthopedics* 161(2): 220–227.

Juloski, J., Radovic, I., Goracci, C. et al. (2012). Ferrule effect: A literature review. *Journal of Endodontics* 38(1): 11–19.

Juntavee, P., Kumchai, H., Juntavee, N. et al. (2020). Effect of ceramic surface treatment and adhesive systems on bond strength of metallic brackets. *International Journal of Dentistry* 2020: 7286528.

Kokich, V. (2001). Managing orthodontic-restorative treatment for the adolescent patient. In: J.A. McNamara and W.L. Brudob (eds.), *Orthodontics and Dentofacial Orthopedics*. Ann Arbour, MI: Meedham Press, pp. 423–452.

Kokich, V., Jr. (2005). Early management of congenitally missing teeth. *Seminars in Orthodontics* 11(3): 146–151.

Kokich, V. (2008). Altering vertical dimension in the perio-restorative patient: The orthodontic possibilities. In M. Cohen (ed.), *Interdisciplinary Treatment Planning: Principles, Design, Implementation*. Chicago, IL: Quintessence, ch. 2.

Kokich, V.G., and Spear, F. (2007). Interdisciplinary management of anterior guidance: A case report. *Advanced Esthetics & Interdisciplinary Dentistry* 3(3): 2–6.

Kokich, V.G., and Spear, F.M. (1997). Guidelines for managing the orthodontic-restorative patient. *Seminars in Orthodontics* 3(1): 3–20.

Kokich, V.O., Jr. (2002). Congenitally missing teeth: Orthodontic management in the adolescent patient. *American Journal of Orthodontics and Dentofacial Orthopedics* 121(6): 594–595.

Kokich, V.O., Kinzer, G.A., and Janakievski, J. (2011). Congenitally missing maxillary lateral incisors: Restorative replacement. *American Journal of Orthodontics and Dentofacial Orthopedics* 139(4): 441.

Korayem, M., Flores-Mir, C., Nassar, U. et al. (2008). Implant site development by orthodontic extrusion: A systematic review. *Angle Orthodontist* 78(4): 752–760.

Kurol, J., and Thilander, B. (1984). Infraocclusion of primary molars with aplasia of the permanent successor: A longitudinal study. *Angle Orthodontist* 54(4): 283–294.

Kwak, J.-Y., Jung, H.-K., Choi, I.-K. et al. (2016). Orthodontic bracket bonding to glazed full-contour zirconia. *Restorative Dentistry & Endodontics* 41(2): 106–113.

Lopez, J.I. (1980). Retentive shear strengths of various bonding attachment bases. *American Journal of Orthodontics* 77(6): 669–678.

Mantzikos, T., and Shamus, I.I. (1998). Case report: Forced eruption and implant site development. *Angle Orthodontist* 68(2): 179–186.

Maryanchik, I., Brendlinger, E.J., Fallis, D.W. et al. (2010). Shear bond strength of orthodontic brackets bonded to various esthetic pontic materials. *American Journal of Orthodontics and Dentofacial Orthopedics* 137(5): 684–689.

Pinho, M., Manso, M., Martin, C. et al. (2017). Adhesion strength of orthodontic brackets to acrylic surfaces. A systematic review on in vitro studies. *Revista Portuguesa de Estomatologia, Medicina Dentária e Cirurgia Maxilofacial* 58(2): 65–70.

Polder, B.J., Van't Hof, M.A., Van der Linden, F.P. et al. (2004). A meta-analysis of the prevalence of dental agenesis of permanent teeth. *Community Dentistry and Oral Epidemiology* 32(3): 217–226.

Pontoriero, R., Celenza, F., Jr., Ricci, G. et al. (1987). Rapid extrusion with fiber resection: A combined orthodontic-periodontic treatment modality. *International Journal of Periodontics & Restorative Dentistry* 7(5): 30–43.

Potashnick, S., and Rosenberg, E. (1982). Forced eruption: Principles in periodontics and restorative dentistry. *Journal of Prosthetic Dentistry* 48(2): 141–148.

Rakhshan, V. (2015). Congenitally missing teeth (hypodontia): A review of the literature concerning the etiology, prevalence, risk factors, patterns and treatment. *Dental Research Journal* 12(1): 1–13.

Revah, A., Rehany, A., Zalkind, M. et al. (1985). The tilted posterior tooth. Part III: Abutment for a fixed partial denture. *Journal of Prosthetic Dentistry* 54(3): 325–330.

Rosa, M., and Zachrisson, B.U. (2001). Integrating esthetic dentistry and space closure in patients with missing maxillary lateral incisors. *Journal of Clinical Orthodontics* 35(4): 221–238.

Rosa, M., and Zachrisson, B.U. (2007). Integrating space closure and esthetic dentistry in patients with missing maxillary lateral incisors. *Journal of Clinical Orthodontics* 41(9): 563–573.

Sabri, R. (2004). Management of congenitally missing second premolars with orthodontics and single-tooth implants. *American Journal of Orthodontics and Dentofacial Orthopedics* 125(5): 634–642.

Scholtes, E., Suttorp, C.M., Loomans, B.A. et al. (2018). Combined orthodontic, surgical, and restorative approach to treat a complicated crown-root fracture in a maxillary central incisor. *American Journal of Orthodontics and Dentofacial Orthopedics* 154(4): 570–582.

Schwimer, C.W., Rosenberg, E.S., and Schwimer, D.H. (1990). Rapid extrusion with fiberotomy. *Journal of Esthetic and Restorative Dentistry* 2(3): 82–88.

Shahin, S.Y., Abu Showmi, T.H., Alzaghran, S.H. et al. (2021). Bond strength of orthodontic brackets to temporary crowns: In vitro effects of surface treatment. *International Journal of Dentistry* 2021: 9999933.

Sharma, P.K., and Sharma, P. (2015). Interdisciplinary management of congenitally absent maxillary lateral incisors: Orthodontic/prosthodontic perspectives. *Seminars in Orthodontics* 21: 27–37.

Simon, R.L. (1984). Rationale and practical technique for uprighting mesially inclined molars. *Journal of Prosthetic Dentistry* 52(2): 256–259.

Spear, F.M., Mathezus, D.M., and Kokich, V.G. (1997). Interdisciplinary management of single-tooth implants. *Seminars in Orthodontics* 3(1): 45–72.

Thilander, B., Ödman, J., Gröndahl, K. et al. (1992). Aspects on osseointegrated implants inserted in growing jaws. A biometric and radiographic study in the young pig. *European Journal of Orthodontics* 14(2): 99–109.

Torbjörner, A., and Fransson, B. (2004). Biomechanical aspects of prosthetic treatment of structurally compromised teeth. *International Journal of Prosthodontics* 17(2): 135–141.

Turner, K.A., and Missirlian, D.M. (1984). Restoration of the extremely worn dentition. *Journal of Prosthetic Dentistry* 52(4): 467–474.

Wesemann, C., Muallah, J., Mah, J. et al. (2017). Accuracy and efficiency of full-arch digitalization and 3D printing: A comparison between desktop model scanners, an intraoral scanner, a CBCT model scan, and stereolithographic 3D printing. *Quintessence International* 48(1): 41–50.

Wiens, J.P. (ed.) (2015). *Fundamentals of Occlusion*. Chicago, IL: American College of Prosthodontists.

Zachrisson, B.U., Rosa, M., and Toreskog, S. (2011). Congenitally missing maxillary lateral incisors: Canine substitution. *American Journal of Orthodontics and Dentofacial Orthopedics* 139(4): 440.

20
Integrated Management of the Orthognathic Patient

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Summary

This chapter gives an overview of our approach to the management of dentofacial deformities, which are commonly corrected through a combination of orthodontic treatment and orthognathic surgery. The importance of the multidisciplinary team in comprehensively assessing and diagnosing the patient is emphasized, including the role of the psychologist. Even though there have been no profound changes in orthognathic surgical techniques or in the fundamentals of orthodontics, there have been some significant developments in the process of soft tissue prediction and occlusal planning, as well as the treatment pathways. Three-dimensional digital planning is increasingly being adopted and we will describe our state-of-the-art process in detail, along with discussion of recent developments and future aspirations. The conventional, orthodontics-first approach to orthognathic treatment is typically long, with presurgical orthodontics often accentuating the patient's dentofacial deformity prior to surgical correction. The surgery-first approach has gained increasing attention in recent years, offering a potentially more time-efficient pathway, with immediate correction of the skeletal jaw discrepancy. We will give an account of both treatment pathways, including their benefits and limitations, and discuss their indications. Evidence will be cited, where possible, to support our views.

Multidisciplinary Team

The management of dentofacial deformities requires a multidisciplinary team (MDT). While the make-up of the team will vary from one center to another, it should ideally include a clinical psychologist, an orthodontist, an oral and maxillofacial surgeon, and a maxillofacial technologist. A clinic coordinator is also invaluable for direct liaison with patients and organization of the clinic logistics. The literature highlights the importance of the psychological aspects of patient care, with more than 50% of those referred having

experienced psychological distress as a result of their dentofacial deformity (Selvaraj et al., 2019). It has been suggested that careful patient selection, based on psychological evaluation, and ongoing support throughout the treatment journey are the cornerstones of successful orthognathic care.

In our clinic, patients are interviewed by the psychologist before their first appointment with the rest of the team. The main role of the psychologist, prior to any treatment commencing, is the early identification of potential problems that could affect patients' expectations or their ability to cope with treatment. The psychologist also has an integral role in providing advice and support to both patients and clinicians in the postoperative period, particularly for those patients who have the potential for deterioration in their psychological status while trying to cope with the morbidity and dentofacial changes resulting from surgery.

Based on initial psychological assessment, patients are categorized using a "flag" system: red, amber, and green. These flags are essential for the safe progression of patients onto the orthognathic pathway. Patients allocated a red flag are generally contraindicated for surgery and should not be operated on. Examples of red flag conditions include body dysmorphic disorder (BDD; Dons et al., 2022). Despite the low prevalence of BDD in the general population, the prevalence of BDD in patients seeking orthognathic surgery is much higher, ranging from 5.2% up to 13% (Dons et al., 2022). Evidence has shown that BDD patients are rarely satisfied with surgical outcomes (Phillips and Crerand 2016) and can show litigious or violent tendencies, of which clinicians must be aware. Patients with unrealistic expectations, or who are insistent on surgery for reasons that are very poorly defined, should therefore be very carefully assessed (Ayoub et al., 2013b).

Amber flags are usually raised on patients with vague chief complaints, but who give exaggerated descriptions of their appearance and are preoccupied with minor dentofacial defects. They may express dissatisfaction with previous treatment and possess narcissistic traits, demanding extensive unnecessary surgical intervention (Ayoub et al., 2013b). Patients with green flags are

usually allowed to proceed to our dentofacial clinic (DFC) for clinical assessment.

Orthodontists are often best placed to coordinate orthognathic clinics, because the patients are commonly referred to them for initial assessment by general dentists and they provide orthodontic treatment for them throughout their journey. For this reason, our DFC is held in the orthodontic department. The surgeon and the orthodontist must work closely together to agree and explain the treatment options to the patient and arrive at the final combined plan. We also consider the presence of the maxillofacial technologist to be essential in our clinics, both to participate in the planning discussions and to ensure that instructions regarding the required surgical jaw movements and planned occlusion are clearly and precisely communicated. This applies whether it is physical model surgery or virtual digital planning that is being carried out.

Systematic approach

Clinical assessment and diagnosis

General medical and dental history

Medical-surgical and dental histories must be obtained for every orthognathic patient prior to examination. While most patients will have been seen already at an orthodontic diagnostic clinic and a medical history recorded, the surgeon will wish to probe any reported issues in greater depth to reduce the risk of patients entering the treatment pathway for whom surgery may turn out to be complicated or even contraindicated when the time for arranging admission comes. A social history is also important, to try to ascertain accurate information about the levels of any smoking habits or alcohol consumption, which can affect fitness for surgery and subsequent recovery.

Patients should be attending their general dental practitioner regularly, but it is important to establish if they have been through periods of dental neglect or experienced significant problems with their teeth, including episodes of treatment or extractions. In some

cases, a patient's malocclusion, and the detrimental esthetics associated with it, may have discouraged them from looking after their teeth and detailed questioning may be needed to gain an accurate history.

Patient's concerns

It is important that a patient seeking treatment for a dentofacial deformity can express clearly defined concerns, and it is essential that these are fully explored early in the assessment process. Severe malocclusions will often be accompanied by functional difficulties, such as incising food in the case of an anterior open bite or reverse overjet. Esthetic concerns can be related to either the jaw discrepancy, the teeth, or a combination of both. Where dental appearance is the main concern, it may be that orthodontic alignment alone is all that is required for a satisfactory result, but where occlusal function and/or facial appearance are the major concerns, surgery is more likely to be required. The clinical psychologist plays a key role in identifying patients who have disproportionate concerns or, in more severe cases, BDD, which would contraindicate surgery.

Facial assessment

The first step in evaluating a patient's face is to gain a subjective impression of his or her dentofacial deformity. The eye of an experienced clinician can assess the region and extent of any key deficiencies or excesses, and observing patients as they walk into the room and then during conversation, with its accompanying facial animation, yields valuable information about how their facial esthetics may differ from the accepted norm. Viewing the face in all three planes of space is essential and the bird's-eye (from above) and worm's-eye (from below) views can be very informative, particularly where an asymmetry is present. We consider it essential that both the surgeon and the orthodontist examine the patient together, since both clinicians will naturally tend to focus on slightly different aspects of the dentofacial complex and discussing their combined observations will then allow the most accurate and complete picture to be assembled.

It is important to then look at specific aspects of the facial soft tissues in a more objective manner, and numerous soft tissue profile analyses are available, which include variables such as facial convexity, naso-labial angle, labio-mental angle, lip-chin-submental plane angle, submental plane-neck angle, Frankfort-mandibular planes angle (FMPA), upper lip length, lower lip length, and so on. It is important for the lips to be relaxed during the examination to avoid posturing, which can distort the profile and the vertical relationship of the lips to the teeth. Patients should be evaluated in an upright sitting position and encouraged to adopt a natural head position (NHP). This should ensure that the antero-posterior jaw relationship and profile are accurately assessed (Ayoub et al. 2013a; Figure 20.1). Where angles are being measured and compared to published norms, analysis of profile photographs and/or a lateral cephalogram may be more useful. However, we would emphasize that numerical values should be regarded only as supplementary information, which can serve to confirm clinical judgment in many cases, but should not be relied on to dictate treatment planning.

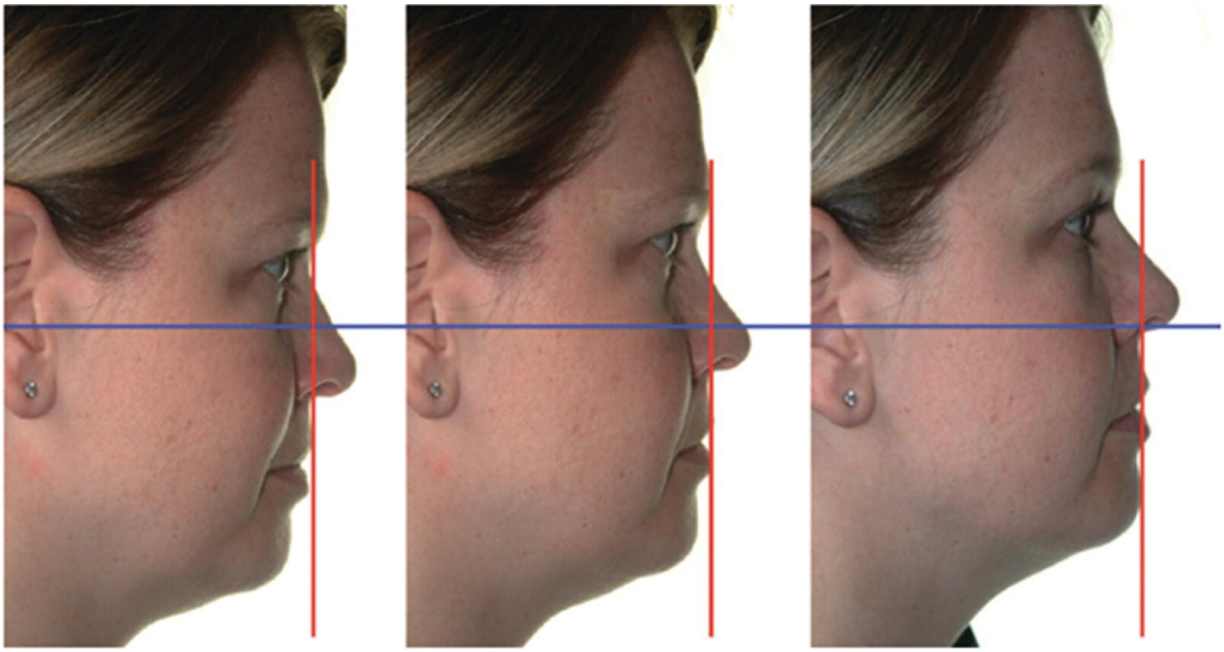


Figure 20.1 The impact of head position on the clinical impression of the antero-posterior jaw relationship. These three images illustrate the importance of the head position in avoiding a misleading impression.

Source: Ayoub et al. (2013a) / with permission of John Wiley and Sons.

In the average facial type, the clinically observed vertical dimension can be divided into two equal parts: the lower anterior face height (LAFH), measured from subnasale to soft tissue menton, and the upper anterior face height (UAFH), measured from glabella to subnasale. The ratio of the LAFH to the total anterior face height (TAFH) should therefore be 50%. For the evaluation of transverse proportions, the rule of fifths can be used as a practical guide, in which the face comprises five equal portions. This is particularly useful in assessing the width of the alar base (the middle fifth), which should ideally be equal to the intercanthal width (Naini and Gill, 2016). The balance between vertical and horizontal proportions should be maintained where possible to achieve facial harmony (Ayoub et al., 2013a). Asymmetry should be assessed in each step during the systematic approach of dentofacial examination for each component, including the level of the eyes and ears. Any cant of the occlusal plane should be carefully examined and documented. A practical method of assessing this is to lay a wooden spatula across the occlusal surfaces of the maxillary posterior teeth, which can be

compared to another horizontal reference plane (usually the interpupillary line). A detailed discussion of dentofacial assessment and clinical parameters is beyond the scope of this chapter, but further information is available in other texts, including our *Handbook of Orthognathic Treatment* (Ayoub et al., 2013a).

It is also important to consider the patient's overall physical build, including height and general body shape. A tall, thin patient is likely to suit dolichocephalic dentofacial features, while a short, stocky patient is more likely to fit well with brachycephalic features, and this can influence the surgical plan. For example, a short female patient who presents with an increased LAFH and moderate Class III discrepancy, due to mild maxillary deficiency and mild mandibular prognathism, will tend to derive a pleasing esthetic outcome from mandibular setback, rather than maxillary advancement. A key step in this scenario, therefore, is combining dentofacial assessment and body status information for the planning of optimal surgical goals.

Both soft and hard tissues of the dentofacial complex require systematic assessments to identify any dentofacial dysmorphology. A systematic approach to guide clinical evaluation should ensure accurate and complete information and avoid missing fundamental parameters that may be important in planning surgery for optimal facial esthetics (Figure 20.2). Clinicians should consider the philosophy of aiming to achieve balance, proportions, and harmony of the dentofacial components, based primarily on clinical assessment, rather than surgical correction based on numerical values derived from objective analysis.

Nose

The size and morphology of the nose can affect overall facial esthetics and therefore needs special consideration during the assessment and planning of orthognathic treatment. Dentofacial deformities are commonly associated with some nasal deformities. For example, maxillary deficiency is often coupled with a narrow alar base, drooping of the nasal tip, and a mild dorsal hump, which often improve as a result of Le Fort I advancement osteotomy (Seah et al., 2012). However, other nasal deformities may require a separate rhinoplasty, particularly where asymmetry and septal deviation are

involved. The nose may look bigger or smaller than its actual size based on the position of the maxilla (Posnick, 2022). For example, Le Fort I advancement with clockwise rotation in cases of maxillary deficiency associated with Class III jaw discrepancies will improve the nasal profile, midface prominence, and overall facial harmony.

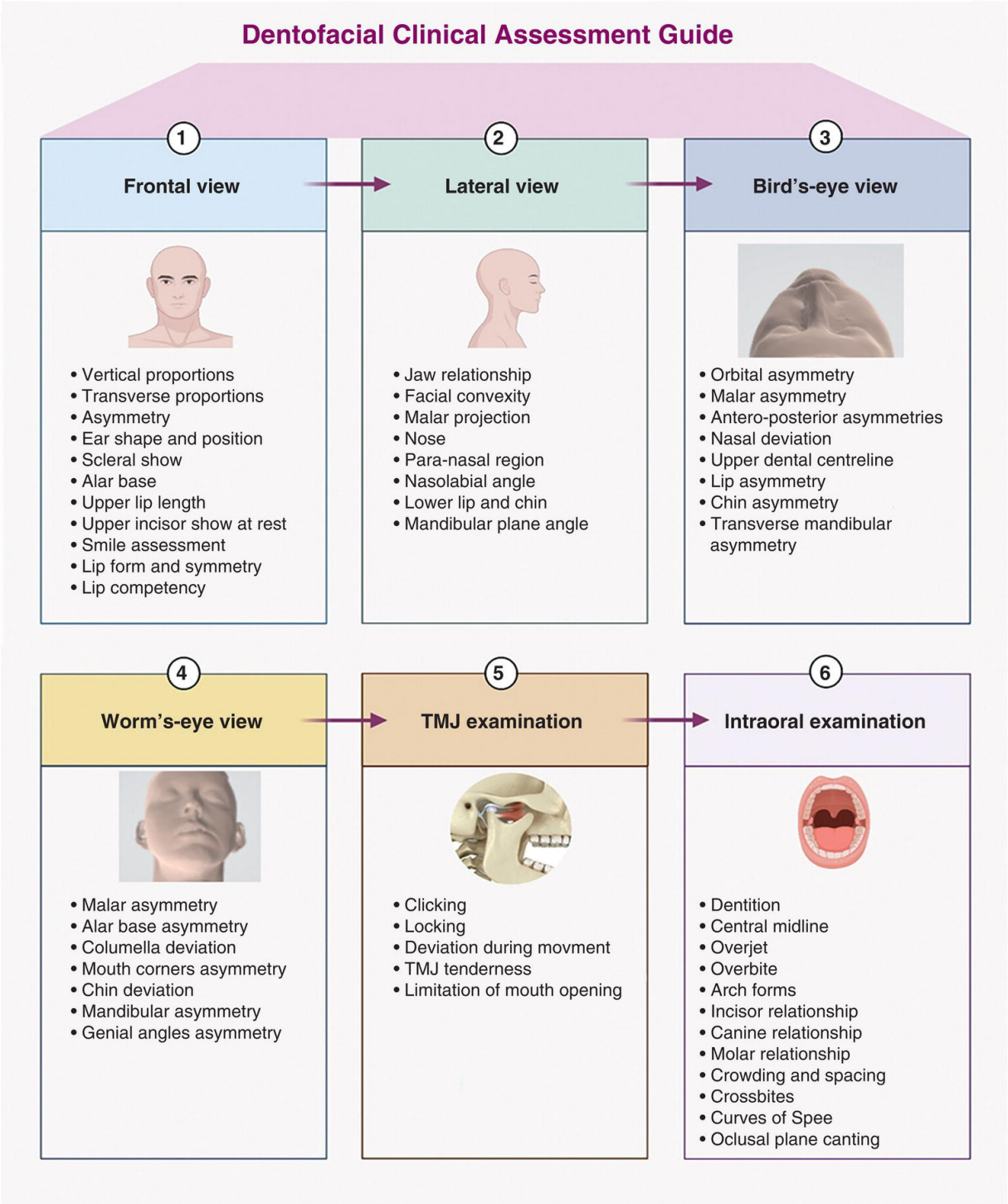


Figure 20.2 Dentofacial clinical assessment guide. Systematic clinical assessment using six steps: frontal view, lateral view, bird's-eye view, worm's-eye view, temporomandibular joint (TMJ), and intraoral examination. Analysis of key features for each step eases clinical diagnosis and decision making.

Where maxillary impaction is required to correct vertical maxillary excess, clinicians should be aware of the potential negative effects on nasal esthetics. In particular, flaring of the alar base can result, as well as asymmetry of the nostrils, nasal septum, and tip (Almukhtar et al., 2018; Ubaya et al., 2012; Ayoub et al., 2016). These abnormalities can usually be managed simultaneously with Le Fort I osteotomy through adequate trimming of the nasal septum and placement of a cinch suture to control the alar base width.

Temporomandibular joints

Details of any temporomandibular joint (TMJ) problems should be recorded, followed by a comprehensive examination, as part of orthognathic patient assessment. Abnormalities of the TMJs include symptoms such as pain, clicking, or grinding noises, in addition to a history of any previous therapy. Clinical signs of TMJ abnormalities in radiographic assessments include limitation of mouth opening or locking of the joints, while radiographs may suggest lysis of the condylar heads, which might warrant further investigation. Temporomandibular dysfunction (TMD) has a multifactorial etiology. Al-Moraissi et al. (2017) reported on a systematic review and meta-analysis of 29 studies on the effects of orthognathic surgery on TMD. They concluded that there were no identified preoperative symptoms of TMD, nor any specific skeletal deformity, which could have predicted the TMD outcome after orthognathic surgery. Several limitations were associated with this review, including different study designs and short follow-up, as well as lack of controls and considerable variability. There is therefore a need for more prospective randomized control trials using appropriate sex-matched and age-matched controls to identify more clearly the effects of orthognathic surgery, if any, on TMJs. Clinicians must inform TMD patients that orthognathic surgery could not be guaranteed to improve their condition and that there is also a chance that they could be negatively affected. Moreover, there is a possibility that new symptoms can develop after orthognathic surgery (Al-Moraissi et al., 2017; Dujoncquoy et al., 2010; Dolwick and Widmer, 2018).

Intraoral examination

For patients referred through the orthodontic clinic, dental and periodontal health will already have been assessed, but it is important to ensure that patients do not have uncontrolled dental or periodontal disease that could cause complications with the surgery or adjunctive orthodontic treatment (Musich, 2012). As a general rule, dental or periodontal disease should be treated and the patient made fully "dentally fit" before progressing further along the orthognathic pathway; oral hygiene should also be satisfactory. If good plaque control is not being maintained prior to any surgical or orthodontic intervention, it is less likely that the patient will cope with the cleaning regime required during the early postoperative period, when oral access is restricted and uncomfortable. In addition, any areas of gingival recession, whether secondary to disease or physiological bony dehiscence, should be noted and photographed, since both orthodontic tooth movement and surgery could result in one or more of these progressing.

For most patients, an orthodontic assessment will have been carried out on a previous clinic, but it is worth going through this again as part of the orthognathic assessment. Trimmed study models (or virtual models produced from intraoral scans) should be available for the MDT clinic, and this helps greatly with accurate assessment and documentation of the occlusal relationships. The overjet, overbite, and any crossbites, along with the arch forms and the presence of an accentuated curve of Spee, must be assessed. However, it is important to check that the study models are correctly trimmed or articulated, particularly if the patient tends to posture the mandible forward or off to one side. It is essential to make sure the patient's condyles are fully seated, so that the true extent of the antero-posterior occlusal discrepancy is known and recorded, prior to planning any treatment. In our experience, patients with retrognathic mandibles and backward growth rotations frequently have a habitual forward posture and can be difficult to induce into a retruded contact position. It is equally important in Class III cases with a reverse overjet and increased overbite to ascertain if the patient is able to contact their incisors edge to edge, before displacing them forward into a more comfortable occlusion. Failure to unmask these postural habits can result in surgical planning

starting from the erroneous position and adversely affect the outcome.

The upper incisal show at rest and on smiling, along with any gingival show, are essential baseline measurements since they must be considered in planning any vertical maxillary movement. The relation of the maxillary dental midline to the envisaged midline of the face, as well as to the mandibular dental midline, should be assessed. Where there is an asymmetry of the upper face it can be difficult to find a mid-facial line and clinical judgment is needed. The mandibular dental midline should also be assessed in relation to the midpoint of the chin, so that any mandibular asymmetry is accounted for.

The presence of a deep overbite or open bite requires measurement and documentation. The nature and extent of an open bite are important, and whether it is associated with an accentuated upper curve of Spee or level arches. The size and posture/function of the tongue need to be evaluated, particularly in cases of open bite, where it may be part of the etiology and could affect stability after surgical correction. Macroglossia and scalloping of the tongue's lateral sides are commonly associated with open bite or excessive bimaxillary dental proclination (Wolford and Cottrell, 1996).

The presence of unerupted and impacted teeth should be assessed, using radiographs where necessary. Unerupted third molars may require surgical removal in advance of orthognathic surgery, usually leaving at least nine months for healing, but this is down to surgical preference and some surgeons are content to remove 8s, where necessary, at the time of surgery (Verweij et al., 2016).

Diagnostic records

This section describes the various diagnostic records involved in the management of the orthognathic patient and their specific roles at the different stages of the care pathway. As with the rest of dentistry and medicine, there is an ongoing transition toward digital imaging that is profoundly altering the way in which orthognathic planning and treatment are carried out. These changes will be discussed along with their benefits and limitations.

Radiographic assessment

The patient's general dental practitioner will usually have taken whatever intraoral radiographs have been required to diagnose and then manage any dental or periodontal disease, but a dental panoramic tomograph (DPT), taken as part of the initial orthognathic assessment, will occasionally identify caries, bone loss, apical areas, or other pathology. In such cases, further investigation and management may be indicated before the patient can progress further along the pathway. Apart from acting as a hard tissue screen, the DPT provides information regarding the morphology of the mandible and its condyles, which can vary significantly with the vertical dimension of the face. More detailed tomography of the condyles may be indicated in cases where lysis is suspected with, for example, a progressive anterior open bite. Where mandibular asymmetry is present, a DPT can give some information about any difference in size and shape of the condyles and their necks, and this may be supplemented by radioisotope scanning in some cases if progressive asymmetrical growth is suspected. Asymmetries in the length and depth of the body of the mandible will also be apparent, although accurate positioning of the patient in the machine is essential to avoid distortion of the image, which can give a false perception of asymmetry.

The presence and position of unerupted and impacted teeth, including third molars, must be identified. The DPT is a useful image in this regard, but it provides very limited information in the transverse plane. This makes the orientation and relative positions of hard tissue structures difficult to determine. This is particularly true of the transverse position and course of the inferior dental canal, which is of relevance in the planning of the sagittal split osteotomy. The DPT also gives no information about the thickness of the mandibular cortical plates or cancellous space, which can influence the quality of the sagittal split procedure. An image that provides three-dimensional (3D) information is therefore of superior value, for both diagnosis and contemporary surgical planning.

The advent of cone-bean computed tomography (CBCT) has brought about a paradigm shift in the diagnosis and planning of orthognathic patients. Traditionally, lateral and postero-anterior cephalometric

radiographs have been used for routine radiographic assessment of dentofacial deformities, with numerous analyses available, aimed at quantifying the various aspects of the craniofacial dysmorphology using linear, angular, and proportional variables. Most of these analyses relate to the lateral cephalogram, which represents only the antero-posterior and vertical planes and is therefore a two-dimensional (2D) representation of a complex 3D object composed of multiple bilateral structures. While comparing mean values to published norms is informative, the information should be carefully interpreted and correlated to the clinical findings. In addition, facial asymmetry cannot be readily analyzed using lateral cephalometry due to its complexity. We are now of the opinion that it is the 3D morphology of the patient's face, as assessed subjectively by the clinicians, that should guide treatment planning, rather than numerical data. The 3D cephalometric analysis of CBCT images is a potentially valuable tool that could overcome some of the limitations of 2D cephalometry, but normative values have not yet been established and its validity and accuracy have yet to be confirmed. Further work is therefore required around landmark identification and standardization of measurements on CBCT images before this becomes a widely accepted method for the 3D quantification of dentofacial deformities (Weiss and Read-Fuller, 2019; Wang et al., 2020; Yitschaky et al. 2011).

In contemporary orthognathic clinics, CBCT may now be considered as the gold standard for assessment of hard tissues, including facial asymmetry, and 3D orthognathic planning (Weiss and Read-Fuller, 2019; Almutairi et al., 2018). In our clinic, it has now largely replaced conventional 2D cephalograms. The thresholding of the CBCT image can be adjusted to show both the craniofacial soft and hard tissues, which allows it to be used for both surgical planning as well as soft tissue prediction, with the aid of dedicated software, which is now widely available.

It is important to be mindful of the higher levels of radiation that CBCT exposes the patient to, and each clinician must be able to justify the radiographic views he or she requests on the grounds of their diagnostic yield.

Clinical photographs

Conventional 2D clinical photographs consist of a series of intraoral and extraoral images, which should be as standardized as possible. Extraoral photographs should include frontal views at rest and on smiling; right and left profiles; right and left three-quarter profiles; and bird's-eye and worm's-eye views. Together, these provide a comprehensive record of the patient's facial appearance and should be taken before any treatment starts and then at key stages throughout, to monitor progress and change. Intraoral photographs should consist of upper and lower occlusal views, front and lateral views of the teeth in occlusion, and overjet (or reverse overjet). It is our protocol to take postoperative photographs annually for five years for patients who continue to attend review appointments.

In our clinic, we also use stereophotogrammetry to record standardized 3D images of the face, which can be rotated and viewed from any angle. These give a true 3D representation of the face, and the presurgical capture is used in conjunction with the CBCT image for photo-realistic orthognathic planning. In addition, these images can be used to show topographical changes to the soft tissues produced by surgery, or due to growth, such as asymmetries, by superimposing sequential captures on stable regions of the face (Al-Rudainy et al., 2019).

Study models

Dental study models should be available at the first MDT clinic appointment. They allow detailed assessment of the patient's occlusion, as well as allowing the clinicians to try out different possible postoperative occlusions by freehand articulation. Having two sets of models is advisable so that one set can be used, if necessary, for provisional model surgery at the early planning stage, particularly if segmental surgery is being considered.

Where intraoral scanners are being used to produce digital models only, it may be more challenging and time consuming to manipulate the models into new trial occlusions because of the absence of haptic feedback (feel) from the occlusal surfaces of the teeth. One of the advantages of physical models at the initial planning stage is the ease with which the clinicians can assess how the teeth would fit together

in the proposed postoperative occlusion. Study models, whether physical or digital, should be acquired at the key stages of treatment, at least up to and including the removal of any orthodontic appliances following surgery.

Problem list

After the required information and records have been collected, it is helpful to set out a problem list. This should be agreed by both surgeon and orthodontist together, to ensure that all aspects are accounted for. A possible structure is shown in Box 20.1 along with common examples in italics.

The problem list is intended to concisely record the main features of relevance and provide the basis for discussion of the treatment options. The psychology report must be carefully considered in conjunction with the patient's concerns.

Treatment planning

First, the surgeon and orthodontist must discuss and agree what they consider the patient's treatment options to be. In some cases, the options can range from no intervention at all, or a simple orthodontics-only compromise, to complex combined treatment involving bimaxillary surgery, depending on the desired objectives. The objectives of each option should be carefully aimed at addressing the patient's concerns, to a greater or lesser extent, and they should be explained to the patient along with the risks and benefits of each. The patient should be provided with supporting information and given ample time to think over what he or she wishes to do. Seeing the patient again at a subsequent appointment, after a few weeks, is usually advisable. The process of diagnosis and management of dentofacial deformities are summarized in Figure 20.3.

Box 20.1 The structure of a problem list.

Patient's concerns	
Functional:	*Difficulty biting between front teeth*
Aesthetic	
Facial:	*Lower jaw "sticks out"*
	Chin off to right side
	Shows "too much gum" on smiling
Dental:	*Appearance of reverse bite*
	Crooked lower front teeth
Medical conditions	*Type 1 diabetes (well controlled)*
Local pathology	
Skeletal:	*Possible left condylar hyperplasia (nonprogressive)*
Soft tissue:	*Recurrent oral ulcers (mild)*
Dental:	*Secondary caries of tooth 36*
Antero-posterior discrepancies	
Skeletal:	*Severe Class III*
	Moderate mandibular prognathism
	Mild maxillary deficiency

Soft tissue:	
	Mild paranasal hollowing
Occlusal:	
	4 mm reverse overjet
	Retroclined and crowded lower incisors
Vertical discrepancies	
Skeletal:	
	Increased LAFH
	Mild vertical maxillary excess
Soft tissues:	
	Reduced upper incisor show at rest
	3 mm gingival show on smiling
	Short upper lip
Occlusal:	
	Mild anterior open bite (1 mm)
Transverse discrepancies	
Skeletal:	
	Chin point to right approx. (3 mm)
Occlusal:	
	Cant of maxillary occlusal plane down on left (2 mm)
	Right-sided buccal segment crossbite

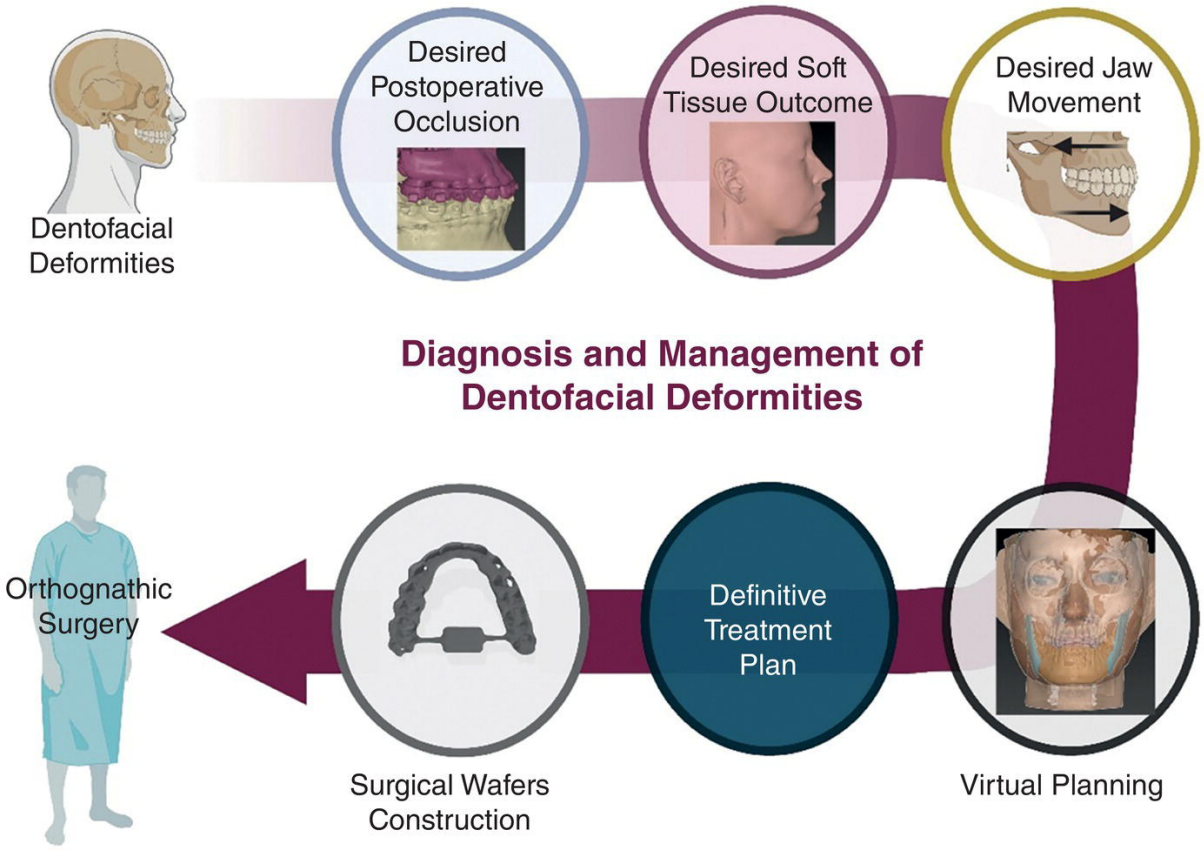


Figure 20.3 The "surgically led" treatment planning process.

Treatment planning process

The process of conventional orthognathic treatment planning can be approached in two fundamental ways. The first could be called "orthodontically led" planning, where the initial aim is to set the upper and lower incisors as near as possible to their cephalometric norms in relation to their respective skeletal bases. The overjet (or reverse overjet) produced by this presurgical decompensation then largely dictates the size of the surgical jaw movements and, in turn, the corresponding soft tissue changes. The potential problem with this approach, in our opinion, is that the orthodontic tooth movements achieved may not necessarily deliver the jaw movements required for optimal facial esthetics. In addition, complete decompensation, carried out with the aim of achieving ideal incisor inclinations, may create an excessive overjet or reverse overjet, requiring bimaxillary surgery, where partial decompensation would

have allowed single-jaw surgery and still produced satisfactory esthetics.

The second method could be called “soft tissue-guided” planning, in which the starting point is to decide the soft tissue changes that will deliver the desired esthetic result, and then plan the jaw movements to produce those changes. The orthodontic treatment is then planned to facilitate the jaw movements, and may involve partial, rather than complete, decompensation in some cases. It is this second method that the authors prefer, because orthognathic surgery will inevitably produce a change in facial appearance. Considering the soft tissues first should increase the likelihood that the treatment is targeted at addressing the patient’s concerns. However, the orthodontist must be careful to consider what orthodontic tooth movements are possible. If the magnitude of surgical jaw correction decided on requires tooth movements that cannot be achieved, a compromise will have to be agreed. Envisaging the soft tissue changes required for optimal esthetics relies on the experience of the clinicians and is subjective. Where there is disagreement among the team members regarding the desired goals, it is important to involve the patient as much as possible in the decision-making process, focusing carefully on the patient’s concerns and expectations.

For most patients, in addition to a functional deficit, the lack of soft tissue harmony is their main concern. Our orthognathic treatment planning process starts with identifying the required soft tissue changes, which guide the movements of the osteotomy segments and inform the orthodontic tooth movements. The need for clockwise or anti-clockwise rotation of the maxillo-mandibular complex should be considered, taking into consideration the need to adjust the chin. The position of the maxilla is planned to place the upper incisors in their ideal relationship to the upper lip, both at rest and on smiling, as well as correcting the upper dental midline. Careful consideration should be given to the effect of any proposed maxillary movements on the nose and lips, as well as any deficiencies of the zygomatic bones or infraorbital rims. Any repositioning of the mandible should also consider the throat length and possible effects on the airway. Carrying out soft tissue prediction planning can be helpful at this stage, to illustrate different options such as single-jaw versus

bimaxillary surgery, but the limitations of whichever software is used must be made clear to the patient.

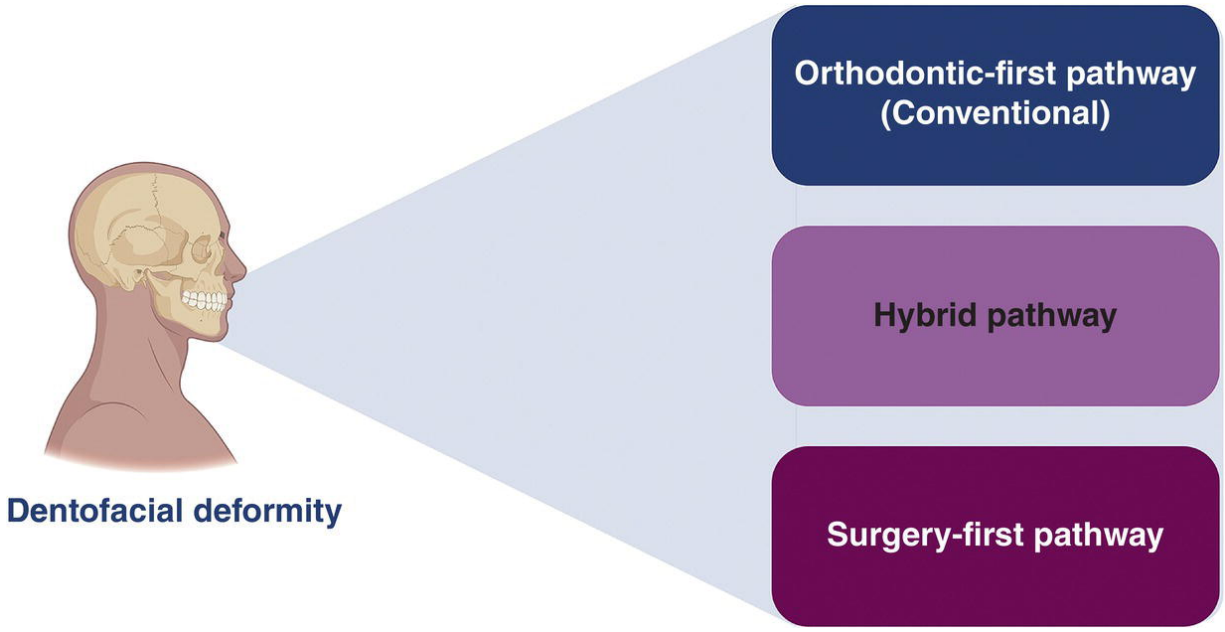


Figure 20.4 Three different approaches to orthognathic treatment.

Once there is agreement between the clinicians and the patient as to what the treatment objectives are, consideration can be given to the way in which the treatment is to be carried out.

Treatment pathways

Conventionally, orthognathic treatment involves an initial phase of presurgical orthodontics to partially, or completely, decompensate the incisors, followed by surgery to place the teeth in the planned occlusion and correct the skeletal jaw discrepancy. However, the concept of carrying out treatment on a surgery-first basis is gaining recognition, with some potential advantages reported in the literature in suitable cases. Some cases may not be entirely suited to either approach, but can benefit from a "hybrid" of both (Figure 20.4).

Orthodontics-first approach

In the conventional or "orthodontics-first" approach (OFA), a provisional surgical plan is made prior to the start of presurgical

orthodontics, with is then aimed at positioning the teeth to allow the desired surgical jaw movements and produce the best possible arch coordination. Final surgical planning is not carried out until up-to-date records have been taken with the teeth in their final decompensated positions. The positions of the teeth will then dictate the magnitude of the antero-posterior skeletal jaw correction, which should be guided by the required soft tissue changes. This can be predetermined to some extent by agreeing a "target (reverse) overjet" that the orthodontist aims to achieve. Final surgical planning is then carried out to confirm the individual jaw movements, whether single-jaw or bimaxillary, along with the vertical dimension and any necessary chin adjustment. Following surgery, postoperative orthodontics continues, with the aims of achieving optimal arch coordination and interdigitation. Despite the widespread use of the conventional pathway, it has been shown to have a long duration, with presurgical orthodontics taking between 15 and 24 months, and 36 months for the total treatment on average (Behrman and Behrman, 1988). In addition, presurgical dental decompensation tends to exaggerate the patient's malocclusion, particularly in Class III cases, and this has been shown to have adverse psychological effects (Liao and Lo, 2018). (See Cases 20.1–20.4.)

Surgery-first approach

The surgery-first approach (SFA) has been widely reported in the literature over the past decade or so (Nagasaka et al., 2009; Sugawara et al., 2010; Villegas et al., 2010; Hernández-Alfaro et al., 2011a; Anwar et al., 2022). Because the surgery is carried out at the start of the treatment journey, the orthodontic treatment is carried out in a single continuous phase afterwards. For the patients, this means that the correction of what is usually their main problem, the jaw discrepancy, happens right at the start, and they do not have to suffer the adverse functional and esthetic effects of presurgical orthodontic decompensation.. In addition, the treatment duration is greatly reduced, partly due to the uninterrupted nature of the pathway, but also because the soft tissue environment of the teeth has been normalized, which would be expected to aid dental decompensation rather than resist it (Behrman and Behrman, 1988). In addition, there is some evidence that the rate of tooth movement

is increased through the “regional acceleratory phenomenon” due to surgical trauma in the early postoperative period (Peiro-Guijarro et al., 2016; Baek et al., 2010; Hernández-Alfaro et al., 2014). Another contributory factor to the rapid treatment progress is the reduced appointment intervals that the SFA requires, because of the need to closely monitor patients in the postoperative healing phase. Their orthodontic mechanics also demand intensive supervision to ensure that the teeth are moving in the desired way to correct the secondary malocclusion. Appliance adjustments therefore tend to be carried out much more frequently than for nonsurgical orthodontic patients, with appointments every few weeks (Barone et al., 2020). Such intensive supervision along with the reduced treatment duration would also be expected to reduce the risk of orthodontically induced iatrogenic damage.

Case 20.1

This 26-year-old female presented with severe skeletal Class III jaw and incisor relationships due to a combination of mandibular prognathism and maxillary deficiency. Her reverse overjet measured 4 mm, but her lower incisors were severely retroclined and crowded. Previous extractions have been carried out in the upper arch for relief of crowding (Figure 20.5). An orthodontics-first approach was employed with the aim of achieving full decompensation, but had the adverse effect of exaggerating the facial disharmony (Figure 20.5). Bimaxillary surgery was carried out involving Le Fort I maxillary advancement of 8 mm and bilateral sagittal split mandibular setback of 7 mm (Figure 20.5).

(a)

(b)

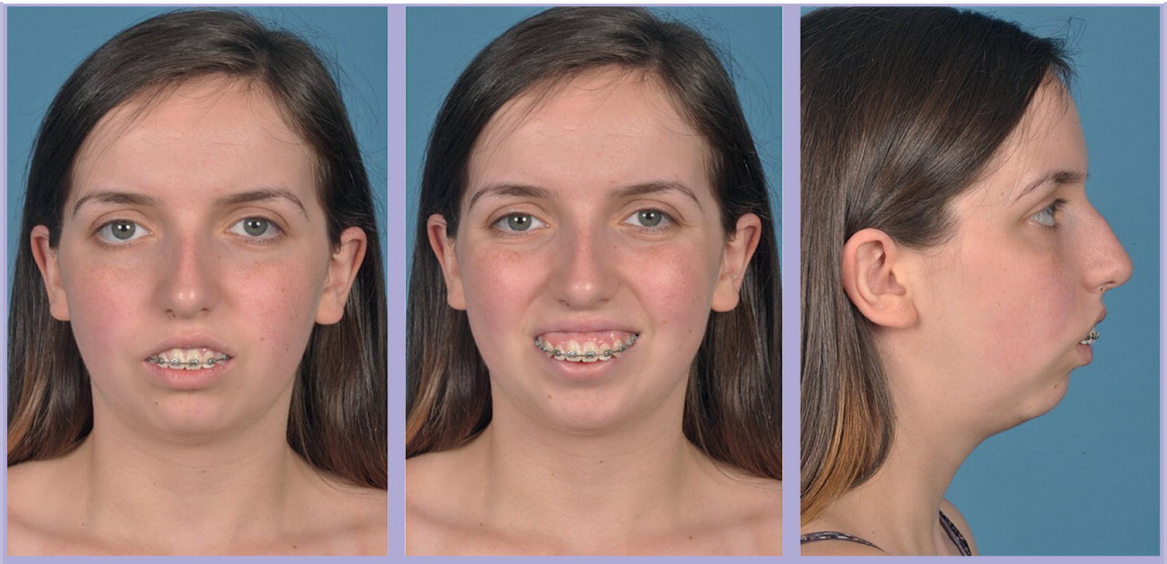
(c)

Figure 20.5 Pretreatment (top), immediate pre-surgery (middle), and end-of-treatment (bottom), facial and intraoral views.

Case 20.2

This 13-year-old female presented with a severe Class II skeletal pattern and a long facial type, accompanied by anterior open bite, an increased overjet of 11 mm, and severe upper and lower crowding (Figure 20.6a). Presurgical orthodontics was carried out, which involved extraction of teeth #34 and 44 to avoid proclination of the lower incisors and maximize the overjet prior to surgery (Figure 20.6b). Bimaxillary surgery was aimed at impacting the maxilla, both anteriorly and posteriorly, to reduce the vertical show of the upper incisors and allow autorotation of the mandible, which was also advanced by 10 mm. An advancement genioplasty of 6 mm was also carried out to balance the profile and further reduce the lower anterior face height (Figure 20.6c).

(a)



(b)

(c)

Figure 20.6 Pre-treatment (top), immediate pre-surgery (middle), and end-of-treatment (bottom), facial and intraoral views.

Case 20.3

This 27-year-old female was complaining of a deep and traumatic overbite. She presented with a severe Class II Division 2 incisor relationship with severely retroclined upper incisors and a deep and traumatic overbite. Her severe Class II skeletal jaw relationship was primarily due to mandibular deficiency and her vertical dimension was reduced. Previous orthodontic treatment had been carried out, involving extraction of upper premolars (Figure 20.7a). Presurgical orthodontics was carried out to procline the upper incisors and achieve the largest possible overjet (Figure 20.7b). Surgery was carried out to advance the mandible by 10 mm using bilateral sagittal split osteotomy (Figure 20.7c).

(a)

(b)

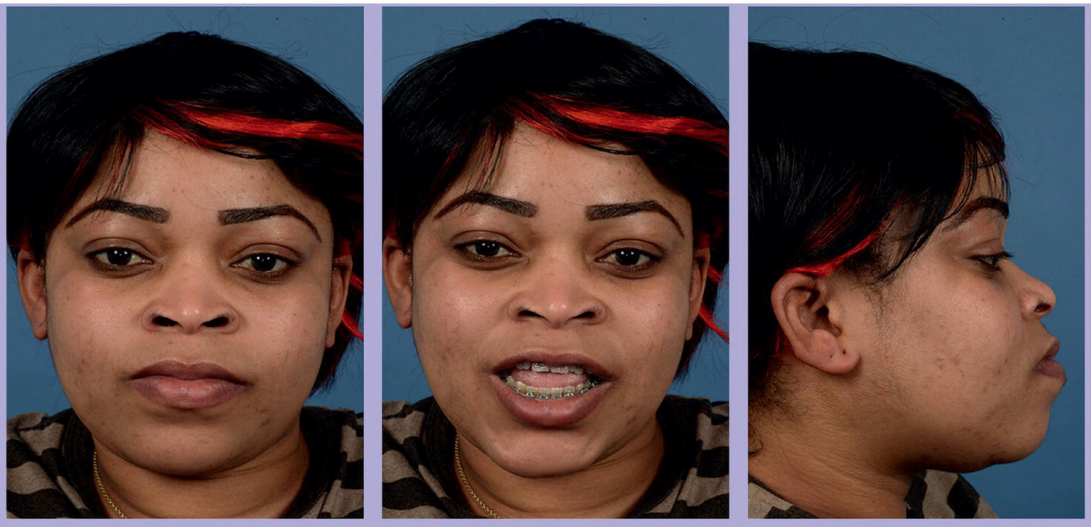
(c)

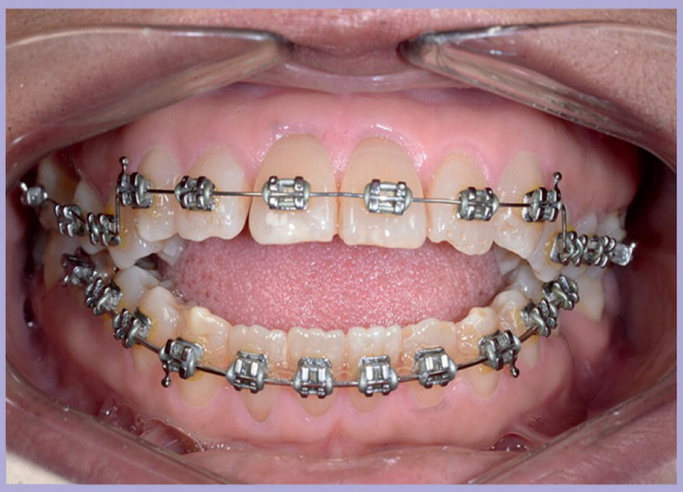
Figure 20.7 Pre-treatment (top), immediate pre-surgery (middle), and end-of-treatment (bottom), facial and intraoral views.

Case 20.4

This 32-year-old female had a history of digit sucking, but the shape and size of her anterior open bite were not consistent with the features of a habit alone. She was diagnosed with skeletal Class III, anterior bimaxillary protrusion, and an anterior open bite of 10 mm (Figure 20.8a). Her tongue tended to habitually posture between her upper and lower incisors, which may have been the primary etiological factor (Figure 20.8b). Presurgical orthodontics was aimed at creating a vertical step in the maxillary occlusal plane, while avoiding extrusion of the upper incisors. Care was taken to ensure that adequate separation of the roots of the upper canines and first premolars was achieved in preparation for a two-part segmental Le Fort I osteotomy (Figure 20.8c). Surgery involved a combination of downgrafting of the anterior segment and impaction of the posterior segment. This, in conjunction with a degree of mandibular autorotation, enabled closure of the open bite.

(a)





(b)

(c)

Figure 20.8 Pre-treatment (top), immediate pre-surgery (middle), and end-of-treatment (bottom), facial and intraoral views.

The SFA is distinct from the OFA in that the jaw movements are not guided to the same extent by the occlusion. Instead, the surgery must be planned to correct the skeletal discrepancy and achieve optimal facial esthetics, as judged by the clinicians. This produces a "secondary malocclusion" that will vary in its severity, depending on how well aligned and coordinated the dental arches are. It is primarily the role of the orthodontist to judge whether the secondary malocclusion will be amenable to orthodontic correction, and not all cases are suitable for this approach. The most favorable cases are those with good arch coordination and minimal dental compensations and irregularities, such that only small, predictable tooth movements will be required to achieve an ideal outcome (Choi et al., 2019). However, many cases have vertical and transverse interarch discrepancies that result in less favorable occlusions, and the orthodontist must judge whether they think the SFA will be successful. For example, in cases where an accentuated curve of Spee exists in the upper arch, posterior open bites may be present immediately postoperatively, but these should readily close as orthodontics progresses (Huang et al., 2015).

It is important for the orthodontist to recognize when correcting the postoperative malocclusion would be unpredictable, or where it is difficult to envisage the tooth movements needed to achieve a satisfactory occlusal result. In such cases, the OFA will continue to be the approach of choice. The type of surgery may also dictate that presurgical orthodontics is required, such as segmental osteotomies where root separation is needed. However, in more borderline cases the decision can be challenging, and it is important for the MDT to carefully evaluate the risks and potential benefits of each approach on a case-by-case basis, involving the patient in the discussion as much as possible. In carrying out soft tissue prediction planning for SFA cases, there is the disadvantage that the incisors are still in their compensated positions, which in some cases may affect the predicted lip posture. (See Cases 20.5–20.8.)

Hybrid approach (early surgery)

In some cases a particular feature of the malocclusion is not ideal for the SFA, such as a slightly narrow upper intercanine width, and presurgical orthodontics is required in the upper arch only to

produce a more favorable postoperative occlusion. Other features, such as lower incisor decompensation, can be left until after surgery. Such a “hybrid” approach is intended to allow the patient to gain some of the key advantages of the SFA, while making the final surgical planning and postsurgical orthodontics more straightforward. Where surgically assisted palatal expansion (SARPE) is planned, this can be carried out separately in advance of the definitive surgery, which requires an additional general anesthetic, as would be the case with the OFA. Alternatively, it is possible for this to be carried out postoperatively using a bone-borne expander, which is placed at the time of surgery. Two paranasal fixation plates only are used, to allow the maxilla to widen posteriorly. (See Case 20.9.)

Intermaxillary anchorage

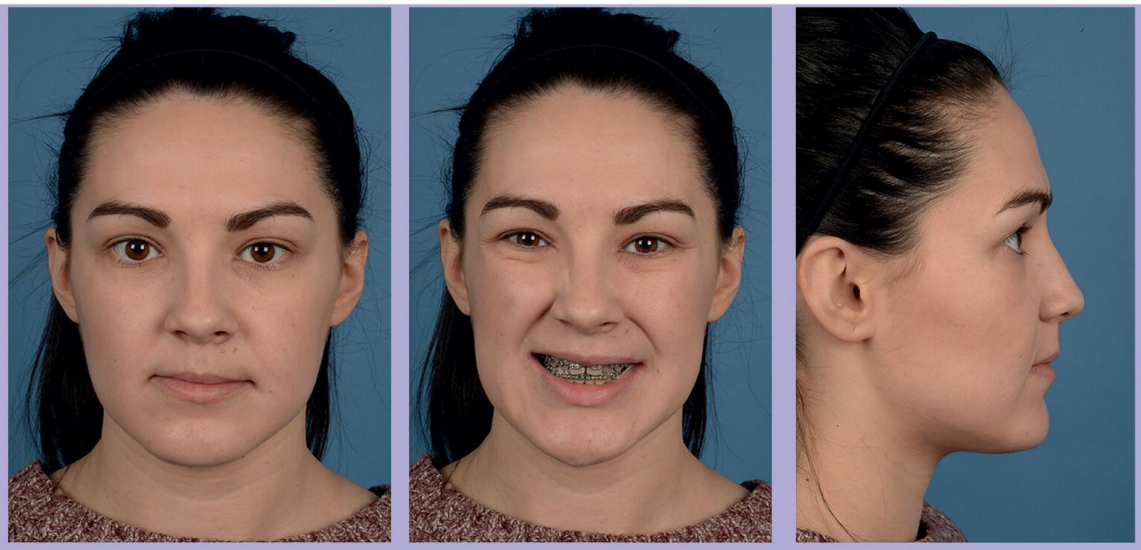
One of the advantages of fixed orthodontic appliances in orthognathic treatment is to enable the clinicians to apply intermaxillary elastics in the early postoperative period, to counteract muscle pull and ensure that the planned occlusion is being maintained. In the OFA this is accepted practice, because the archwires in place at the time of surgery are usually rectangular stainless steel, to which surgical hooks can be attached. They also help to distribute the elastic traction force among the roots of the teeth. In the SFA, the appliances, which are placed the day before surgery, have only light nickel–titanium aligning archwires in place, which cannot hold surgical hooks and provide little or no splinting effect. In most cases it is therefore more desirable to apply the forces directly to the bone, using either surgical intermaxillary fixation screws or orthodontic temporary anchorage devices (TADs; Nagasaka et al., 2009). In our clinic, the surgeon and orthodontist plan the sites for the bone screws prior to surgery and these are placed intraoperatively. Most commonly, we aim to place them mesial to the roots of the first molar and distal to the canine. This allows an antero-posterior force vector to counteract surgical relapse and avoids trauma to the gingival margins from the elastics. The formation of the screws will vary depending on the jaw movements and the direction of pull required. In anterior open bite cases, screws can also be placed between the upper and lower central incisors for

control of the vertical dimension. The screws usually remain *in situ* for at least six weeks, until initial healing is complete. Once the teeth have aligned and rectangular archwires are in place, elastics can be run between the fixed appliances for occlusal fine tuning, as they would in an OFA case. There is some evidence that the stability of SFA and OFA cases is similar, despite the different management of postoperative anchorage (Barone et al., 2020), and a study completed in our unit recently on Class III cases has found the occlusal outcomes for SFA patients to be comparable to those of OFA patients (Anwar et al., 2022).

Case 20.5

This 20-year-old female presented with a Class III jaw discrepancy, primarily due to maxillary deficiency. The show of her upper incisors at rest and on smiling was slightly reduced. Her reverse overjet measured 5 mm and her lower incisors were retroclined by way of compensation (Figure 20.9a). A surgery-first approach was adopted, involving maxillary advancement of 6 mm and mandibular setback of 4 mm (Figure 20.9b). The fixed appliances were placed shortly before surgery and the incisor alignment and decompensation were carried out entirely postoperatively. In this way, the exaggerated Class III profile associated with presurgical decompensation was avoided and the final result was achieved in a greatly reduced time of 10 months (Figure 20.9c).

(a)



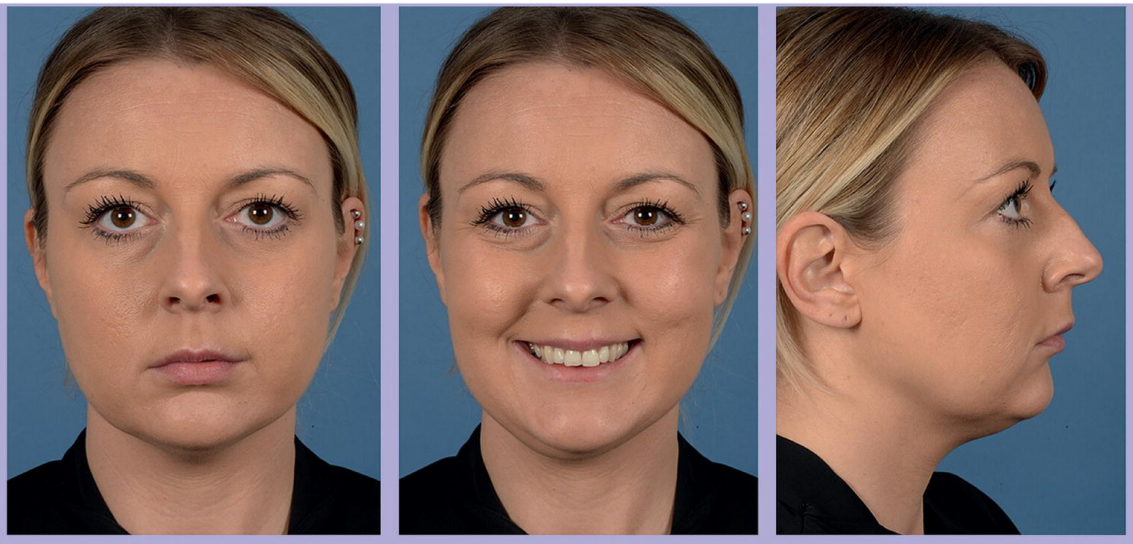
(b)

(c)

Figure 20.9 Pre-treatment (top), post-surgery (middle), and end-of-treatment (bottom), facial and intraoral views.

Case 20.6

This 20-year-old female presented with a severe Class II Division 1 incisor relationship on a Class II skeletal base, due to a retrognathic mandible. Her upper and lower incisors were of average inclination clinically, with only very mild crowding. Her overjet of 12 mm and her overbite were incomplete. There was some gingival recession associated with the upper incisors and canines, but oral hygiene and periodontal condition were satisfactory (Figure 20.10a). The surgery-first approach was adopted, with the fixed appliances placed the day before surgery. Mandibular advancement of 10 mm, using bilateral sagittal split osteotomy, was aimed at placing the incisors approximately edge to edge, to achieve a degree of overcorrection in anticipation of minor relapse. An advancement genioplasty was also carried out for optimal facial harmony (Figure 20.10b). The postoperative orthodontic treatment was completed in eight months (Figure 20.10c).



(a)

(b)

(c)

Figure 20.10 Pre-treatment (top), immediate pre-surgery (middle), and end-of-treatment (bottom), facial and intraoral views.

Case 20.7

This 35-year-old female presented with a severe Class II Division 2 incisor relationship and severe mandibular retrusion. She had mildly crowded and severely retroclined upper incisors, and her lower incisors were also retroclined, but well aligned. She showed a degree of facial asymmetry, with a reduced vertical dimension on the right side and a cant of the maxillary occlusal plane. Tooth # 23 (upper left canine) was diminutive, but nevertheless a permanent tooth (Figure 20.11a). The patient was treated using the surgery-first approach, with her fixed appliances placed the day before surgery. The mandibular position was corrected using bilateral sagittal split osteotomy and advancement genioplasty, following interactive three-dimensional planning and careful consideration of the postoperative occlusion (Figure 20.11b). Postoperative orthodontic treatment was then aimed at correcting the anterior crossbite, which was associated with the secondary malocclusion (Figure 20.11c). Torque adjustments in upper rectangular archwires and intermaxillary elastics were required to achieve sufficient proclination of the upper incisors (Figure 20.11d). The total treatment duration was about 12 months.

(a)

(b)

(c)

(d)

Figure 20.11 Pre-treatment (top), immediate post-surgery (second from top), intraoral views showing progress of post-operative orthodontic treatment (second from bottom), and end-of treatment (bottom), facial and intraoral views.

Case 20.8

This case consists of images derived from preoperative (Figure 20.12a) and postoperative (Figure 20.12b) cone beam computed tomography scans. The patient was a young adult male who was concerned about his anterior open bite and keen to have it corrected surgically. However, he wanted to minimize the duration of treatment and we proposed a surgery-first approach, which included a two-part maxillary osteotomy (Le Fort I), in conjunction with extraction of both upper first premolars to allow reduction of the overjet, but also to give ample clearance for the surgical cuts, which were made distal to teeth # 13 and 23. The open bite was closed through a combination of posterior maxillary impaction and anterior downgraft. The orthodontic fixed appliances were placed the day before surgery, but with sectional archwires in the upper arch, leaving the first premolars unbonded for extraction. A continuous upper archwire was placed following the initial healing phase and treatment was completed within about nine months.

(a)

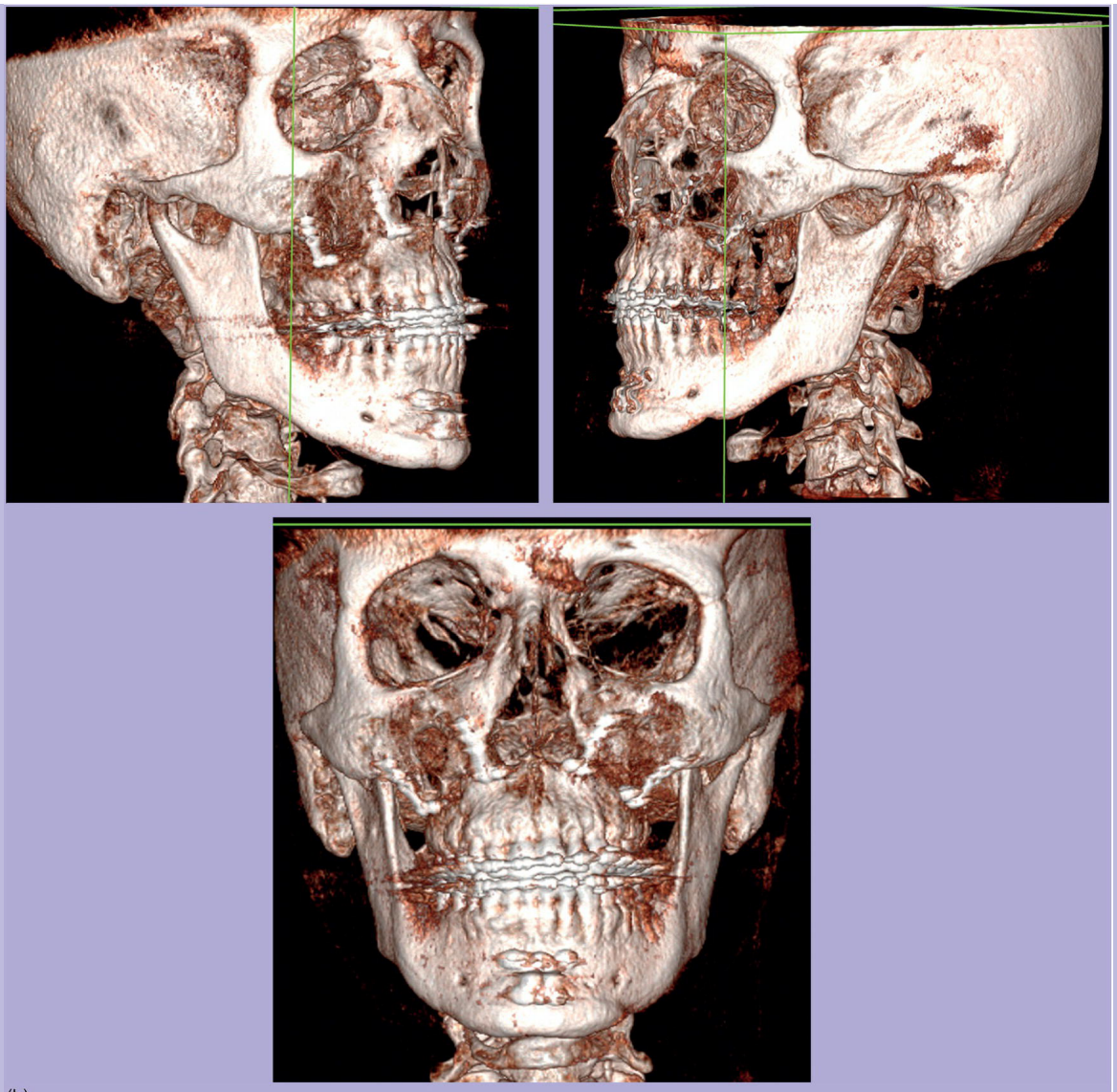
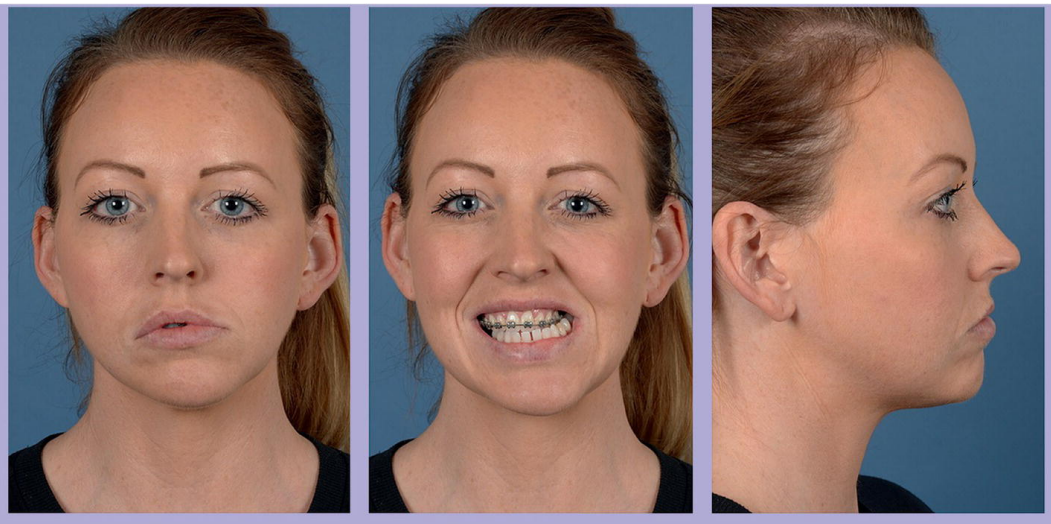


Figure 20.12 Pre-treatment CBCT images showing anterior open bite and accentuated curve of Spee on maxillary dental arch (top), and post-surgical CBCT images showing closure of anterior open bite by Le Fort I segmental osteotomy. The patient had a simultaneous advancement genioplasty (bottom).

Case 20.9

This 29-year-old female presented complaining of her chin being shifted to the left side. It was established that the asymmetry was no longer progressive and there was no associated pathology. Her malocclusion involved a cant of both occlusal planes up to the right side, and a unilateral left-sided buccal segment crossbite, with a lower midline shift to the left of approximately 4 mm. Tooth # 12 was palatally displaced. There were edentulous spaces in the region of # 15, 25, and 46. Antero-posteriorly, there was a mild Class III jaw relationship (Figure 20.13a). A surgery-first approach was prevented by the position of tooth # 12, which interfered with the planned occlusion, so a "hybrid" approach was adopted, whereby treatment was commenced with a brief phase (three months) of an upper fixed appliance to align and expand the upper dental arch (Figure 20.13b). Bimaxillary surgery was then carried out, involving maxillary downgraft on the left side (5 mm) and rotation of the mandible to the right, as well as leveling of the occlusal plane in order to achieve the planned occlusion, using bilateral sagittal split osteotomy. An advancement genioplasty of 5 mm and left-sided malar onlay using iliac crest bone graft were added to optimize facial harmony. Bondable arch bars (Baurmash, TP Orthodontics, La Porte, IN, USA) were placed on the lower teeth to facilitate intermaxillary elastics in the immediate postoperative healing phase (Figure 20.13c). A full lower fixed appliance was added following the initial healing phase and postoperative orthodontics was completed in the region of 12 months, accepting the edentulous spaces in the upper left and lower right quadrants, but largely closing the space in the upper right quadrant (Figure 20.13d).

(a)



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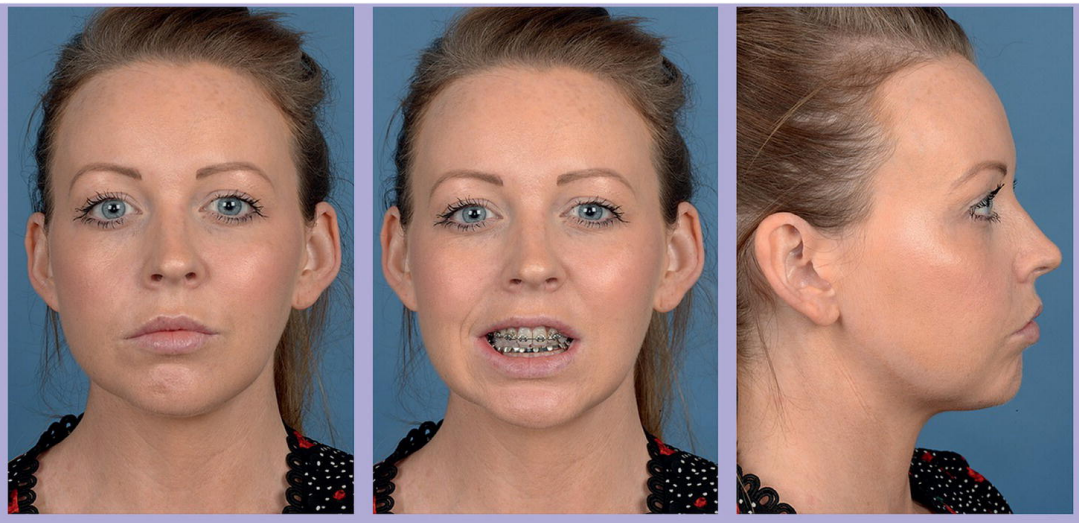

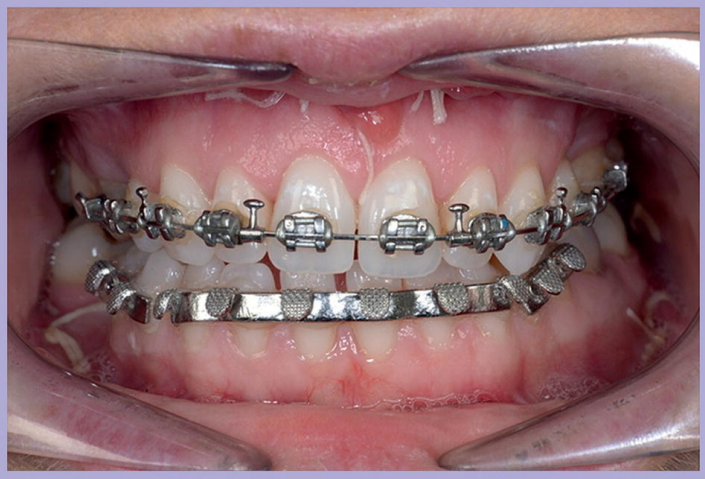

(c)

(d)

Figure 20.13 Pre-treatment (top), pre-surgery (second from top), immediate post-surgery (second from bottom), and end-of treatment (bottom), facial and intraoral views.

Timing of surgery

In most cases, orthognathic surgery is carried out on adult patients, whose facial growth is largely complete. In the experience of the authors, surgery can occasionally be indicated in a growing patient, particularly on the grounds of psychosocial issues such as teasing at school. In these patients, the potential benefits of early surgery must be weighed up against the risks of postoperative adverse growth, which is unpredictable. In this age group, psychological assessment is of paramount importance and is likely to be decisive in whether to provide or withhold treatment.

The decision to operate on patients who are seeking surgery well into adulthood, and have lived with their dentofacial deformity for a large proportion of their lives, requires careful evaluation. In addition to greater potential for surgical complications, their ability to adapt to the changes produced by surgery may be more limited, both physically and psychologically. The scope of adjunctive orthodontic treatment is also likely to be more limited and of higher risk, particularly where the dentoalveolar tissues have suffered age-related deterioration.

Definitive surgical planning

Once the combined orthodontic and surgical plan has been agreed in the clinic, the next step is to accurately plan the surgical movements. The main aims of surgical planning are to simulate the surgical jaw movements, facilitate the fabrication of the surgical wafer(s), and transfer the plan to the operating theater. Conventionally this has been carried out using physical models in the maxillofacial laboratory, but contemporary technology now allows the entire process to be carried out using digital records. This section will outline both methods and discuss their advantages and disadvantages.

Conventional model surgery

For conventional physical model surgery, final impressions are taken a few weeks prior to surgery, and the models mounted on a semi-adjustable or fully adjustable articulator, using a facebow transfer.

The facebow transfers the relationship of the maxillary dental arch to the condylar hinge axis of the temporomandibular joints from the patient to the articulator. The mounting of the maxillary model in relation to the upper member of the articulator also aims to replicate the angle of the maxillary occlusal plane to the Frankfort plane, although this can be prone to error (Walker et al., 2008). The mandibular model is then mounted with the teeth in the preoperative occlusion, as recorded using a wax wafer. It is essential for the mandible to be in its most retruded position when the wax wafer is recorded, with any habitual posture eliminated. The surgical moves are then simulated by physically repositioning the maxillary model according to the prescription provided by the clinicians, then setting the mandibular model to the agreed postoperative occlusion. This must be agreed in the clinic and the models clearly marked or waxed together. This is particularly important where the teeth are not well interdigitated, as with the SFA, and there might be scope for misinterpretation of the correct occlusion by the technologist. The surgical wafer(s) are then manufactured by hand using conventional laboratory methods (Figure 20.14).

A disadvantage of physical articulator-based model surgery is that any inaccuracies in the facebow recording, or the occlusal wafer, will produce errors in the mounting of the casts on the articulator. Repositioning the casts from an incorrect starting point can result in errors in the surgical movements, which will then transfer to the intraoperative positioning of the jaws and occlusion, and adversely affect the treatment outcome. In addition, the dental models are vulnerable to damage, which can affect the accuracy of the occlusion.

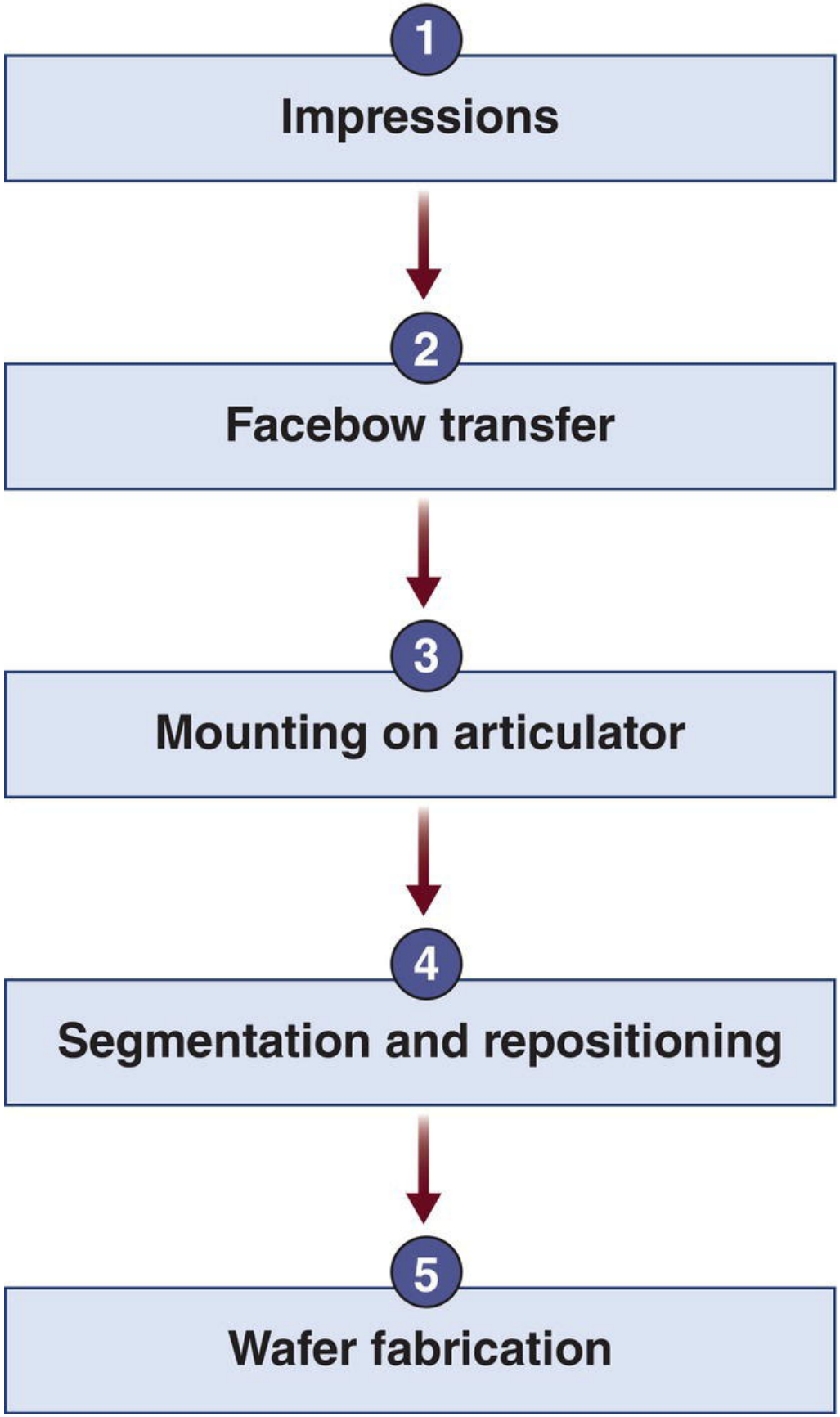
1
Impressions
2
Facebow transfer
3
Mounting on articulator
4
Segmentation and repositioning
5
Wafer fabrication

Figure 20.14 Conventional model surgery.

The articulators used in many centers are designed primarily for restorative purposes and are not well suited to surgical planning of patients with significant facial asymmetries. Attempts have been made to overcome this problem with innovative designs (Barbenel et al., 2010), but, from the point of view of the surgeon, articulators in general give no information about the anatomy of the jaws or TMJs.

Stereolithographic model surgery

For more anatomically realistic planning, a 3D model is printed using the stereolithographic (STL) file derived from a CBCT scan. This allows the surgeon to assess the morphology of the jaws more accurately, and the 3D radiographic images provide valuable cross-sectional information, such as the thickness of the ramus and the position of the inferior dental canal. In addition, the need for a facebow recording is eliminated.

One complication with STL models is that the dentition is distorted as a result of magnification and radiographic artefacts due to the scattering effect and metallic halation of high-density structures like enamel, dental implants, metal restorations, and orthodontic brackets (Almutairi et al., 2018; Rangel et al., 2013; Baan et al., 2021a). This can make the occlusal surfaces of the teeth difficult or impossible to see and renders them useless as a template for surgical wafers. To overcome this problem, the "defective dentition" must be replaced by inserting accurate dental casts (O'Neil et al., 2012; Figure 20.15). This then allows the model surgery and surgical wafer production to be carried out in much the same way as on a conventional articulator. A second potential problem is the location of the mandibular condyle in the glenoid fossa, which is lost due to the absence of the meniscus and the need to separate the mandible from the skull base. A spacer can be inserted into the glenoid fossa to simulate the meniscus, but the accuracy of this for planning autorotational movements of the mandible has not been validated.

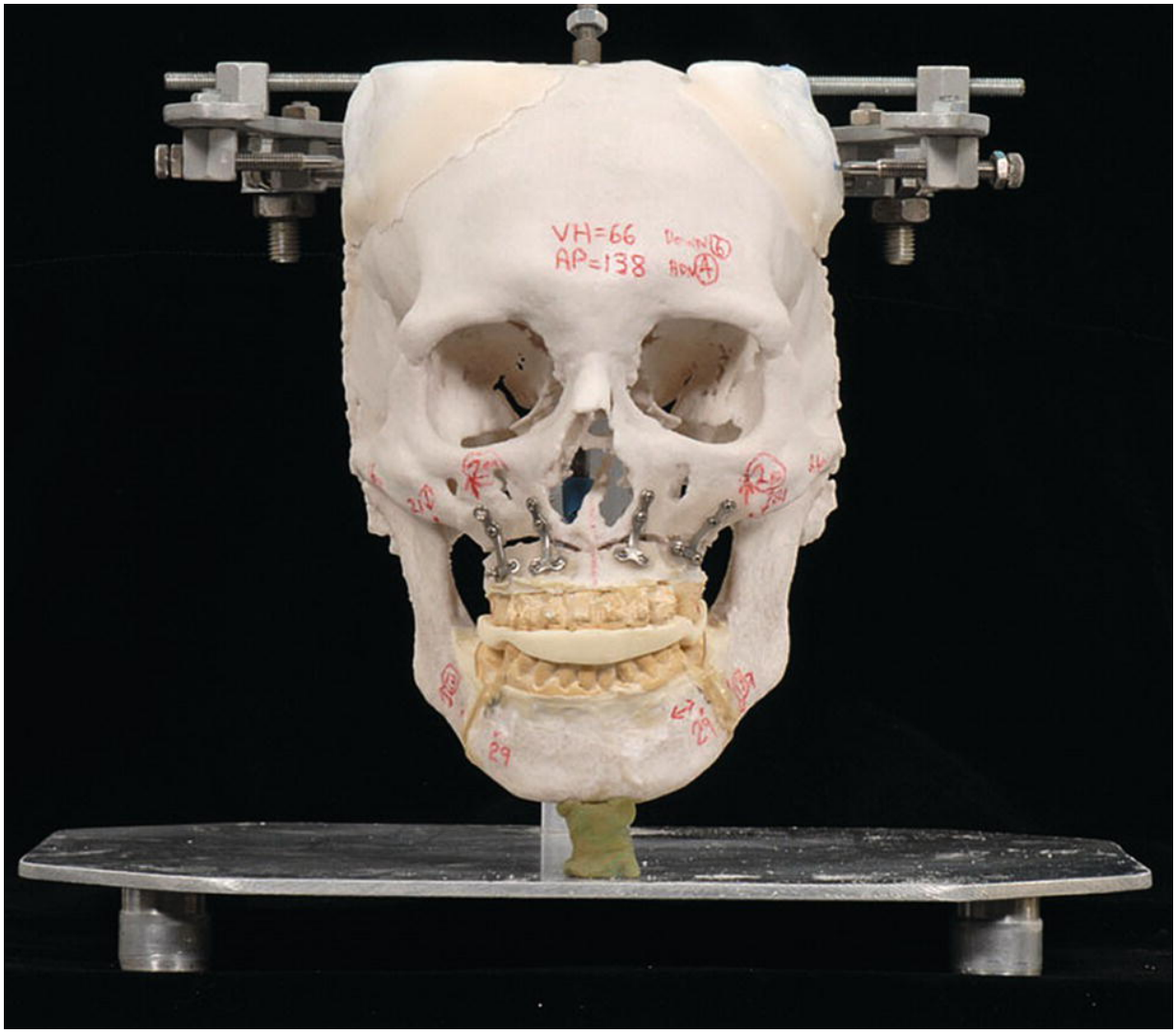

Figure 20.15 Three-dimensional stereolithographic model surgery.

Source: O'Neil et al. (2012) / with permission of Elsevier.

Virtual model surgery

As technology has progressed, several computer-aided surgical simulation systems have become available that enable both surgical and occlusal planning to be carried out entirely in a virtual environment. All allow the surgical movements of the osteotomy segments in six degrees of freedom: pitch, yaw, roll, x-direction, y-direction, and z-direction. A CBCT scan, along with separate digital captures of the dentition, is used to construct a 3D composite model, which includes the facial skeleton, the dentition, and the covering soft tissues of the face (Figure 20.16). The image of the soft tissue

surface is rendered by adjusting the thresholding of the CBCT image. This potentially provides an “all-in-one” orthognathic planning solution, incorporating 3D soft tissue prediction planning (see later; Figure 20.17). If the CBCT image is to be used as the basis for soft tissue prediction, it is essential that the lips and facial muscles are relaxed during scan acquisition, to avoid distortion. Lip distortion can also occur in patients with reduced vertical dimensions, where bringing their teeth into occlusion results in overclosure of the mandible. In such cases it is helpful to make a wax wafer, which the patient wears for all 3D imaging procedures, to hold the mandible in a consistent rest position.

With virtual planning there are two possible methods for providing the software with the planned postoperative occlusion. The first involves the use of conventional physical models, which are captured both separately and in the desired occlusion, using either CBCT or laser scanning. The second method involves direct intraoral scanning of the teeth, with the virtual model images then being manipulated on the screen into the planned occlusion using dedicated software. This can eliminate the need for physical models entirely, but has the potential disadvantage of the lack of haptic feedback (surface contact) that physical models provide and that allows the clinicians to feel how the teeth fit together. With virtual occlusal planning, the clinician must rely on visualization of the teeth, as well as the software’s color-coded occlusal maps, which show the extent of separation or perforation of the occlusal surfaces. The IPS CaseDesigner software incorporates a rigid motion engine to detect collisions between the virtual models, which helps to prevent penetration of the tooth surfaces (Baan et al., 2021b). Several studies have shown virtual occlusal planning in orthognathic surgery to be reliable and accurate (Baan et al., 2021b; Liu et al., 2016; Nadjmi et al., 2010).

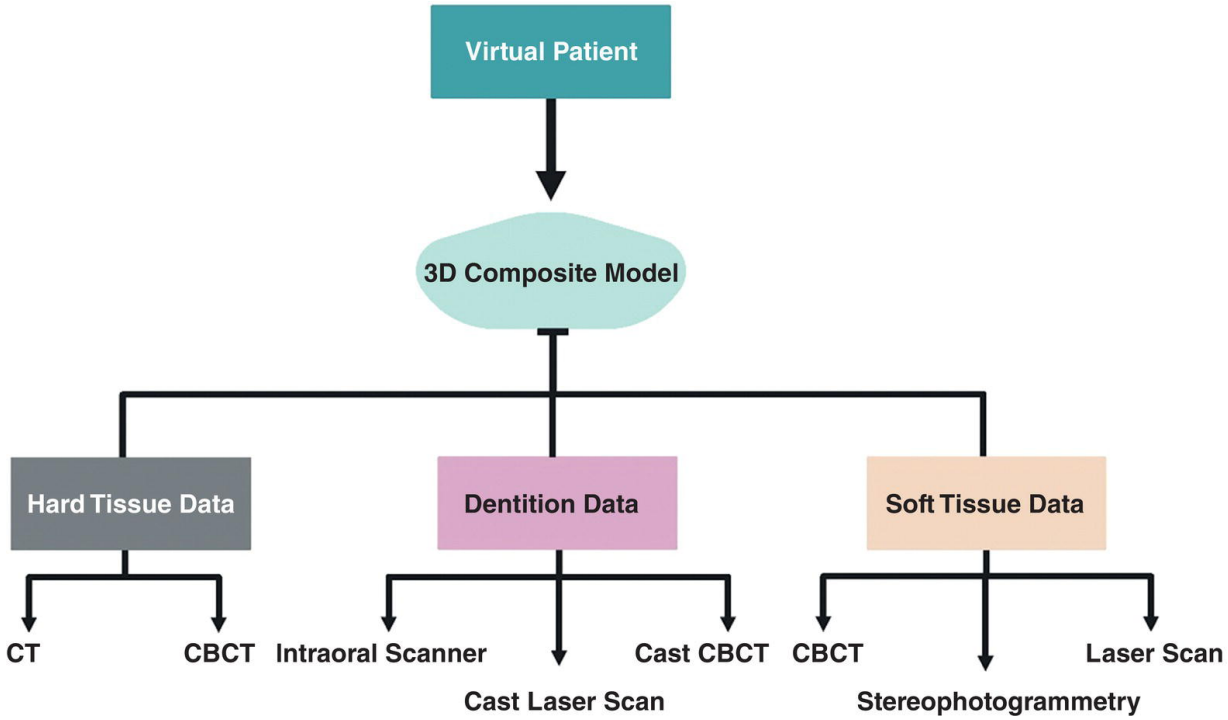

Figure 20.16 Acquisition of three-dimensional (3D) data for 3D virtual model. CBCT, cone beam computed tomography; CT, computed tomography.

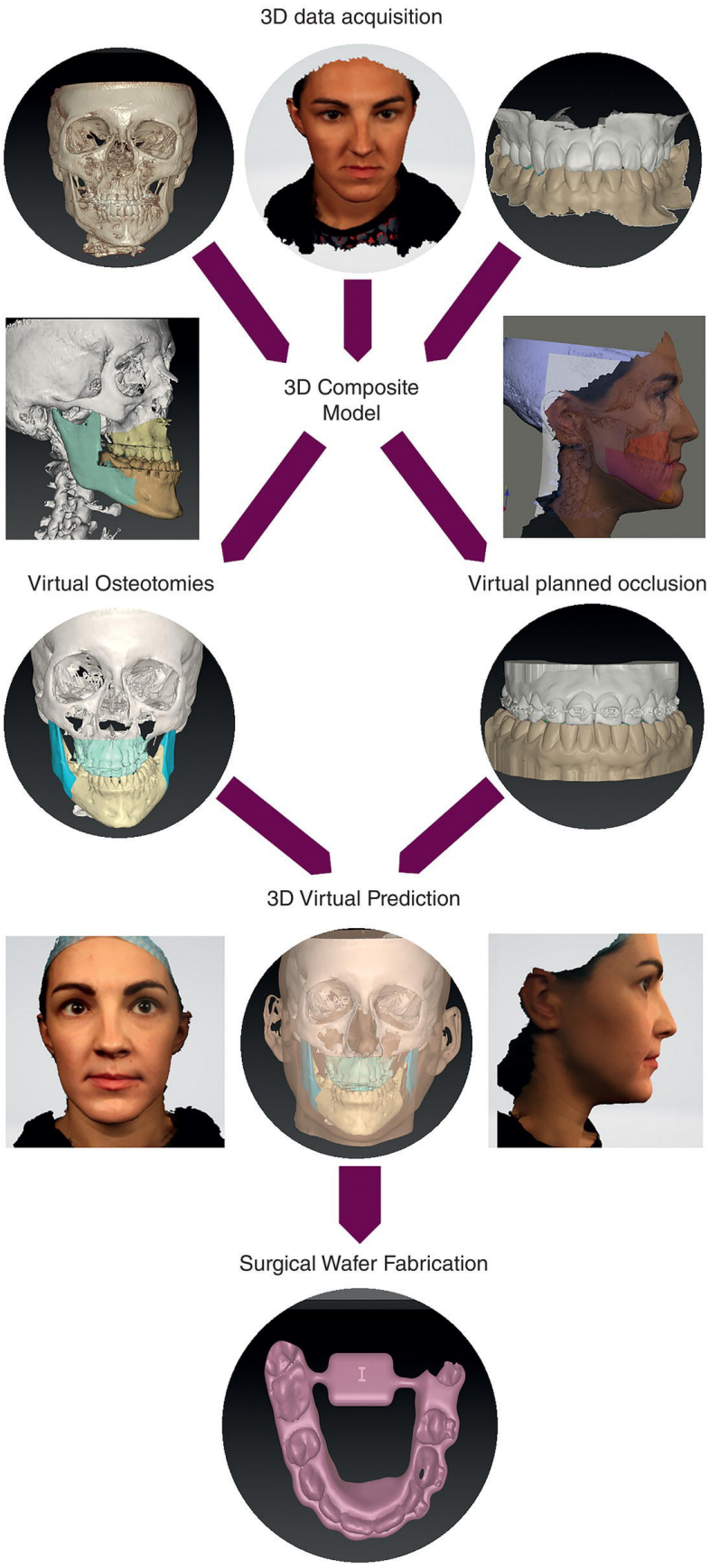
3D data acquisition
3D Composite Model
Virtual Osteotomies
Virtual planned occlusion
3D Virtual Prediction
Surgical Wafer Fabrication

Figure 20.17 Workflow of virtual model surgery for orthognathic planning.

Certain software manufacturers provide a service, at additional cost, whereby a biomedical engineer is involved in the surgical planning, via video conference, and then manufactures the surgical wafer(s) along with preformed plates, which aid the surgeon in delivering the segments to their planned positions intraoperatively.

Note: In bimaxillary orthognathic cases, when the surgical sequence is maxilla first, it is important to capture the CBCT in centric relation where both condyles are seated in the glenoid fossa. Some cases require a wax wafer to hold the mandible in its rest position during the capture of the CBCT and 3D stereophotogrammetry.

Soft tissue prediction planning

When orthognathic patients express concerns about their facial appearance, they are mainly referring to the drape of the soft tissues overlying their facial bones. Any surgical jaw movements carried out will, in addition to correcting their malocclusion, bring about a change in their facial appearance, and it is important for them to be satisfied with this. Prediction of these soft tissue changes is therefore an essential part of the planning process and can provide a powerful tool for both the MDT and the patient in finalizing the surgical plan. However, the ratios of soft tissue to hard tissue movements is multi-factorial and depends on lip thickness, muscle tone and ethnic variations and this must be clearly communicated to the patient from the outset to avoid unrealistic expectations. As mentioned previously, it is our routine to start the planning process by trying to envisage the desired soft tissue changes and then estimate the skeletal and dental movements required to achieve those changes. In this way, planning is focused from the start on facial esthetics.

Two-dimensional prediction

Predicting facial soft tissue changes in response to surgical jaw movements was originally conducted manually using a lateral cephalogram and profile photograph that is scaled to achieve a 1 : 1 ratio before the manual superimposition for prediction planning according to the Henderson method. The traced hard tissue outlines

were moved manually to simulate the planned surgical jaw movements and the soft tissue outlines were then manually repositioned in predetermined ratios, derived from studies, to show an estimate of how the profile would change (Henderson, 1974). To overcome the limitations of manual prediction planning, several 2D software packages were developed and remain in common use. These packages allow the superimposition of the digital cephalometric radiographs and profile photographs to adjust the soft tissue profile automatically in response to movements of the skeletal components. Whether manual or digital, soft tissue profile prediction has the limitation that it is a 2D representation of the 3D dentofacial complex and does not allow effective visualization of structures away from the midline.

Three-dimensional prediction

Predicting soft tissue changes in three dimensions presents additional challenges because it requires data relating not just to the ratio of hard to soft tissue movements in the midline, but in other areas of the face as well. These include the malar regions, the paranasal areas, the alar base, and the lateral parts of the lips and chin. Because of the scarcity of these data, and the difficulty in obtaining them, software producers have tended to opt for the development of algorithms, based on the thickness and characteristics of the soft tissues.

Several software packages have emerged, including 3dMDvultus (3dMD, Atlanta, GA, USA), Maxilim (Medicim, Mechelen, Belgium), IPS CaseDesigner (KLS Martin, Tuttlingen, Germany), Dolphin Imaging (Dolphin Imaging & Management Solutions, Chatsworth, CA, USA), InVivoDental (Anatomage, San Jose, CA, USA), and SimPlant OMS (Materialise, Leuven, Belgium). A study aimed at validating one of these systems found satisfactory accuracy in soft tissue prediction following the correction of facial asymmetry with Le Fort I osteotomy (Mundluru et al., 2017).

The soft tissue surface rendered by the CBCT scan has no texture, and does not give a life-like appearance. To enhance this, a photorealistic 3D image of the face can be captured using stereophotogrammetry and, where the software allows it, this can

then be superimposed on the CBCT image. This undoubtedly increases the realism of the prediction, although not its accuracy. Patients have reported a high level of satisfaction following a session of interaction with their 3D prediction plan, where they were allowed to rotate and view the image on the screen (Hertanto et al., 2021).

Orthognathic surgery

The correction of dentofacial deformities can be achieved with either single-jaw surgery, in which only the maxilla or mandible is moved, or double-jaw (bimaxillary) surgery, involving both jaws. The surgical movements are planned according to the desired soft tissue changes, the magnitude of the dentofacial disharmony, and the presence of any facial asymmetry or occlusal canting. Single-jaw surgery is generally indicated in mild maxillo-mandibular deformities, but in moderate cases a decision often must be made regarding whether single-jaw surgery will provide adequate correction, or whether bimaxillary surgery is required. In such cases, the aims of surgery must be to achieve the maximum improvement in esthetics and function, while minimizing the associated risks and morbidity (Borba et al., 2016), and bimaxillary surgery may not always be justifiable where one of the jaws alone is responsible for a large proportion of the deformity. In some cases, the decision regarding single- or double-jaw surgery can be heavily influenced using 3D interactive soft tissue planning, with the patient participating in the process.

Bimaxillary osteotomy is usually considered in the correction of severe antero-posterior skeletal jaw discrepancies, canting of the occlusal planes, facial asymmetry, and bimaxillary retrusion, where advancement of both jaws is indicated to achieve the aesthetic and functional objectives (Hernández-Alfaro et al., 2011b; Park et al., 2012; Almuzian et al., 2016). The surgeon must decide on the sequence in which the surgical procedures are to be executed. Generally, the Le Fort I osteotomy is performed first, and fixed in place, before the mandibular osteotomy is carried out. In asymmetrical cases, it may be advantageous to carry out the mandibular correction first, since repositioning the maxilla first would require a cumbersome intermediate wafer design and make

the application of intermaxillary fixation difficult intraoperatively. Other indications for carrying out mandibular surgery first are where anti-clockwise rotation of the maxillo-mandibular complex is required, where there is uncertainty about condylar positioning and centric relation registration, or in cases requiring simultaneous TMJ surgery or segmental maxillary surgery (Perez and Ellis, 2011; Borba et al., 2016). In summary, the four most commonly listed indications for a mandible-first approach include instability of condylar centric relation position, posterior maxillary downgrafting, where rigid fixation of the maxilla might be difficult, and where large maxillo-mandibular advancements are required.

In most cases, orthognathic treatment requires both orthodontics and surgery. As mentioned previously, the MDT decides whether the surgery should be carried out first or after a phase of presurgical orthodontics. This will depend on the features of the dentofacial deformity, the experience of the team, and the individual patient's needs.

Adjunctive surgical procedures

Genioplasty

Genioplasty is a versatile surgical procedure for the correction of retrogenia, progenia, vertical chin deficiency or excess, and asymmetry. The procedure can be performed separately or in conjunction with the major orthognathic procedures. Genioplasty can improve esthetic outcomes by enhancing the labiomental fold, restoring the chin–throat length, and the correct vertical proportions. In our experience, the decision regarding the magnitude and direction of movement of the genial segment is greatly aided by virtual 3D soft tissue prediction planning, and it is beneficial for patients to take part in this process.

Malar augmentation

In cases where malar prominence is lacking, augmentation can enhance facial harmony, particularly in conjunction with Le Fort I maxillary advancement, which can accentuate the flat appearance of the malar bones in patients with mid-face deficiency. Malar

projection can be restored using onlays or autografts (usually iliac crest or fat), as well as patient-specific implants made of polyetheretherketone (PEEK; French et al., 2020). Autografts have several drawbacks, including donor site morbidity and the potential for excessive resorption. Alloplastic malar implants carry a greater risk of migration, underlying bone resorption, foreign body reaction, and infections (Keyhan et al., 2021).

Rhinoplasty

The nose is the most noticeable facial structure, and correction of nasal deformities may be indicated to achieve optimal facial esthetics. Seah and collaborators (2012) reported that over 61% of dentofacial deformities were associated with nasal deformities. Because of nasal intubation, simultaneous rhinoplasty and orthognathic surgery is not possible unless submental intubation is considered. In such a case, submental intubation or switching to oral intubation after completion of the orthognathic procedure can be used. The details of rhinoplasty and soft tissue surgery are beyond the scope of this chapter. The authors would not generally consider recommending rhinoplasty as a secondary procedure to a patient until after one year following Le Fort I osteotomy.

Stability and relapse

Relapse, in orthognathic treatment, is defined as partial or complete movement of the osteotomy segments, the teeth, or both toward their original positions. Various factors contributing to relapse can be classified as patient related, orthodontics related, or surgery related. Surgical factors include the magnitude and direction of the movements of the osteotomy segments and the type of fixation used. For example, larger mandibular advancements are associated with more horizontal relapse than vertical relapse, whereas the larger changes in mandibular plane angle are associated with more vertical relapse. Orthodontic factors include tooth extrusion, de-rotations, and movement of teeth into a position of soft tissue imbalance. Patient factors are usually related to poor compliance with removable retainers in addition to genetic and congenital anomalies (cleft lip and palate).

The short-term and long-term skeletal stability of the SFA remains debatable and controversial (Ko et al., 2013; Yang et al., 2017; Wei et al., 2018). It has been postulated that the less well interdigitated postoperative occlusion in SFA cases may result in greater relapse compared with OFA cases (Choi et al., 2019; Liao et al., 2010). However, a recent study suggests that there is no difference in stability between the two approaches following bimaxillary surgery in Class III patients (Park et al., 2021). In addition, several studies have shown comparable long-term stability between the approaches in all three planes of space (transverse, vertical, and sagittal; Huang et al., 2014; Montian Manosudprasit et al., 2012; Peiro-Guijarro et al., 2016; Sharma et al., 2015). Based on the current evidence, the relapse with the SFA occurs more in counter-clockwise surgical movements of the mandible (Wei et al., 2018). To maximize the stability of the orthognathic treatment outcome, the MDT should consider the potential factors in postoperative relapse during patient screening, treatment pathway selection, surgical movements, and methods of fixation.

Follow-up

All orthognathic patients are seen frequently and closely monitored during their early postoperative period and until the completion of their postoperative orthodontic treatment. After this, our standard protocol is to follow them up annually for five years, where possible, to monitor surgical and orthodontic stability, any areas of sensory deficit, and any problems with surgical fixation components. Plates can occasionally cause infection or dehiscence through the oral mucosa and approximately 20%, on average, will require removal at some stage. It is also important to monitor the patient's level of satisfaction with their treatment and their degree of concern regarding any residual features of facial dysmorphology or malocclusion, as well as any relapse that has occurred.

Digital innovations in orthognathic surgery

Four-dimensional imaging

There is no doubt that orthognathic surgery can affect facial expressions, and real-time recording of facial expressions in 3D provides a high-technology method for analyzing these postoperative changes that would be difficult otherwise (Shujaat et al., 2014; Al-Hiyali et al., 2015). Our team also uses 4D imaging to assess dynamic facial asymmetry in orthognathic patients. High-definition stereophotogrammetry images are recorded at a rate of 60 per second, generating 180 3D captures of each facial expression over a period of three seconds. Sophisticated software packages are available for analysis of the dynamics and symmetry of facial expressions, but little in the way of research has been carried out in this area to date.

Dynamic navigation

Dynamic navigation provides a real-time method for accurately localizing and orienting around vital anatomical structures and enables the precise execution of the planned orthognathic surgical procedure. The sagittal split osteotomy is most commonly used for the correction of mandibular deformities and it has been reported that the use of navigation reduces the incidence of injury to the inferior dental nerve related to this procedure (Shim et al., 2013). In Le Fort I osteotomy, navigation allows visualization of the pterygoid plates during pterygomaxillary disarticulation, thereby minimizing surgical complications, which include fracture of the plates and related vascular injuries of the internal maxillary artery and pterygoid venous plexus. Shiba and colleagues (2015) reported the use of navigation systems in 46 orthognathic cases. They confirmed its usefulness in guiding the osteotomy at the pterygomaxillary fissure, in horseshoe Le Fort I osteotomy above the molar roots, and in mandibular sagittal split, for repositioning of the proximal mandibular segment. Despite the advantages of navigation-guided surgery, several obstacles prevent its wide clinical application, including the cost, the required additional training, and the complex registration, calibration, and tracking required before surgery.

Robotic arms

Systems have recently been developed that combine robotic technology with a dynamic navigation system. The robotic arm performs osteotomies according to the virtual surgical plan and repositions the osteotomy segments with a high level of accuracy (Wu et al., 2020), potentially minimizing complications. Most of the available evidence is based on preclinical studies (Wu et al., 2020; Seo and Choi, 2021; Han et al., 2021). Given the rate of advance of digital technology, it is possible that robotic-assisted orthognathic surgery will become widely applied clinically in the foreseeable future.

Conclusion

This chapter has aimed to provide the reader with an overview of the contemporary approaches for the diagnosis and management of dentofacial deformities. It has highlighted the importance of soft tissue–based diagnosis and treatment planning to achieve optimal facial harmony. It has included recent advances in 3D imaging and provided a detailed, step-by-step guide to digital planning of orthognathic treatment. We hope the selection of cases has helped to illustrate the concept of the surgery-first approach, which has been clearly shown to reduce the overall duration of treatment in suitable cases, as well as to minimize the negative psychological impact of presurgical orthodontic decompensation, but without compromising the quality of the occlusal outcomes. Most of all, we hope that the content of this chapter will inspire readers to think about how their own orthognathic service can be refined for the benefit of their patients.

References

Al-Hiyali, A., Ayoub, A., Ju, X. et al. (2015). The impact of orthognathic surgery on facial expressions. *Journal of Oral and Maxillofacial Surgery* 73(12): 2380–2390.

Al-Moraissi, E.A., Wolford, L.M., Perez, D. et al. (2017). Does orthognathic surgery cause or cure temporomandibular disorders? A systematic review and meta-analysis. *Journal of Oral and Maxillofacial Surgery* 75(9): 1835–1847.

Almukhtar, A., Khambay, B., Ju, X. et al. (2018). Comprehensive analysis of soft tissue changes in response to orthognathic surgery: Mandibular versus bimaxillary advancement. *International Journal of Oral and Maxillofacial Surgery* 47(6): 732–737.

Almutairi, T., Naudi, K., Nairn, N. et al. (2018). Replacement of the distorted dentition of the cone-beam computed tomography scans for orthognathic surgery planning. *Journal of Oral and Maxillofacial Surgery* 76(7): 1561-e1–1561-e8.

Almuzian, M., Almukhtar, A., Ju, X. et al. (2016). Effects of Le Fort I osteotomy on the nasopharyngeal airway—6-month follow-up. *Journal of Oral and Maxillofacial Surgery* 74(2): 380–391.

Al-Rudainy, D., Ju, X., Mehendale, F.V. et al. (2019). Longitudinal 3D assessment of facial asymmetry in unilateral cleft lip and palate. *Cleft Palate-Craniofacial Journal* 56(4): 495–501.

Anwar, M., Benington, P.C.M., Gillgrass, T.J. et al. (2022). Surgery-first approach for correction of class III dentofacial deformity with Le Fort I osteotomy; is it advantageous? *British Journal of Oral and Maxillofacial Surgery* 60(9): 1234–1239.

Ayoub, A., Khambay, B., Benington, P. et al. (2013a). Dentofacial assessment. In: A. Ayoub, B. Khambay, P. Benington et al. (eds.), *Handbook of Orthognathic Treatment: A Team Approach*. Chichester: Wiley, pp. 16–50. doi: 10.1002/9781118751695.

Ayoub, A., Khambay, B., Benington, P. et al. (2013b). Psychological considerations for the orthognathic patient. In: A. Ayoub, B. Khambay, P. Benington et al. (eds.), *Handbook of Orthognathic Treatment: A Team Approach*. Chichester: Wiley, pp. 1–15.

Ayoub, A.A., Khambay, A.B., and Mcdonald, J.X. (2016). State of the art analysis of soft tissue changes in response to Lefort I maxillary

advancement. *British Journal of Oral and Maxillofacial Surgery* 54(7): 812–817.

Baan, F., Bruggink, R., Nijsink, J. et al. (2021a). Fusion of intra-oral scans in cone-beam computed tomography scans. *Clinical Oral Investigations* 25(1): 77–85.

Baan, F., Bruggink, R., Nijsink, J. et al. (2021b). Virtual occlusion in orthognathic surgery. *International Journal of Oral and Maxillofacial Surgery* 50(9): 1219–1225.

Baek, S.-H., Ahn, H.-W., Kwon, Y.-H. et al. (2010). Surgery-first approach in skeletal class III malocclusion treated with 2-jaw surgery: Evaluation of surgical movement and postoperative orthodontic treatment. *Journal of Craniofacial Surgery* 21(2): 332–338.

Barbenel, J.C., Paul, P.E., Khambay, B.S. et al. (2010). Errors in orthognathic surgery planning: The effect of inaccurate study model orientation. *International Journal of Oral and Maxillofacial Surgery* 39(11): 1103–1108.

Barone, S., Morice, A., Picard, A. et al. (2020). Surgery-first orthognathic approach vs conventional orthognathic approach: A systematic review of systematic reviews. *Journal of Stomatology, Oral and Maxillofacial Surgery* 122(2): 162–172.

Behrman, S.J., and Behrman, D.A. (1988). Oral surgeons' considerations in surgical orthodontic treatment. *Dental Clinics of North America* 32(3): 481–507.

Borba, A.M., Borges, A.H., Cé, P.S. et al. (2016). Mandible-first sequence in bimaxillary orthognathic surgery: A systematic review. *International Journal of Oral and Maxillofacial Surgery* 45(4): 472–475.

Choi, D.-S., Garagiola, U., and Kim, S.-G. (2019). Current status of the surgery-first approach (part I): Concepts and orthodontic protocols. *Maxillofacial Plastic and Reconstructive Surgery* 41(1): 1–8.

Dolwick, M.F., and Widmer, C.G. (2018). Orthognathic surgery as a treatment for temporomandibular disorders. *Oral and Maxillofacial Surgery Clinics* 30(3): 303–323.

Dons, F., Mulier, D., Maleux, O. et al. (2022). Body dysmorphic disorder (BDD) in the orthodontic and orthognathic setting: A systematic review. *Journal of Stomatology, Oral and Maxillofacial Surgery* 123(4): e145–e152.

Dujoncquoy, J.-P., Ferri, J., Raoul, G. et al. (2010). Temporomandibular joint dysfunction and orthognathic surgery: A retrospective study. *Head & Face Medicine* 6(1): 1–7.

French, K.E.M., Gormley, M., Kana, A. et al. (2020). Outcomes and complications associated with malar onlays: Literature review and case series of 119 implants. *British Journal of Oral and Maxillofacial Surgery* 58(9): 1110–1115.

Han, J.J., Woo, S.-Y., Yi, W.-J. et al. (2021). Robot-assisted maxillary positioning in orthognathic surgery: A feasibility and accuracy evaluation. *Journal of Clinical Medicine* 10(12): 2596.

Henderson, D. (1974). The assessment and management of bony deformities of the middle and lower face. *British Journal of Plastic Surgery* 27(3): 287–296.

Hernández-Alfaro, F., Guijarro-Martínez, R., Molina-Coral, A. et al. (2011a). “Surgery first” in bimaxillary orthognathic surgery. *Journal of Oral and Maxillofacial Surgery* 69(6): e201–e207.

Hernández-Alfaro, F., Guijarro-Martínez, R., and Peiró-Guijarro, M.A. (2011b). Effect of mono-and bimaxillary advancement on pharyngeal airway volume: Cone-beam computed tomography evaluation. *Journal of Oral and Maxillofacial Surgery* 69(11): e395–e400.

Hernández-Alfaro, F., Guijarro-Martínez, R., and Peiró-Guijarro, M.A. (2014). Surgery first in orthognathic surgery: What have we learned? A comprehensive workflow based on 45 consecutive cases. *Journal of Oral and Maxillofacial Surgery* 72(2): 376–390.

Hertanto, M., Ayoub, A.F., Benington, P.C.M. et al. (2021). Orthognathic patient perception of 3D facial soft tissue prediction planning. *Journal of Cranio-Maxillofacial Surgery* 49(9): 783–788.

Huang, C., Hsu, S.S.-P., and Chen, Y.-R. (2014). Systematic review of the surgery-first approach in orthognathic surgery. *Biomedical Journal* 37(4): 184.

Huang, C.S., Hsu, S., and Chen, Y.-R. (2015). Orthodontic principles and guidelines for the surgery-first approach to orthognathic surgery. *International Journal of Oral and Maxillofacial Surgery* 44(12): 1457–1462.

Keyhan, S.O., Bagheri, S.C., Cheshmi, B. et al. (2021). Malar bone augmentation using malar osteotomies. In: S.O. Keyhan, T. Fattahi, S.C. Bagheri et al. (eds.), *Integrated Procedures in Facial Cosmetic Surgery*. New York: Springer, pp. 145–161.

Ko, E.W.-C., Lin, S.C., Chen, Y.R. et al. (2013). Skeletal and dental variables related to the stability of orthognathic surgery in skeletal Class III malocclusion with a surgery-first approach. *Journal of Oral and Maxillofacial Surgery* 71(5): e215–e223.

Liao, Y.-F., Chiu, Y.-T., Huang, C.-S. et al. (2010). Presurgical orthodontics versus no presurgical orthodontics: Treatment outcome of surgical-orthodontic correction for skeletal Class III open bite. *Plastic and Reconstructive Surgery* 126(6): 2074–2083.

Liao, Y.-F., and Lo, S.H. (2018). Surgical occlusion setup in correction of skeletal Class III deformity using surgery-first approach: Guidelines, characteristics and accuracy. *Scientific Reports* 8(1): 1–8.

Liu, X.J., Li, Q.Q., Zhang, Z. et al. (2016). Virtual occlusal definition for orthognathic surgery. *International Journal of Oral and Maxillofacial Surgery* 45(3): 406–411.

Montian Manosudprasit, D., Tasanee Wangsrimongkol, D., Palakorn Surakunprapha, M. et al. (2012). Surgery first orthognathic

approach for skeletal Class III malocclusion corrections—a literature review. *Journal of the Medical Association of Thailand* 95(11): S172–S180.

Mundluru, T., Almukhtar, A., Ju, X. et al. (2017). The accuracy of three-dimensional prediction of soft tissue changes following the surgical correction of facial asymmetry: An innovative concept. *International Journal of Oral and Maxillofacial Surgery* 46(11): 1517–1524.

Musich, D.R. (2012). Orthodontic treatment in patients requiring orthognathic surgical procedures. In: V. Krishnan and Z. Davidovitch (eds.), *Integrated Clinical Orthodontics*. Oxford: Wiley Blackwell, pp. 332–365.

Nadjmi, N., Mollemans, W., Daelemans, A. et al. (2010). Virtual occlusion in planning orthognathic surgical procedures. *International Journal of Oral and Maxillofacial Surgery* 39(5): 457–462.

Nagasaka, H., Sugawara, J., Kawamura, H. et al. (2009). "Surgery first" skeletal Class III correction using the Skeletal Anchorage System. *Journal of Clinical Orthodontics* 43(2): 97–105.

Naini, F.B., and Gill, D.S. (2016). Patient evaluation and clinical diagnosis. In: F.B. Naini and S.D. Gill (eds.), *Orthognathic Surgery: Principles, Planning and Practice*, Chichester: Wiley, pp. 116–170.

O'Neil, M., Khambay, B., Bowman, A. et al. (2012). Validation of a new method for building a three-dimensional physical model of the skull and dentition. *British Journal of Oral and Maxillofacial Surgery* 50(1): 49–54.

Park, S.-B., Kim, Y.-I., Son, W.-S. et al. (2012). Cone-beam computed tomography evaluation of short-and long-term airway change and stability after orthognathic surgery in patients with Class III skeletal deformities: Bimaxillary surgery and mandibular setback surgery. *International Journal of Oral and Maxillofacial Surgery* 41(1): 87–93.

Park, Y.-W., Kwon, K.-J., Kang, Y.-J. et al. (2021). Surgery-first approach reduces the overall treatment time without damaging long-term stability in the skeletal Class III correction: A preliminary study. *Maxillofacial Plastic and Reconstructive Surgery* 43(1): 1–8.

Peiro-Guijarro, M.A., Guijarro-Martínez, R., and Hernández-Alfaro, F. (2016). Surgery first in orthognathic surgery: A systematic review of the literature. *American Journal of Orthodontics and Dentofacial Orthopedics* 149(4): 448–462.

Perez, D., and Ellis, E. (2011). Sequencing bimaxillary surgery: Mandible first. *Journal of Oral and Maxillofacial Surgery* 69(8): 2217–2224.

Phillips, K.A., and Crerand, C.E. (2016). Psychological evaluation and body dysmorphic disorder. In: F.B. Naini and S.D. Gill (eds.), *Orthognathic Surgery: Principles, Planning and Practice*. Chichester: Wiley, pp. 235–244.

Posnick, J.C. (2022). Orthognathic surgery treatment planning. In: J.C. Posnick, *Orthognathic Surgery: Principles and Practice*. *St*. Louis, MO: Elsevier Health Sciences, pp. 382–418.

Rangel, F.A., Maal, T.J.J., Bronkhorst, E.M. et al. (2013). Accuracy and reliability of a novel method for fusion of digital dental casts and cone beam computed tomography scans. *PLoS One* 8(3): e59130.

Seah, T.E., Bellis, H., and Ilankovan, V. (2012). Orthognathic patients with nasal deformities: Case for simultaneous orthognathic surgery and rhinoplasty. *British Journal of Oral and Maxillofacial Surgery* 50(1): 55–59.

Selvaraj, A.K. Benington, P.C.M., Murphy, L. et al. (2019). Psychology input to an orthognathic clinic: Patients' perception of service quality. *Surgeon* 17(6): 340–345.

Seo, H.J., and Choi, Y.-K. (2021). Current trends in orthognathic surgery. *Archives of Craniofacial Surgery* 22(6): 287.

Sharma, V.K., Yadav, K., and Tandon, P. (2015). An overview of surgery-first approach: Recent advances in orthognathic surgery. *Journal of Orthodontic Science* 4(1): 9.

Shiba, H., Kato, S., and Nakagawa, T. (2015). Use of navigation systems in orthognathic surgery. *International Journal of Oral and Maxillofacial Surgery* 44: e288.

Shim, B.K., Shin, H.S., Nam, S.M. et al. (2013). Real-time navigation-assisted orthognathic surgery. *Journal of Craniofacial Surgery* 24(1): 221–225.

Shujaat, S., Khambay, B.S., Ju, X. et al. (2014). The clinical application of three-dimensional motion capture (4D): A novel approach to quantify the dynamics of facial animations. *International Journal of Oral and Maxillofacial Surgery* 43(7): 907–916.

Sugawara, J., Aymach, Z., Nagasaka, D.H. et al. (2010). "Surgery first" orthognathics to correct a skeletal Class II malocclusion with an impinging bite. *Journal of Clinical Orthodontics* 44(7): 429–438.

Ubaya, T., Sherriff, A., Ayoub, A. et al. (2012). Soft tissue morphology of the naso-maxillary complex following surgical correction of maxillary hypoplasia. *International Journal of Oral and Maxillofacial Surgery* 41(6): 727–732.

Verweij, J.P., Houppermans, P.N.W.J., Gooris, P. et al. (2016). Risk factors for common complications associated with bilateral sagittal split osteotomy: A literature review and meta-analysis. *Journal of Cranio-Maxillofacial Surgery* 44(9): 1170–1180.

Villegas, C., Uribe, F., Sugawara, J. et al. (2010). Expedited correction of significant dentofacial asymmetry using a "surgery first" approach. *Journal of Clinical Orthodontics* 44(2): 97–103.

Walker, F., Ayoub, A.F., Moos, K.F. et al. (2008). Face bow and articulator for planning orthognathic surgery: 2 articulator. *British Journal of Oral and Maxillofacial Surgery* 46(7): 573–578.

21

The Role of the Orthodontist in Managing Disorders of the Temporomandibular Joint

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Summary

Orthodontists routinely see patients reporting signs and symptoms of temporomandibular joint (TMJ) problems before, during, and after orthodontic treatment. Because of the close anatomical and functional relationship between the dental occlusion and the TMJs, orthodontic treatment has been historically considered either a remedy or a cause of TMJ disorders. An "abnormal" condyle fossa relationship has been often considered a putative risk factor for temporomandibular disorders (TMDs) by many orthodontists, despite the lack of any reliable evidence in support of this belief. Some local or systemic pathologies affecting the TMJs, such as arthritis, hypoplasia, and hyperplasia, may result in occlusal changes. The management of these conditions requires a deep understanding of the underlying pathology and typically also complex multidisciplinary treatment. It is therefore crucial for orthodontists to understand the relationship between occlusion and TMJ problems and to develop the diagnostic skills that are necessary to assess the TMJs and jaw function. In this chapter we will discuss the most common TMDs, such as joint pain and disc displacement, and will provide suggestions on how to diagnose and manage these conditions. We will also review a number of TMJ conditions and developmental problems that may affect dental occlusion, and provide clinical guidelines for a differential diagnosis of these pathologies.

Why should orthodontists deal with the temporomandibular joint?

The correct functioning of the temporomandibular joint (TMJ) is of paramount importance for patients' well-being and oral health-related quality of life (Chanthavisouk et al., 2022; Häggman-Henrikson et al., 2022; John, 2020). Orthodontists routinely work on dental occlusion, and occlusal changes may also result from a number of TMJ pathologies. A deep understanding of the relationship between occlusion and TMJ problems is therefore crucial for orthodontists (Michelotti and Iodice, 2010).

The collective term temporomandibular disorders (TMDs) includes a set of heterogeneous conditions that affect the masticatory muscles, the TMJ, and the surrounding tissues and structures. The most common conditions are classified in the diagnostic criteria for temporomandibular disorders (DC/TMD) and are characterized by regional acute or persistent pain in the facial and/or preauricular areas, limitation of or interference with jaw function, and/or TMJ noises during jaw movements (Schiffman et al., 2014). However, other possible conditions might affect the TMJ. These are classified in the expanded taxonomy of TMDs and include joint diseases, fractures, and congenital/developmental disorders (Peck et al., 2014).

Some occlusal features, such as unilateral crossbite and overjet larger than 7 mm, have been historically considered risk factors for TMDs (Pullinger et al., 1988); nowadays, however, the role of occlusal factors is not supported by strong evidence and it is considered irrelevant within the etiological framework of the biopsychosocial model for TMDs (Manfredini et al., 2017; Olliver et al., 2020; Suvinen et al., 2005).

Changes in the occlusal relationship may result from changes in TMJ morphology, which are associated with degenerative joint disease, neoplasm, or fractures. It is therefore important that orthodontists have the diagnostic skills that are necessary to assess TMJ problems (Caldas et al., 2016). Finally,

orthodontists were also blamed for provoking TMDs, and for this it is important to know what the effects of orthodontic treatment on the TMJ could be (Al-Moraissi et al., 2017; Owen, 1988).

Anatomy of the temporomandibular joint

The TMJ is a double bicondylar diarthrosis. The mandibular condyle seats in the glenoid fossa and articulates with the articular eminence of the temporal bone. Unlike other joints, articular surfaces are covered with fibrocartilaginous tissue instead of hyaline cartilage, and there is a fibrous disc between the two articular surfaces. The joint cavity contains synovial fluid. The articular disc divides the joint into two compartments: an upper space called the temporo-discal space, and a lower space called the condylar-discal space.

The *mandibular condyle* is the most superior part of the condylar process along the condylar neck. It presents an ovoid form with rounded medial and lateral poles. The condyle antero-posterior axis is approximately 1 cm, while the latero-medial axis is around 2 cm; the major axes of the two condyles converge at the foramen magnum at an angle of 145°. The antero-superior portion of the condyle that articulates with the disc and with the tubercular eminence is covered with fibrocartilage and serves as the area under the heaviest load among all the body joints (50–80 kpa; Koolstra, 2002).

The *glenoid fossa* is part of the squamous portion of the temporal bone. It is a very thin, concave bony layer that extends forward with the temporal tubercle, giving to the temporal articular surface the classic "saddle" morphology. The posterior part of the temporal tubercle is called the eminence plane and changes its inclination throughout life. In newborns the eminence plane is almost flat, but with functional loading and changes in dentition it becomes steeper, up to a 45° slope during adulthood. However, with aging it changes again to a flat plane. The eminence plane is covered with fibrocartilage, but not the posterior part of the glenoid fossa, as this is not an articular surface.

The mandibular condyle is surrounded by the fibrous *joint capsule*, which has a protective and proprioceptive role. It extends from the perimeter of the cranial articular surface to the condylar neck of the mandible. The inner part of the joint capsule is a synovial membrane producing fluid for lubrification and trophism of the joint. The outer part of the joint capsule, instead, is made of collagen and elastic fibers, which allow a degree of movement freedom to the joint, but at the same time also restrict excessive excursions. Indeed, the joint capsule limits both the forward translation of the condyle and in part its distraction and posterior movement. The ligaments stabilizing the TMJ are the temporomandibular ligament, the stylomandibular ligament, and the sphenomandibular ligament.

Within the two articular surfaces the TMJ presents the *articular disc*, which is described as a biconcave fibrous lamina that can be subdivided into three zones: anteroinferior, intermediate, and posterior. The intermediate zone is the thinnest part of the disc, while the posterior zone is the thickest at around 3 mm. The part that bears the highest load is the intermediate part, which is formed by collagen fibers. The articular disc is extremely viscoelastic, due to the presence of elastic fibers that allow shape variation and exchange of fluids (blood, synovial fluid, water) during functional and postural activities (Fanghänel and Gedrange, 2007). The disc is avascular and inserts anteriorly to the articular capsule, where it is partially connected to the tendon of the lateral pterygoid muscle; laterally and medially the condylar disc ligaments (polar ligaments) connect the disc to the condyle. When the disc is in a "physiological position" relative to the condyle, the intermediate zone is facing the tubercular eminence, while the posterior zone is on the top of the condyle in the middle of the glenoid fossa (Figure 21.1; Academy of Prosthodontics, 2017). The disc presents several receptors (i.e. Pacinian corpuscles, Golgi tendon organs, and muscle Ruffini endings) that increase their density from the disc center to its periphery, and provide feedback during mastication together with the periodontal receptors (Wink et al., 1992).

Posteriorly to the disc there is a retrodiscal space or bilaminar zone formed by two laminae separated by an interlaminar space, made of connective and fat tissues, which contain nerves and the retrodiscal venous plexus. The retrodiscal space also contains branches of the deep auricular, anterior tympanic, and middle meningeal arteries, of the auriculotemporal nerve, and of the temporomandibular veins. The role of the retrodiscal space is to protect the posterior part of the glenoid fossa during jaw closure, and to provide the blood supply to the TMJs.

Should orthodontists care about condylar position?

Since the early 1970s it has been hypothesized that a malocclusion can have a negative impact on the physiological condylar–disc relationship, which in turn can result in the onset of TMDs (Roth, 1973, 1981a).

Nowadays, several occlusal features like Class II Division 2, deep bite, discrepancies between centric occlusion and centric relation, and occlusal interferences are still considered risk factors for TMDs altering the physiological condylar–disc relationship. In order to prevent or treat TMDs, Roth's philosophy has emphasized the search for an optimal condyle position as one main goal of orthodontic treatment. This position was determined using a particular bite registration (power centric) followed by articulator mounting of the patient's dental casts (Roth, 1973, 1981a, 1981b; Roth and Rolfs, 1981). However, the existence of an ideal centric relation (CR), with condyles centered in the glenoid fossa, has been questioned (Rinchuse, 2021). The term CR refers to a reproducible relationship between the condyle and the glenoid fossa, independently of the tooth contacts. First, in the 1970s, it was defined as a retruded postero-superior condyle position; in the 1980s it changed to the antero-superior position of the condyle (Rinchuse, 2021). The operational criteria to identify CR are not only difficult to define, but they also appear to lack reliability and validity (Kandasamy et al., 2013). Indeed, in a study conducted on magnetic resonance to assess the validity of three different methods to find the CR, neither the maximum intercuspation, not the retruded CR, nor the power-centric bite registration was able to achieve the CR (Kandasamy et al., 2013).

(a) (b)

Figure 21.1 Magnetic resonance imaging of a temporomandibular joint showing condyle, articular disc, and articular eminence, with both (a) closed and (b) open mouth.

Finally, as mentioned before, the relationship between glenoid fossa and mandibular condyle is continuously changing throughout life due to ongoing remodeling. The most significant changes occur during growth with eruption of the permanent dentition and growth at the condyle and the tubercular eminence. Also during adulthood there are small but continual changes in the relationship between glenoid fossa and mandibular condyle, as a result of the physiological aging of the stomatognathic system (tooth wear, TMJ remodeling, muscular changes; Ingervall, 1968). Considering these aspects, it is difficult to assume that this relationship would remain stable over the years, and that the maximum intercuspation (MI) will always coincide with the CR, as indicated as primary goal of so-called orthodontic gnathology (CR–MI coincidence). However, it has been considered that, although the physiological relationship between articular disc and condyle exists and presents the posterior band covering the head of the condyle and the intermediate band between the condyle and the articular eminence (Academy of Prosthodontics, 2017), this relationship changes frequently both within and between individuals. Indeed, the position of the condyle in the fossa is influenced by the circadian variation of muscle tone and many other factors such as parafunction, stress levels, tongue posture, and hydration of the disc, among others (Michelotti et al., 1997).

Furthermore, the need for CR–MI coincidence as prevention or treatment of TMDs is not supported by scientific evidence (Greene and Manfredini, 2020). First, the CR appears to be an unreliable and unachievable position; second, the transfer of the CR to the articulators may be flawed; and finally, there are no studies supporting the notion that CR is more common in healthy subjects or less common in TMD patients (Bonilla-Aragon et al., 1999; Lelis et al., 2015; Paknahad et al., 2015). The current evidence indicates that the position of the TMJ in healthy subjects is variable, ranging from retruded to centered and anterior, hence it can be speculated that an ideal three-dimensional position of the condyle that can be used to prevent or treat TMDs does not exist (Bean and Thomas, 1987; Kircos et al., 1987; Türp et al., 2016). Finally, current evidence suggests that there is a range of acceptable condylar positions for all individuals, and that usually most patients adapt well to changes in this position (Zonnenberg et al., 2021). The condyle–fossa relation is strongly influenced by anatomical variation of the fossa, varying from narrow and deep to wide and shallow. Asymptomatic patients may present three possible scenarios of condyle–fossa relation: a concentric position of the condyle in the fossa, a posterior position of the condyle in the fossa, or an anterior position of the condyle in the fossa, but with an average ratio of fossa depth to fossa width. In contrast, patients with disc displacement more commonly present a wider and shallower fossa or a very narrow posterior joint space associated with a narrow or deep fossa, depending on the type of disc displacement (Pullinger, 2013). Hence, anatomical factors seem to have a more important role than condylar position in the onset of TMDs. When considering that it is not possible to change the morphology of the TMJs, one aim of orthodontic treatment should be to reach an acceptable maximal intercuspation position, without sliding that is clinically significant, independently of the CR position (Kandasamy et al., 2018).

Temporomandibular joint disorders

TMJ problems are routinely encountered by orthodontists in daily practice, and therefore it is important to have a correct diagnosis and management of these conditions. TMJ signs and symptoms include pain (arthralgia), condylar disc incoordination (disc displacement), and anatomical or degenerative changes (arthrosis, systemic arthritis, and growth disturbances; Greene et al., 2017). In general, the management of signs and symptoms of TMDs, such as pain or dysfunction, should include reversible therapies based on the biopsychosocial model (Sharma et al., 2020; Suvinen et al., 2005). The biopsychosocial model suggests biological, clinical, and behavioral characteristics of the patient as factors involved in the onset, maintenance, and remission of TMDs (Sharma et al., 2020). Hence, the focus of occlusion as a risk factor for TMD has shifted, and other putative factors have been identified, such as genetic predisposition, central neural system pain control mechanisms, psychosocial status, and parafunctions, with all of these playing an important role in TMD evolution (Slade et al., 2016). Based on current evidence, changing the occlusion to treat TMD is not recommended (Kandasamy et al., 2018). Conversely, reversible treatments should be preferred, also because of large fluctuations in the signs and symptoms of TMDs. Symptoms may spontaneously decrease or even disappear without any treatment; hence, conservative management is recommended including cognitive behavioral therapies, biofeedback, oral occlusal appliances, physical therapies, and pharmacological agents (Al-Moraissi et al., 2020, 2022). Epidemiological studies indicate an increased prevalence of TMJ disorders, such as clicking sounds, in the age range between 15 and 25 years or younger (Magnusson et al., 1994; Rauch et al., 2020); this age range corresponds to the time when adolescents or young adults more frequently seek orthodontic treatment. Considering that the average duration of orthodontic treatment is around 20 months, it is very likely that TMDs occur during or after the orthodontic treatment and patients may assume that they causally relate to that treatment (Michelotti and Iodice, 2010).

How should orthodontists manage a patient with signs and symptoms of TMD before or during treatment (Figure 21.2)? In general, before the orthodontic treatment it is important to screen the patient for TMD, and DC/TMD is a good instrument for identifying TMD (Schiffman et al., 2014). If a patient presents signs or symptoms of TMD before starting orthodontic treatment, the first step is to make a diagnosis, considering possible differential diagnoses, and then, in the case of TMD, start conservative therapy such as pharmacotherapy, counseling, behavioral therapy, home exercises, physical therapy, and/or occlusal appliances to manage signs and symptoms. In general, the orthodontic treatment should not be initiated if TMD pain is significant (Michelotti and Iodice, 2010). Moreover, patients with a positive history of TMD might be more prone to developing TMD during the treatment, or sometimes TMD might occur for the first time during the orthodontic treatment. In this case, the first step is to make a correct diagnosis, temporarily suspend or reduce the active orthodontic phases (e.g. intermaxillary elastics), and then manage the signs and symptoms until remission. When the patient is

pain free or symptoms become very mild, orthodontic treatment can be continued as previously planned or, if necessary, modified according to the patient's condition. Furthermore, the doctor should emphasize that TMDs are highly prevalent in the general population and present a multifactorial etiology, and evidence does not support a possible cause–effect relationship between orthodontic treatment and TMD (Michelotti and Iodice, 2010).

There is no convincing evidence supporting the idea that occlusion or malocclusion or orthodontic treatment might cause TMDs; but some TMDs, such as osteoarthrosis or arthralgia, might cause occlusal alterations like open bite, crossbite, or Class II malocclusion. Hence, an appropriate TMJ examination before starting orthodontic treatment is needed and could affect treatment planning, which should be tailored to the patient's conditions and expectations (Caldas et al., 2016). In the next section we discuss the most common TMDs that occur before, during, or after orthodontic treatment (joint pain and disc displacement), and then we consider local or systemic conditions that may affect the TMJs and also have an impact on dental occlusion.

Joint pain: Arthralgia

Arthralgia is defined as joint pain that is affected by jaw movement, function, or parafunction, and replication of this pain occurs with provocation testing of the TMJs.

The DC/TMD provides a flow diagram for the diagnosis of arthralgia and its diagnostic accuracy (Table 21.1; Schiffman et al., 2014). When arthralgia is present, the pain is reported to be directly in front of the ear, the lateral pole of the condyle is usually tender to palpation, and the pain is usually constant and increased by jaw movements.

Arthralgia might be a symptom linked to several conditions, such as inflammation of different components of the TMJ (ligaments, retrodiscal tissue, bone, fibrocartilage), and it is often present in the case of arthritis. Arthritis is defined as an inflammation or infection associated with edema, erythema, and/or increased temperature over the affected joint, and it includes inflammation not only of the bone structures but also other TMJ structures such as synovia (synovitis) or capsule (capsulitis), and retrodiscal structures (retrodiscitis). The majority of inflammatory conditions affecting the joint are secondary to macro- or microtrauma to the tissues within the joint, such as a bump to the chin (microtrauma), onychophagia, tooth grinding, or tooth clenching (microtrauma; Sierwald et al., 2015; Slade et al., 2016). Furthermore, internal derangements of the TMJ (disc displacement with or without reduction) might also be a cause of arthralgia due to a possible inflammation of the retrodiscal tissue (Naeije et al., 2013). Retrodiscal tissue is not as able to adsorb the stress as the articular disc, hence the load present on this area will provoke inflammation and pain. In this case, the patient usually reports trauma and/or joint sounds and/or limitation of mouth opening, and pain is modified during jaw movements.

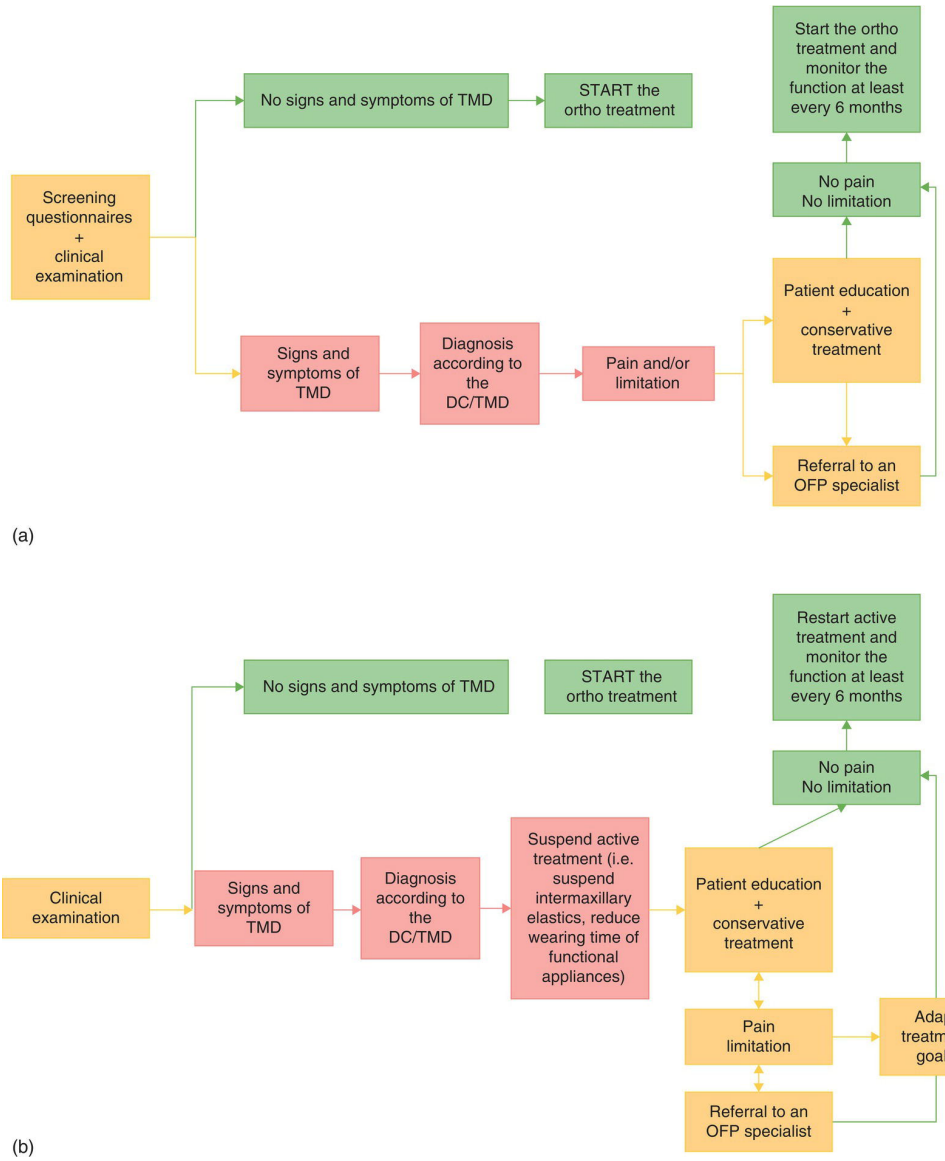


Figure 21.2 Scheme for patient management before (a) or during (b) orthodontic treatment. DC/TMD, diagnostic criteria for temporomandibular disorders; OFP, orofacial pain; TMD, temporomandibular disorders.

Table 21.1 Diagnostic criteria for temporomandibular disorders.

Source: Adapted from Peck et al. (2014).

Diagnosis	History	Clinical examination	Imaging	Notes
Arthralgia	Positive for both of the following: 1. Pain in the jaw, temple, in front of the ear, or in the ear AND	Positive for both of the following: 1. Confirmation of pain location in the area of the TMJ(s) AND		The pain is not better accounted for by another pain diagnosis

Diagnosis	History	Clinical examination	Imaging	Notes
	2. Pain modified with jaw movement, function, or parafunction	2. Report of familiar pain in the TMJ with at least one of the following provocation tests: a. Palpation of the lateral pole or around the lateral pole OR b. Maximum unassisted or assisted opening, right or left lateral movements, or protrusive movements		
Arthritis	Positive for both of the following: Arthralgia as defined previously AND Swelling, redness, and/or increased temperature in front of the ear OR Dental occlusal changes resulting from articular inflammatory exudate (e.g. posterior open bite)	Positive for both of the following: Arthralgia as defined previously AND Presence of edema, erythema, and/or increased temperature over the joint OR Reduction in dental occlusal contacts noted between two consecutive measurements (unilateral/ bilateral posterior open bite), and not attributable to other causes		Rheumatological consultation when needed: 1. Negative for rheumatological disease, including those in systemic arthritides Note: The pain is not better accounted for by another pain diagnosis
Osteoarthrosis	Positive for at least one of the following: 1. In the last 30 days any TMJ noise(s) present with jaw movement or function OR 2. Patient report of any noise present during the exam	Positive for the following: Crepitus detected with palpation during maximum unassisted opening, maximum assisted opening, lateral or protrusive movements	When this diagnosis needs to be confirmed, TMJ CT/CBCT criteria are positive for at least one of the following: 1. Subchondral cyst(s) OR 2. Erosion(s) OR	Rheumatological consultation when needed: 1. Negative for rheumatological disease, including those in systemic arthritides

Diagnosis	History	Clinical examination	Imaging	Notes
			3. Generalized sclerosis OR 4. Osteophyte(s)	
Osteoarthritis	Positive for both of the following: In the last 30 days any TMJ noise(s) present with jaw movement or function OR Patient report of any noise present during the exam AND Arthralgia as defined previously	Positive for both of the following: 1. Crepitus detected with palpation during maximum unassisted opening, maximum assisted opening, right or left lateral movements, or protrusive movements AND 2. Arthralgia as defined previously	TMJ CT/CBCT criteria (Ahmad et al. 2009; Mallya et al. 2022) are positive for at least one of the following: 1. Subchondral cyst(s) OR 2. Erosion(s) OR 3. Generalized sclerosis OR 4. Osteophyte(s)	Rheumatological consultation when needed: 1. Negative for rheumatological disease, including those in systemic arthritides
Disc displacement with reduction	Positive for at least one of the following: 1. In the last 30 days any TMJ noise(s) present with jaw movement or function OR 2. Patient report of any noise present during the exam	Positive for at least one of the following: Clicking, popping, and/or snapping noise detected during both opening and closing, with palpation during at least 1 of 3 repetitions of jaw opening and closing OR Clicking, popping and/or snapping noise detected with palpation during at least 1 of 3 repetitions of opening or closing AND Clicking, popping, and/or snapping noise detected with palpation during at least 1 of 3 repetitions of right or left lateral movements, or protrusive movements	When this diagnosis needs to be confirmed, then TMJ MRI criteria are positive for both of the following: 1. In the maximum intercuspal position, the posterior band of the disc is located anterior to the 11:30 position and the intermediate zone of the disc is anterior to the condylar head AND 2. On full opening, the intermediate zone of the disc is located between the condylar head	

Diagnosis	History	Clinical examination	Imaging	Notes
			and the articular eminence	
Disc displacement with reduction with intermittent locking	Positive for both of the following: In the last 30 days, any TMJ noise(s) present with jaw movement or function OR Patient report of any noise present during the exam AND In the last 30 days, jaw locks with limited mouth opening, even for a moment, and then unlocks	Positive for the following: 1. Disc displacement with reduction as defined previously. Although not required, when this disorder is present clinically, examination is positive for inability to open to a normal amount, even momentarily, without the clinician or patient performing a specific manipulative maneuver	When this diagnosis needs to be confirmed: 1. The imaging criteria are the same as for disc displacement with reduction if intermittent locking is not present at the time of imaging. If locking occurs during imaging, then an imaging-based diagnosis of disc displacement without reduction will be rendered and clinical confirmation of reversion to intermittent locking is needed	
Disc displacement without reduction with limited opening	Positive for both of the following: 1. Jaw locked or caught so that the mouth would not open all the way AND 2. Limitation in jaw opening severe enough to limit jaw opening and interfere with ability to eat	Positive for the following: Maximum assisted opening (passive stretch) including vertical incisal overlap <40 mm (maximum assisted opening of <40 mm is determined clinically)	When this diagnosis needs to be confirmed: 1. In the maximum intercuspal position, the posterior band of the disc is located anterior to the 11:30 position and the intermediate zone of the disc is anterior to the	

Diagnosis	History	Clinical examination	Imaging	Notes
			condylar head AND 2. On full opening, the intermediate zone of the disc is located anterior to the condylar head	
Disc displacement without reduction without limited opening	Positive for both of the following: 1. Jaw locked or caught so that the mouth would not open all the way AND 2. Limitation in jaw opening severe enough to limit jaw opening and interfere with ability to eat	Positive for the following: 1. Maximum assisted opening (passive stretch) including vertical incisal overlap ≥40 mm (maximum assisted opening of ≥40 mm is determined clinically)	When this diagnosis needs to be confirmed, then imaging analysis criteria are the same as for disc displacement without reduction with limited opening, as defined previously	
Systemic arthritides	Positive for both of the following: Rheumatological diagnosis of a systemic inflammatory joint disease AND In the past month, any temporomandibular joint pain present OR Temporomandibular joint pain that worsens with episodes/exacerbations of the systemic inflammatory joint disease	Positive for both of the following: Rheumatological diagnosis of a systemic joint disease AND Arthritis signs and symptoms as defined previously OR Crepitus detected with palpation during maximum unassisted opening, maximum assisted opening, right or left lateral movements, or protrusive movements	Imaging: If osseous changes are present, TMJ CT/CBCT or MRI is positive for at least one of the following: 1. Subchondral cyst(s) OR 2. Erosion(s) OR 3. Generalized sclerosis OR 4. Osteophyte(s)	
Idiopathic condylar resorption	Positive for the following: 1. Progressive dental occlusal changes	Positive for both of the following: 1. Anterior open bite AND 2. Evidence of progressive dental occlusal change with at least one of the following:	Positive for at least one of the following: 1. CT/CBCT evidence of resorption of part or all of the condyle(s) OR	Rheumatological consultation when needed: 1. Negative for rheumatological disease, including those in systemic arthritides

Diagnosis	History	Clinical examination	Imaging	Notes
		a. Occlusal facets that cannot be approximated OR b. Change in sequential dental occlusal measurement over time (horizontal overjet; vertical overbite; or intercuspal contacts)	2. Lateral cephalometric change with sequential imaging over time (clockwise mandibular rotation, i.e. increase in mandibular plane angle; increase in ANB)	
Aplasia	Positive for both of the following: 1. Progressive development of mandibular asymmetry or micrognathia from birth or early childhood AND 2. Development of malocclusion, which may include anterior or posterior open bite	Positive for both of the following: 1. Confirmation of mandibular asymmetry, with deviation of the chin to the affected side, or micrognathia AND 2. Unable to detect condyle with palpation during open–close, protrusive, or lateral jaw movements	TMJ CT/CBCT is positive for the following: 1. Aplasia of the condyle AND 2. Severe hypoplasia of the fossa and eminence	
Hypoplasia	Positive for both of the following: 1. Progressive development of mandibular asymmetry or micrognathia from birth or early childhood AND 2. Development of malocclusion, which may include posterior open bite	Positive for the following: Confirmation of mandibular asymmetry, with deviation of the chin to the affected side, or micrognathia	CT/CBCT is positive for at least one of the following: 1. Hypoplasia of the condyle OR 2. Hypoplasia of the fossa OR Shortened mandibular ramus height	

Diagnosis	History	Clinical examination	Imaging	Notes
Hyperplasia	Positive for the following: 1. Progressive development of mandibular or facial asymmetry	Positive for the following: 1. Confirmation of a positive history	Panoramic radiography and/or CT/CBCT and single photon emission computed tomography are positive for both of the following: 1. Asymmetry in mandibular ramus height AND 2. History of increased uptake of Technetium-99m hydroxy diphosphonate on bone scintigraphy	

CT/CBCT, computed tomography/cone beam computed tomography; MRI, magnetic resonance imaging; TMJ, temporomandibular joint.

Another possible condition associated with arthralgia is osteoarthritis/osteoarthrosis; that is, inflammation of the articular surfaces of the joint. It is characterized by degeneration of the bone tissue of the TMJ, and in severe cases can provoke a malocclusion such as anterior or posterior open bite. Overload of the TMJs is an aggravating factor and can be associated with disc displacement with or without reduction (Kurita et al., 2006). Pain is usually unilateral, increases during palpation and during jaw movements, and might be associated with crepitus during auscultation (Alstergren et al., 2018).

Since mechanical overload of the joint structures is an aggravating factor, treatment should attempt to decrease this loading. The management of arthralgia involves elimination of microtrauma, suggestion of a pain-free diet with slow movements during chewing and small bites, prescription of mild analgesics (nonsteroidal anti-inflammatory drugs [NSAIDs], naproxen), physiotherapy, use of minimally invasive therapy (such as arthrocentesis), and use of an occlusal appliance to reduce overload of the joint (Al-Moraissi et al., 2020). Often arthritis may evolve in complete resolution while osteoarthritis may evolve in a remodeling of the TMJ (Han et al., 2021; Rasmussen, 1981).

Disc disorders

TMJ disc disorders include four conditions described as intracapsular disorders involving the condyle–disc complex. According to the DC/TMD (Schiffman et al., 2014), the four conditions are disc displacement with reduction, with intermittent locking, without reduction with limited opening, and without reduction without limited opening. The diagnostic validity of all these conditions has been thoroughly tested (Table 21.1).

Disc displacement with reduction

In the closed mouth position the disc is displaced relative to its normal relation with the condylar head and the disc reduces (that is, relocates) on mouth opening (Figure 21.3a). Clicking, popping, or snapping noises may occur when the disc is reduced. Magnetic resonance imaging (MRI) of the TMJ with closed and open mouth is the gold standard for this diagnosis; indeed, the clinical examination only presents a sensitivity of 0.34 and a specificity of 0.92 (Schiffman et al., 2014).

Disc displacement with reduction with intermittent locking

In the closed mouth position the disc is displaced relative to the condylar head, and the disc intermittently reduces on mouth opening. When the disc does not reduce with opening of the mouth, intermittent limited mandibular opening occurs. When limited opening occurs, a maneuver may be needed to unlock the TMJ.

Clicking, popping, or snapping noises may occur with disc reduction. Also in this case, MRI of the TMJ with closed and open mouth is the gold standard for diagnosis; indeed, the diagnostic value of clinical examination only presents a sensitivity of 0.38 and a specificity of 0.98 (Schiffman et al., 2014).

Disc displacement without reduction without limited opening

In a closed mouth position, the disc is displaced relative to the condylar head and does not reduce with mouth opening. This disorder is not associated with limited mandibular opening (maximum unassisted opening >40 mm; Figure 21.3b). MRI of the TMJ with closed and open mouth is the gold standard for this diagnosis; sensitivity of the clinical examination is 0.54 and specificity 0.79 (Schiffman et al., 2014).

Disc displacement without reduction with limited opening

In the closed mouth position the disc is displaced relative to the condylar head, and the disc does not reduce with mouth opening. This condition is associated with persistent limited mandibular opening (maximum unassisted opening <40 mm) that does not resolve with the clinician or patient performing a specific manipulative maneuver (Figure 21.3c). This is also referred to as “closed lock.” The presence of a TMJ noise (e.g. crepitus) does not exclude this diagnosis. MRI of the TMJ with closed and open mouth is the gold standard for this diagnosis; the sensitivity of clinical examination is 0.80 and specificity 0.97 (Schiffman et al., 2014).

The correct management of disc derangement disorders is based on two factors: making a correct diagnosis and understanding the natural course of the disorder. Disc displacement with reduction and disc displacement with reduction and with intermittent locking are two conditions that may present joint clicking, but that should be managed in different ways.

Disc displacement with reduction is a condition that requires treatment only if associated with pain. The prevalence of joint sounds, which often accompanies disc displacement with reduction, is very high in the general population; indeed, more than 25% of the population present joint sounds, but often they are asymptomatic and are not seeking treatment (Jussila et al., 2017; Talaat et al., 2018). Moreover, in community samples disc displacement with reduction was found in 26–38% of MRIs and was not associated with any sound or symptom.(Talaat et al., 2018; Tasaki et al., 1996). In some cases, however, disc displacement with reduction may cause pain (arthralgia), mainly due to the load applied to the retrodiscal tissue by the condyle when the disc in dislocated. In this case treatment is recommended, considering that pain may alter the mandibular function.

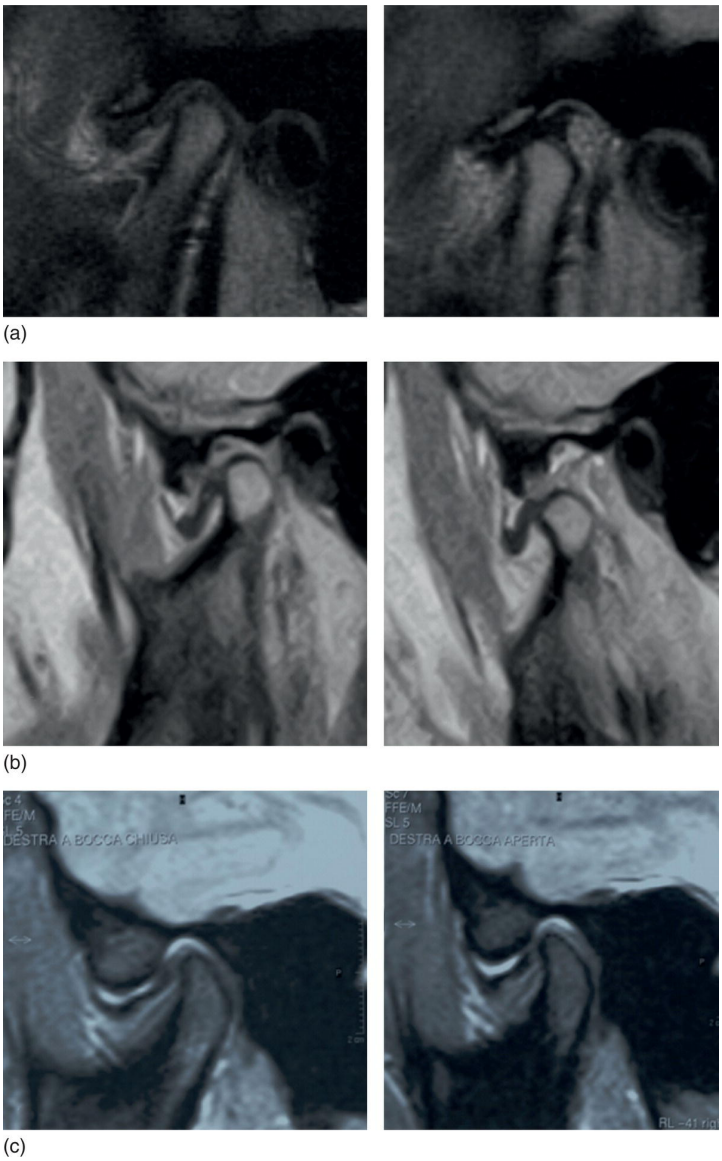


Figure 21.3 Magnetic resonance imaging of a temporomandibular joint showing the temporomandibular joint in a closed (left) and open (right) mouth with (a) disc displacement with reduction; (b) disc displacement without reduction without limited opening; and (c) disc displacement without reduction with limited opening.

In disc displacement with reduction and with intermittent locking, the disc reduction does not always happen during the opening pattern, but the patient should perform a maneuver, often a lateral jaw movement, to reduce the disc and open the mouth fully, while when the dislocation is not reduced the jaw opening is reduced. In this case, treatment should be focused on restoring a sufficient jaw opening, greater than 40 mm, and the elimination of pain.

However, in the absence of pain or mandibular opening reduction, disc displacement with reduction might not need treatment, especially nonreversible treatment. To clarify this concept, the evolution of disc displacement must be considered. First, it was previously mentioned that joint sounds might be asymptomatic and that disc displacement with reduction might be found in MRIs of people who do not present joint sounds (Talaat et al., 2018). Second, it was found that in 30–35% of cases with disc displacement with reduction, joint sounds come and go without any treatment and without any further sign or symptom of TMD, such as arthralgia or reduction of mandibular opening or osteoarthrosis (Magnusson et al., 1994; Okeson and Hayes, 1986). Third, analysis of the evolution of disc displacement

with reduction showed that in less than 10% of cases there is a progression of joint locking or osteoarthrosis (de Leeuw et al., 1994), while disc displacement with intermittent locking may evolve into disc displacement without reduction (Kalaykova et al., 2010, 2011).

Several treatments have been proposed for the management of disc displacement with reduction, both reversible and nonreversible. Reversible therapies include patient education (counseling about disc displacement with reduction), jaw exercises, relaxation techniques (Yoda et al., 2003), stabilization splint, and anterior positioning appliance (Poluha et al., 2019). The first stage of treatment is information from the clinician to the patient about the condition. Self-reports of TMJ clicking are more frequent in care-seeking patients who also have more nonspecific physical symptoms, with a propensity to somatization and with a heightened awareness of their own body image (Ukra et al., 2017). Hence, the doctor should explain that this condition is not an evolving one, that the disc displacement is fluctuating, and that most of the time it disappears without any treatment. Furthermore, the patient must be educated to avoid keeping teeth in touch, avoid excessive joint loading, and avoid self-provoking of the click. One recent study evaluated the treatment outcomes of a jaw exercise intervention program combined with an information/counselling program versus information/counseling alone based on an internet platform, and found that the combined program showed a better outcome compared to counseling alone (Wahlund et al., 2021). In addition, when a patient presents pain or intermittent locking, therapy with a stabilization splint or an anterior repositioning splint, and NSAIDs in the acute phase, may be indicated.

An anterior positioning appliance postures the mandible forward in a position where the joint sound during the opening disappears. This appliance should be worn during the night and in some cases for a few hours during the day, mainly to lower the load on the retrodiscal area, and indeed it may help to reduce joint pain. The aim of this appliance is not to recover the disc position considering the high percentage of relapse (Chen et al., 2017). However, this appliance may lead to unwanted occlusal changes if worn for a long period (Conti et al., 2015).

Good results in controlling joint pain secondary to joint clicking can also be achieved with a stabilization splint with well-distributed occlusal contacts, which has a lower risk of inducing occlusal changes (Conti et al., 2006).

Surgical therapy and occlusal therapy, with prosthodontic or orthodontic approaches, are among the nonreversible treatments for disc displacement with reduction. The basis of occlusal therapy is to shift the mandible into a new intercuspal position where the joint sound disappears. However, the long-term success of the recaptured disc is unpredictable. Indeed, both reversible and nonreversible treatments may present a high percentage of relapse, around 50%, for joint sounds, while arthralgia and locking show a good prognosis with reversible therapies (Okeson, 2013). As Okeson stated, “The reasonable goal of definitive therapy for disc displacements and disc dislocations with reduction is to reduce intracapsular pain, not to recapture the disc” (Okeson, 2013: 417).

Disc displacement without reduction with or without limited opening is not associated with joint sounds, but during the clinical examination a reduced mouth opening (less than 40 mm), a reduced laterotrusion to the contralateral side, and an uncorrected deviation ipsilateral to the affected side might be present. Patients often report a history of a click that suddenly disappears with the reduction of the mouth opening, or a sudden reduction of the opening without a history of joint sounds.

Depending on the time from onset of the condition, two different management approaches are possible: in the first week following the dislocation, a reduction of disc position by means of condylar distraction might be attempted, but then success with reduction becomes very unlikely and the main treatment goal should be to restore function. The natural course of untreated symptomatic disc displacement without reduction was investigated in a cohort of patients with a 2.5-year follow-up; 43% of 40 patients were asymptomatic, 25% did not improve and required treatment, and 33% spontaneously improved. The presence of osteoarthritis and advanced stages of internal derangement was predictive of a poor treatment outcome (Kurita et al., 2006). Hence, while in an acute condition the clinician should try to reduce the disc dislocation, in a chronic condition, when the normal anatomy of the disc is lost and bone remodeling is present, therapy with exercises and mobilization of the joint, and a stabilization splint to reduce the loading of the retrodiscal tissue allowing better natural healing of the TMJ, should be followed (La Touche et al., 2020). Restoring jaw function may require time, up to 8–12 months or more. Surgical treatments such as arthrocentesis can be considered for the management of the pain and dysfunction associated with the condition (Tatli et al., 2017).

Occlusal changes due to temporomandibular disorders

TMDs can also be the cause of occlusal changes that might be misdiagnosed and mistreated by clinicians. In some cases these changes are transient and disappear with TMD treatment, while in other cases the role of the orthodontist is to compensate for the occlusal changes due to TMJ alteration with camouflage; in some other cases it is necessary to prepare the patient for orthognathic surgery. It is important for orthodontists to recognize possible causes of transient occlusal changes that should not be treated by irreversible orthodontic treatment, and the occlusal changes that should be treated by irreversible therapies.

Joint effusion and unilateral open bite

The most common transitory occlusal change due to TMJ problems is unilateral open bite due to joint effusion (Caldas et al., 2016). Joint effusion is defined as the collection of fluid in the TMJ space, and can be assessed by MRI (Khawaja et al., 2017). Fluid in the joint capsule changes the disc and condyle position within the fossa and the patient feels a different teeth contact, which increases on the contralateral canine with deviation of the lower midline and open bite ipsilateral to the affected side. TMJ effusion is not always associated with arthralgia; indeed, sometimes occlusal changes might be the only sign of effusion into the glenoid fossa. In this case it is extremely important to collect an accurate history from the patient, to investigate when this lateral open bite occurred, history of TMD, history of trauma, whether the patient perceives a swelling of the area in front of the ear, and whether there is pain (Marinho and McLoughlin, 1994). Differential diagnosis should include systemic arthritis, coagulopathies (hemarthrosis may create similar signs), neoplasia, and fractures. The treatment must be focused on elimination of the effusion using NSAIDS and eventually liquid aspiration. In a few weeks, the patient should achieve the same intercuspal position as before the acute episode.

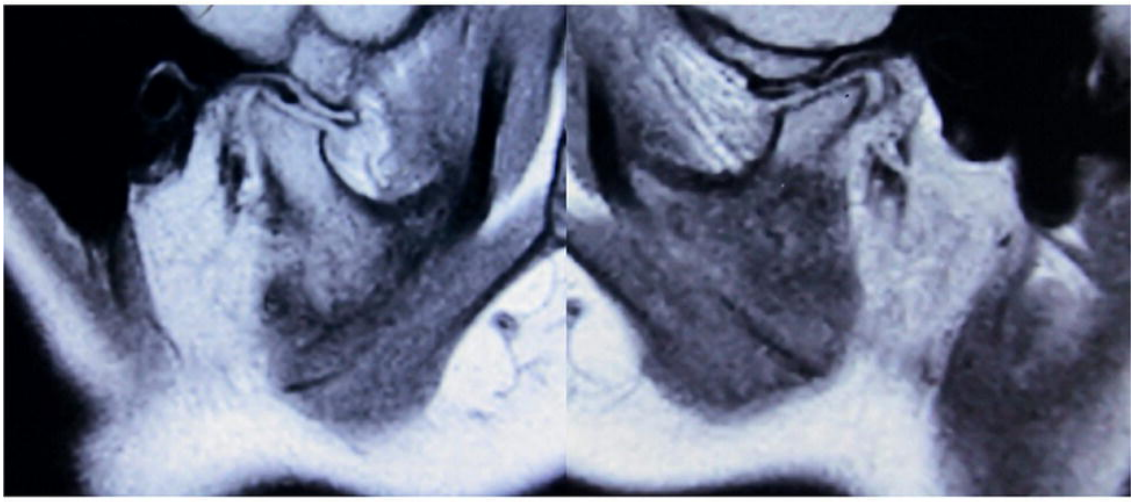
Temporomandibular joint bone alteration and occlusal changes

Systemic arthritides

TMJ inflammation might be the consequence of a generalized systemic inflammatory disease such as rheumatoid arthritis, juvenile idiopathic arthritis (JIA; Figure 21.4), spondyloarthropathies, or other autoimmune or mixed connective tissue disorders. The role of the dentist/orthodontist is mainly to monitor the possible involvement of the TMJs and its evolution.

The expanded taxonomy of DC/TMD describes criteria for the diagnosis of systemic arthritides; however, sensitivity and specificity for the diagnosis of TMJ involvement for each systemic disease have not been established (Peck et al., 2014). Rongo and coworkers assessed the diagnostic performance of the DC/TMD of systemic arthritides for the evaluation of TMJ involvement in patients with JIA. A low sensitivity of 0.15 and a high specificity of 0.92 were found, which is mainly due to two considerations: (i) crepitus is present only when TMJ damage is severe; and (ii) joint pain, instead, is seldom reported in JIA (Rongo et al., 2019). On the other hand, the TMJ is involved in 17–87% of children with JIA depending on subtype, diagnostic criteria used, and ethnicity (Ringold and Cron, 2009; Twilt et al., 2006, 2007).

(a)



(b)

Figure 21.4 (a) Panoramic x-ray and (b) magnetic resonance imaging of a temporomandibular joint in a patient with juvenile idiopathic arthritis and osteoarthrosis.

JIA is the most common inflammatory rheumatic disease of childhood. It develops before 16 years of age, persists for at least six weeks, and has no identifiable cause (Petty et al., 2004). The most challenging aspect for both rheumatologist and dentist/orthodontist in the management of children with JIA is control of the growth disturbances that the TMJ involvement can lead to (Resnick et al., 2019). Indeed, severe cases of TMJ arthritis can present mandibular asymmetry, when unilateral, or mandibular micrognathia, when bilateral, associated with dental Class II, open bite, and crossbite (Billiau et al., 2007). Furthermore, signs of mandibular dysfunction can be reported such as deviation on mouth opening, reduced mouth opening, arthralgia, and myalgia (Stoustrup et al., 2012). Finally, orofacial signs and symptoms of JIA significantly reduce the quality of life of children and also have impacts on their day-to-day life (Rahimi et al., 2018). Orofacial signs and symptoms are often not related to the active phase of the TMJ arthritis, but are consequences of the damage that interferes with the correct functioning of the jaw with abnormal loading of the TMJs, and then the onset of pain or dysfunction. Clinicians should be aware that early identification of TMJ involvement is important, and although the gold standard for the evaluation of TMJ arthritis is MRI with gadolinium, the clinical examination has an important role in screening, making a working diagnosis, and follow-up. Stoustrup and colleagues (2020) identified five domains that must be included in an orofacial examination for JIA

patients: medical history, orofacial symptoms, muscle and TMJ function, orofacial function, and dentofacial growth; and they developed a three-minute screening protocol including these five domains, useful for both clinical and research settings.

The management of TMJ arthritis aims to reduce inflammation, reduce orofacial signs and symptoms, correct or control growth disturbances, and treat possible malocclusion. Orthodontists may play a role in all these aspects. Obviously, the main treatment in these patients is systemic treatment, which with time has evolved from the use of methotrexate to the use of biologic drugs. In addition to this systemic treatment, there is evidence supporting the use of a stabilization splint to reduce the orofacial symptoms, or functional appliances such as the distraction splint to control or correct growth disturbances (Pedersen and Carlalberta, 2015; Stoustrup et al., 2014).

Finally, orthognathic interventions can be performed in these patients to treat growth disturbances, such as orthognathic surgery in skeletal mature patients, distraction osteogenesis in growing subjects, and alloplastic TMJ reconstruction in extremely severe cases. Resnick et al. (2019) proposed an algorithm based on ongoing active disease, skeletal maturity, and degree of facial deformity. This aims to aid clinicians in the treatment planning pathway and to provide a more standardized approach to surgically managing dentofacial deformity in JIA (Resnick et al., 2019; Stoustrup et al., 2021).

It must be considered that TMJ arthritis management is based on a multidisciplinary approach in which, together with the rheumatologist, other specialists are involved such as radiologists, physiotherapists, psychologists, and orthodontists. This can contribute to avoid important sequelae due to JIA involvement of the TMJs.

Idiopathic condylar resorption

Idiopathic condylar resorption (ICR) is defined as “Resorption of the condyles, leading to the idiopathic loss of condylar height, and a progressive anterior open bite” (Peck et al., 2014: 11).

ICR is a rare condition, more frequent in girls between the ages of 15 to the early 20s, is often bilateral, and may provoke important occlusal changes such as open bite, loss of chin projection, and/or asymmetry (Ji et al., 2020). It is a self-limiting condition that may last from six months to two years, can have different degrees of severity, and in many cases the treatment is orthognathic surgery (Hoppenreijs et al., 1999; Wolford, 2001). ICR is characterized by a loss of condylar mass with a decrease in ramus height. The etiology of ICR is mostly unknown; however, orthognathic patients with Class II with severe high mandibular plane are considered the most susceptible to ICR or progressive condylar resorption (PCR), above all in cases of mandibular advancement of more than 5 mm (Scheerlinck et al., 1994). Besides, a recent systematic review highlights not only the role of orthognathic surgery, but also the low level of 17β-estradiol and condylar anatomy as possible etiologies of ICR (Ji et al., 2020).

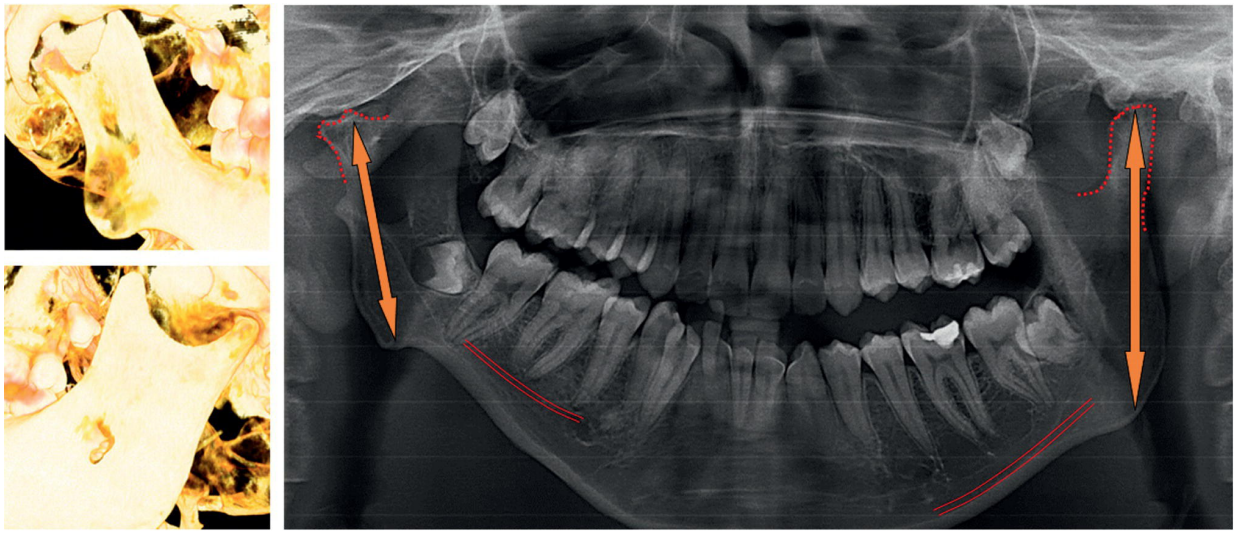
Imaging supports the diagnosis of ICR, and cone beam computed tomography allows three-dimensional evaluation of the condyle and analysis of the possible loss of bone tissue in the TMJ structure, in the ramus, and in the corpus of the mandible. Treatment of ICR depends on the level of activity of the pathology and the grade of condylar alteration. In a case of an acceptable condylar shape that might ensure good stability of the TMJ, the treatment options can include orthodontic camouflage or orthognathic treatment. In a case of more severe condylar resorption, a reconstruction of the condyle or of the ramus may be required (Ji et al., 2020; Peacock et al., 2019). ICR may affect the TMJs independently of orthognathic surgery or orthodontic treatment; indeed, sometimes patients who did not have any treatment present with ICR. However, orthognathic surgery in more severe high-angle Class II patients seems to be an initiating factor of ICR increasing the condyle load in predisposed subjects (Haskin et al., 1995). Unfortunately, there are no biomarkers that can help in identifying these predisposed patients. If ICR starts during orthodontic treatment, usually it produces sudden changes of the occlusion, such as open bite consequent to jaw post rotation. These signs should not be confused with an iatrogenic open bite due to orthodontic mismanagement. Indeed, the clinician should be aware of the possible risk and suggest performing an x-ray to identify possible condylar damage.

Congenital/developmental disorders

Aplasia/hypoplasia

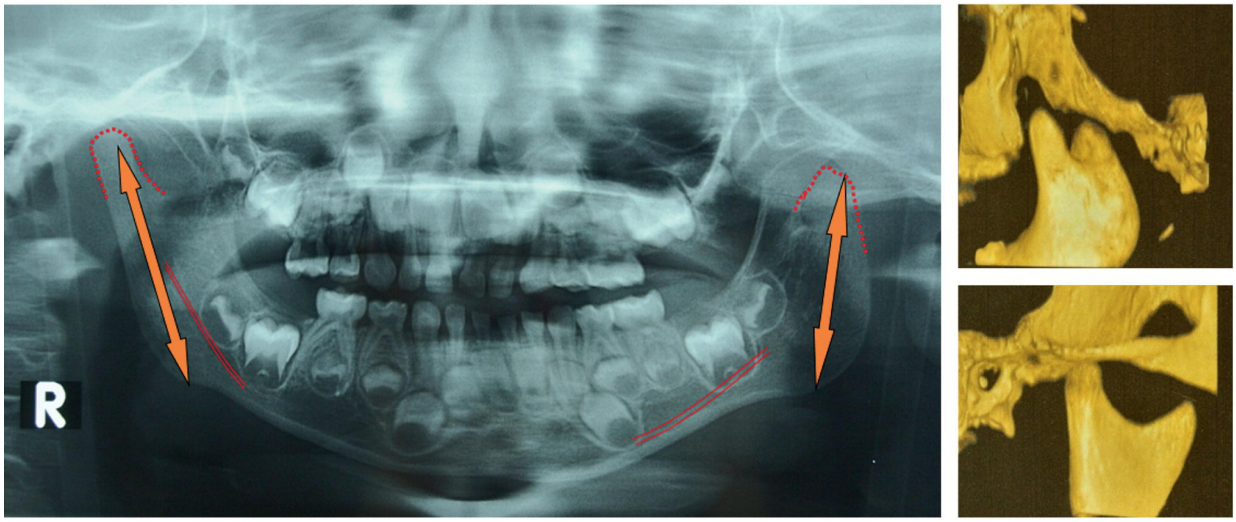
Mandibular aplasia/hypoplasia is characterized by the unilateral absence or underdevelopment of the condyle associated with incomplete development of the fossa and of the eminence, resulting in facial asymmetry; rarely it can be bilateral, resulting in severe micrognathia with possible open bite. Mandibular aplasia/hypoplasia can be either congenital or acquired (Berraquero et al., 1995; Lee et al., 2001). Congenital hypoplasia is usually the expression of more complex congenital syndromes originating in the first and second branchial arches, such as Goldenhar syndrome (Figure 21.5), hemifacial microsomia, or Treacher Collins syndrome. Acquired (secondary) condylar hypoplasia may be caused by local factors (trauma, infection of the mandibular bone or middle ear, irradiation) or by systemic factors (toxic agents, rheumatoid arthritis, mucopolysaccharoidosis; Tank et al., 1998).

Congenital aplasia/hypoplasia treatment includes mainly orthognathic surgery, both with osteodistraction and with mandibular advancement, considering that the affected side of the mandible does not grow (Sadakah, 2009). In this case the role of the orthodontist is critical for the diagnosis, even if in Treacher Collins syndrome or Goldenhar syndrome the diagnosis is made at a very early phase of life, and in the preparation of the occlusion before orthognathic surgery. However, in some cases the functional treatment may help with the management of condylar hypoplasia, like in the case of hemimandibular hypoplasia with condylar-coronoid collapse (HH-CCC; Figure 21.6). HH-CCC is a particular form of condylar hypoplasia that often is misdiagnosed as hemifacial microsomia but has two clear differences: (i) the soft tissues of the patient are normal so there are no malformations of the ears or of the muscles; and (ii) the condyle is collapsed against the coronoid process (Meazzini et al., 2011; Perrotta et al., 2020a). The treatment options for HH-CCC might be functional therapy or distraction osteogenesis (Perrotta et al., 2020a). In a long-term follow-up study comparing patients with hemifacial microsomia and HH-CCC treated by distraction osteogenesis, it was found that patients with HH-CCC had a more stable result, while patients with hemifacial microsomia returned to the original ratio between the affected and unaffected ramus heights. This relapse is probably mainly due to the alteration of the neuromuscular structure of the affected side that tended to return to the starting point (Meazzini et al., 2011).



(a) (b)

Figure 21.5 (a) Cone beam computed tomography and (b) panoramic x-ray of a temporomandibular joint in a patient with Goldenhar syndrome. Red dotted lines show the condylar profile (right side reduced in height and deformed); red solid lines indicate the mandibular canal; orange arrows indicate mandibular ramus heights.



(a) (b)

Figure 21.6 (a) Panoramic x-ray and (b) cone beam computed tomography of a temporomandibular joint in a patient with hemimandibular hypoplasia with condylar-coronoid collapse (HH-CCC). Red dotted lines show the condylar profile (left side reduced in height and with condyle collapsed on coronoid); red solid lines indicate the mandibular canal; orange arrows indicate mandibular ramus heights.

Acquired condylar hypoplasia might instead be mainly associated with a history of trauma or infection or rheumatoid arthritis; however, in this case the possible facial deformity might present later, after the cause of the hypoplasia, depending on the growth rate of the rest of the maxillo-mandibular complex (Kaneyama et al., 2008). If the hypoplasia is unilateral, the normal growth of the contralateral side causes asymmetry toward the affected side, and results in a crossbite and possibly a unilateral open bite on the affected side. If the hypoplasia is bilateral, there is a tendency to micrognathia and possible crowding with severe open bite. However, if the growth is slow, and the mandible grows with clockwise rotation, the compensatory growth of the maxilla may result in a deep bite, vertical maxillary excess, and

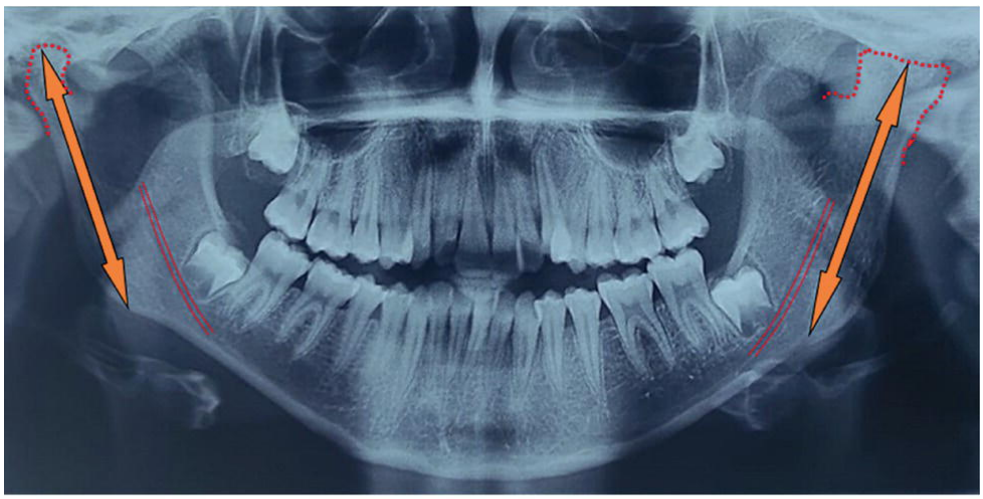
a gummy smile. Orthodontic treatment should start only when the active phase of the inflammation or of the injury is over.

Hyperplasia

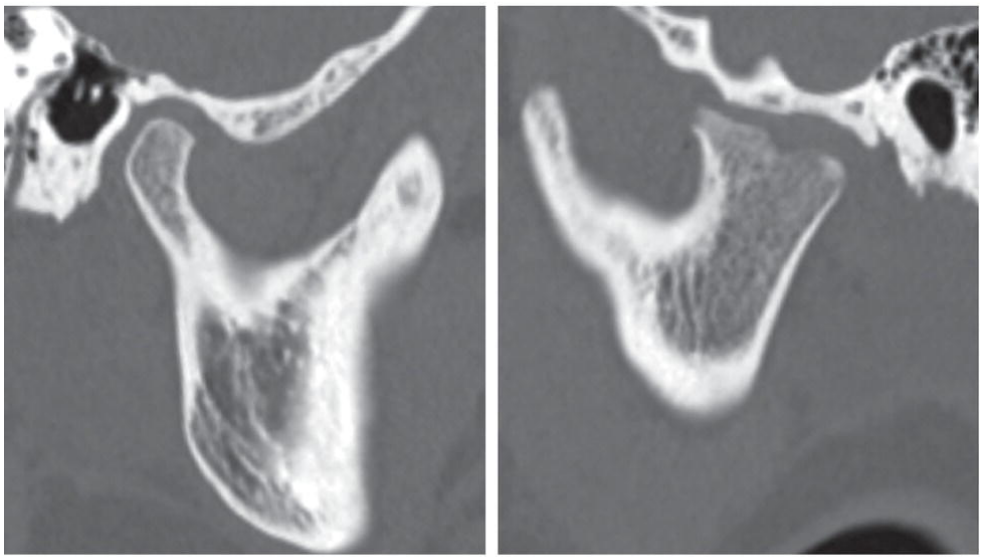
Mandibular hyperplasia is defined as overdevelopment of the mandible. Hyperplasia is typically unilateral, and can be localized at the condyle (condylar hyperplasia) or affecting the whole mandible (mandibular elongation of hemimandibular hyperplasia; Nitzan et al., 2008; Obwegeser and Makek, 1986; Walters et al., 2013).

Condylar hyperplasia is a pathological overgrowth condition in the condylar process, which leads to variable abnormal mandibular and/or facial asymmetry (Figure 21.7). The etiology is unknown, and it is characterized by persistent or increased unilateral condylar growth. Often condylar hyperplasia usually starts around puberty, up to 20 years old (Obwegeser and Makek, 1986).

The continued growth of the condyle provokes facial asymmetry and deviation of the chin to the unaffected side, with a possible crossbite on the unaffected side. Considering the velocity of condylar growth, a compensatory extrusion of the maxillary teeth of the ipsilateral side can induce canting of the occlusal plane. A panoramic radiograph generally shows an elongation of the condylar neck of the affected side; however, cone beam computed tomography allows three-dimensional evaluation with a relatively low dose for the patient (Xiao et al., 2022). An important analysis is bone scintigraphy with 99mTc methylene diphosphonate, to reveal possible asymmetrical growth activity in the mandibular condyles. If the difference in the uptake of the radiotracer between the condyles exceeds 10%, which is considered to be the cut-off value (Deleurant et al., 2008), a high condylectomy or condylar shaving on the affected side is indicated to stop excessive growth (Ghawsi et al., 2016; Li et al., 2022).



(a)



(b)

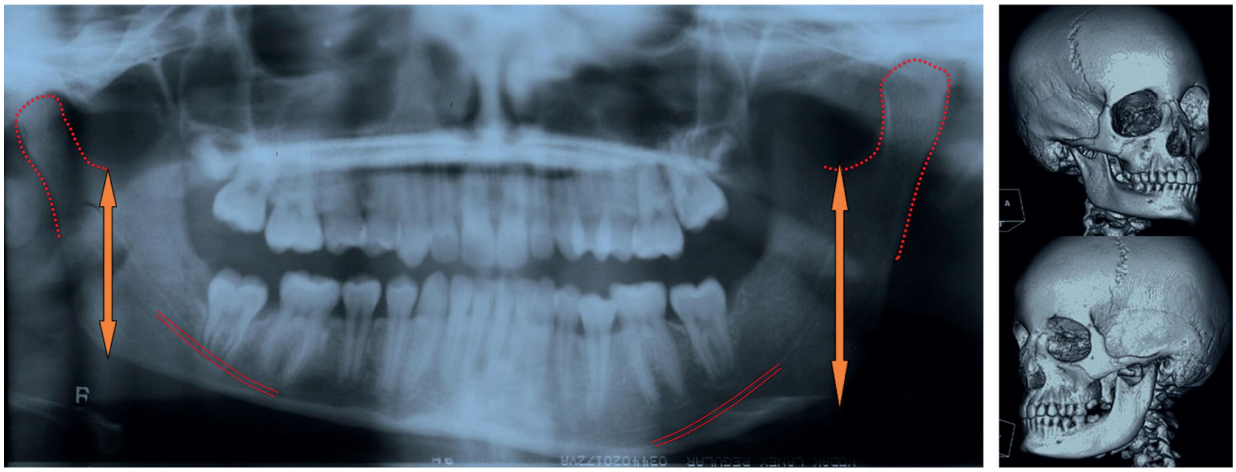
Figure 21.7 (a) Panoramic x-ray and (b) cone beam computed tomography of a temporomandibular joint in a patient with condylar hyperplasia. Red dotted lines show the condylar profile (right condyle increased in height and dimension); red solid lines indicate the mandibular canal; orange arrows indicate mandibular ramus heights.

High condylectomy is a surgical procedure aiming to remove the upper 2–3 mm of the growing cartilage of the condyle and does not affect jaw function. After surgery, orthodontic treatment is necessary to obtain good occlusion and increase the stability of the results. Sometimes the patient needs a second intervention of orthognathic surgery to complete the correction of the skeletal disharmony (Gallagher et al., 2021; Li et al., 2022; Niño-Sandoval et al., 2019).

Hemimandibular hyperplasia is a rare developmental asymmetry characterized by three-dimensional enlargement of half of the mandible (Figure 21.8). It usually involves the condyle, condylar neck, ramus, and body, up to the symphysis, hence half the mandible is hyperplastic. Females are more commonly affected by hemimandibular hyperplasia at any age, and the etiology is not clear (Gateno et al., 2021).

The clinical examination shows an elongated mandibular ramus on one side, generally with minimal shift of the lower dental midline. On the affected side there is elongation of the mandibular alveolar process, bowing down of the lower border with a low running mandibular canal, and an affected gonial angle rounded off in a more caudal position. Maxillary bone and sinuses show compensatory alterations

with downward growth and elongation of the alveolar process on the affected side. Occlusal examination usually shows Class II/2 malocclusion, tilting of the occlusal plane and lip commissure, and rotation of the occlusion in the vertical and axial planes. Diagnosis can be determined by radiographical examination, although clinical diagnosis is still the gold standard. A double mandibular lower contour is noticeable on a lateral cephalogram. An orthopantomogram (OPT) reveals an increased size of the affected mandibular corpus and ramus and increased distance between the tooth root apices and the inferior mandibular border (Perrotta et al., 2020b). Nuclear imaging such as scintigraphy, single-photon emission computed tomography (SPECT), and positron emission tomography (PET) is able to provide helpful insights on the activity level of the disease (Saridin et al., 2011). Treatment planning in adult patients usually requires maxillo-mandibular orthognathic surgery, condylectomy if it is active on scintigraphy scans, reshaping of the mandibular lower margin, and genioplasty (Xu et al., 2014).



(a) (b)

Figure 21.8 (a) Panoramic x-ray and (b) cone beam computed tomography of a temporomandibular joint in a patient with hemimandibular hyperplasia. Red doted lines show the condylar profile (right mandible increased in height and dimension); red lines indicate the mandibular canal; orange arrows indicate mandibular ramus heights.

Hemimandibular hyperplasia is characterized by three-dimensional enlargement of one side of the mandible, that is enlargement of the condyle and the condylar neck, while hemimandibular elongation, another form of mandibular hyperplasia, is characterized mainly by horizontal elongation of the affected hemimandible without involvement of the condylar head and with the mandibular corpus that remains on the same level between the affected and not affected sides (Figure 21.9; Obwegeser and Makek, 1986). At the dental level, it presents a lower midline deviation associated with a crossbite to the unaffected side, and no presence of canting of the occlusal plane. Furthermore, in hemimandibular elongation, as can be detected by observing an OPT, there is an equal distance between the posterior tooth root apices and the inferior mandibular border for the affected and unaffected sides. Regarding the extraoral examination, patients present a chin deviation with noticeable facial asymmetry. Despite condylar hyperplasia being divided into two forms, a combination of these is often seen clinically, called the hybrid or mixed form (Gateno et al., 2021).

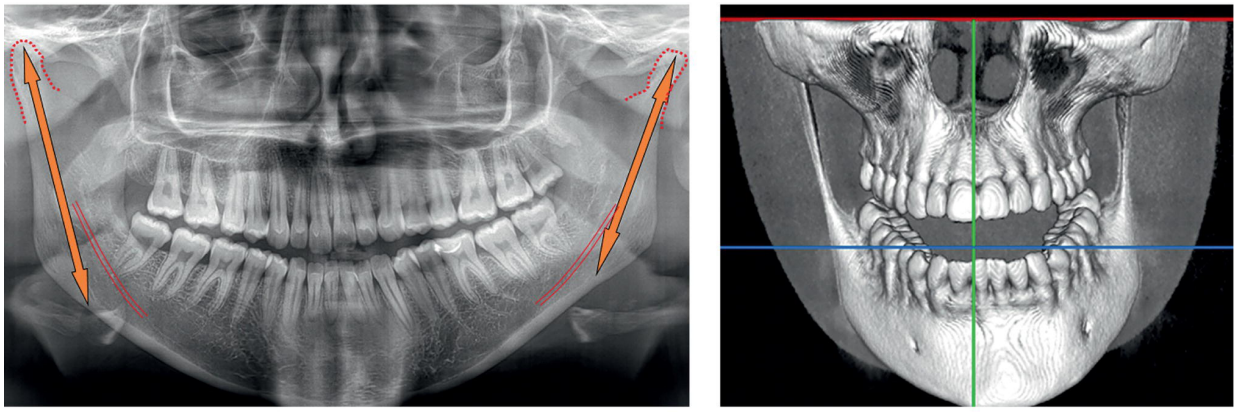


Figure 21.9 (a) Panoramic x-ray and (b) cone beam computed tomography of a temporomandibular joint in a patient with mandibular elongation. Red dotted lines show the condylar profile (left ramus increased in height and dimension); red solid lines indicate the mandibular canal; orange arrows indicate mandibular ramus heights.

The orthodontist is usually the first specialist who identifies patients with these growth alterations, and in this case the treatment options might be orthodontic treatment alone in a case where the malocclusion can be compensated for and there is no more residual growth, or condylar shaving or orthognathic surgery in more severe cases. Usually patients with abnormal mandibular growth are first observed by an orthodontist, who then has the responsibility for the patient's final outcome. Therefore, orthodontists must be familiar with the pathophysiology of condylar hypo- and hyperactivity. An OPT is considered a reliable, simple tool to identify the first signs of mandibular asymmetries, and further examinations should include three-dimensional imaging and bone scintigraphy in order to determine growth activity (Obwegeser and Makek, 1986; Saridin et al., 2011).

Conclusion

- TMJ disorders should be diagnosed by the orthodontist before, during, and after orthodontic treatment.
- There is no convincing evidence supporting the concept that TMJ disorders are causally related to occlusion, the condylar position, or orthodontic treatment, but their etiology is linked to the biopsychosocial model.
- TMJ arthralgia and disc disorders are very often encountered before, during, or after orthodontic treatment, but this high prevalence is mainly due to the high incidence of TMDs in adolescents and young adults.
- TMJ arthralgia can be associated with osteoarthritis and/or osteoarthrosis and should be treated with reversible therapies.
- Disc displacement with reduction should be treated with reversible therapies only in cases of pain of mouth opening reduction. The management of chronic disc displacement without reduction aims to restore TMJ and jaw function.
- TMJ effusion might cause transient occlusal changes, which must not be treated before the effusion disappears. Other TMJ alterations due to systemic arthritis or ICR might cause major occlusal changes that need multidisciplinary management.
- TMJ growth disturbances can also be congenital, and it is important to correctly diagnose the condition before reaching a treatment plan.

References

Academy of Prosthodontics (2017). The Glossary of Prosthodontic Terms: Ninth Edition. *Journal of Prosthetic Dentistry* 117(5S): e1–e105. doi: 10.1016/J.PROSDENT.2016.12.001.

Ahmad, M., Hollender, L., Anderson, Q. et al. (2009). Research diagnostic criteria for temporomandibular disorders (RDC/TMD): development of image analysis criteria and examiner reliability for image analysis. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* 107: 844–860.

Al-Moraissi, E.A., Conti, P.C.R., Alyahya, A. et al. (2022). The hierarchy of different treatments for myogenous temporomandibular disorders: A systematic review and network meta-analysis of randomized clinical trials. *Oral and Maxillofacial Surgery* 26(4): 519–533. doi: 10.1007/S10006-021-01009-Y.

Al-Moraissi, E.A., Wolford, L.M., Ellis, E. et al. (2020). The hierarchy of different treatments for arthrogenous temporomandibular disorders: A network meta-analysis of randomized clinical trials. *Journal of Cranio-Maxillo-Facial Surgery*, 48(1): 9–23. doi: 10.1016/J.JCMS.2019.10.004.

Al-Moraissi, E.A., Wolford, L.M., Perez, D. et al. (2017). Does orthognathic surgery cause or cure temporomandibular disorders? A systematic review and meta-analysis. *Journal of Oral and Maxillofacial Surgery* 75(9): 1835–1847. doi: 10.1016/J.JOMS.2017.03.029.

Alstergren, P., Pigg, M., and Kopp, S. (2018). Clinical diagnosis of temporomandibular joint arthritis. *Journal of Oral Rehabilitation* 45(4): 269–281. doi: 10.1111/JOOR.12611.

Bean, L.R., and Thomas, C.A. (1987). Significance of condylar positions in patients with temporomandibular disorders. *Journal of the American Dental Association* 114(1): 76–77. doi: 10.14219/JADA.ARCHIVE.1987.0043.

Berraquero, R., Palacios, J., Gamallo, C. et al. (1995). Prenatal growth of the human mandibular condylar cartilage. *American Journal of Orthodontics and Dentofacial Orthopedics* 108(2): 194–200. doi: 10.1016/S0889-5406(95)70083-8.

Billiau, A.D., Hu, Y., Verdonck, A. et al. (2007). Temporomandibular joint arthritis in juvenile idiopathic arthritis: Prevalence, clinical and radiological signs, and relation to dentofacial morphology. *Journal of Rheumatology* 34(9): 1925–1933.

Bonilla-Aragon, H., Tallents, R.H., Katzberg, R.W. et al. (1999). Condyle position as a predictor of temporomandibular joint internal derangement. *Journal of Prosthetic Dentistry* 82(2): 205–208. doi: 10.1016/S0022-3913(99)70157-5.

Caldas, W., Conti, A.C. de C.F., Janson, G. et al. (2016). Occlusal changes secondary to temporomandibular joint conditions: A critical review and implications for clinical practice. *Journal of Applied Oral Science* 24(4): 411–419. doi: 10.1590/1678-775720150295.

Chanthavisouk, P., John, M.T., Paulson, D. et al. (2022). Commonalities among dental patient-reported outcomes (dPROs)—a Delphi consensus study. *PloS One* 17(6): e0268750. doi: 10.1371/JOURNAL.PONE.0268750.

Chen, H.-M., Liu, M.-Q., Yap, A.U.-J. et al. (2017). Physiological effects of anterior repositioning splint on temporomandibular joint disc displacement: A quantitative analysis. *Journal of Oral Rehabilitation* 44(9): 664–672. doi: 10.1111/joor.12532.

Conti, P.C.R., da Corrêa, A.S.M., Lauris, J.R.P. et al. (2015). Management of painful temporomandibular joint clicking with different intraoral devices and counseling: A controlled study. *Journal of Applied Oral Science: Revista FOB* 23(5): 529–535. doi: 10.1590/1678-775720140438.

Conti, P.C.R., Dos Santos, C.N., Kogawa, E.M. et al. (2006). The treatment of painful temporomandibular joint clicking with oral splints: A randomized clinical trial. *Journal of the American Dental Association* 137(8): 1108–1114. doi: 10.14219/JADA.ARCHIVE.2006.0349.

de Leeuw, R., Boering, G., Stegenga, B. et al. (1994). Clinical signs of TMJ osteoarthrosis and internal derangement 30 years after nonsurgical treatment. *Journal of Orofacial Pain* 8(1): 18–24.

Deleurant, Y., Zimmermann, A., and Peltomäki, T. (2008). Hemimandibular elongation: Treatment and long-term follow-up. *Orthodontics & Craniofacial Research* 11(3): 172–179. doi: 10.1111/J.1601-

6343.2008.00427.X.

Fanghänel, J., and Gedrange, T. (2007). On the development, morphology and function of the temporomandibular joint in the light of the orofacial system. *Annals of Anatomy* 189(4): 314–319. doi: 10.1016/J.AANAT.2007.02.024.

Gallagher, A.L., Ruellas, A.C. de O., Benavides, E. et al. (2021). Mandibular condylar remodeling characteristics after simultaneous condylectomy and orthognathic surgery. *American Journal of Orthodontics and Dentofacial Orthopedics* 160(5): 705–717. doi: 10.1016/j.ajodo.2020.06.040.

Gateno, J., Coppelson, K.B., Kuang, T. et al. (2021). A better understanding of unilateral condylar hyperplasia of the mandible. *Journal of Oral and Maxillofacial Surgery* 79(5): 1122–1132. doi: 10.1016/j.joms.2020.12.034.

Ghawsi, S., Aagaard, E., and Thygesen, T.H. (2016). High condylectomy for the treatment of mandibular condylar hyperplasia: A systematic review of the literature. *International Journal of Oral and Maxillofacial Surgery* 45(1): 60–71. doi: 10.1016/J.IJOM.2015.09.002.

Greene, C.S., Galang-Boquiren, M.T.S., and Bartilotta, B.Y. (2017). Orthodontics and the temporomandibular joint: What orthodontic providers need to know. *Quintessence International* 48(10): 799–808. doi: 10.3290/J.QI.A39095.

Greene, C., and Manfredini, D. (2020). Treating temporomandibular disorders in the 21st century: Can we finally eliminate the "third pathway"? *Journal of Oral & Facial Pain and Headache* 34(3): 206–216. doi: 10.11607/OFPH.2608.

Häggman-Henrikson, B., Lobbezoo, F., Durham, J. et al. (2022). The voice of the patient in orofacial pain management. *Journal of Evidence-Based Dental Practice* 22(1S): 101648. doi: 10.1016/J.JEBDP.2021.101648.

Han, K., Kim, M.C., Kim, Y.J. et al. (2021). A long-term longitudinal study of the osteoarthritic changes to the temporomandibular joint evaluated using a novel three-dimensional superimposition method. *Scientific Reports* 11(1): 9389. doi: 10.1038/S41598-021-88940-Y.

Haskin, C.L., Milam, S.B., and Cameron, I.L. (1995). Pathogenesis of degenerative joint disease in the human temporomandibular joint. *Critical Reviews in Oral Biology and Medicine* 6(3): 248–277. doi: 10.1177/10454411950060030601.

Hoppenreijs, T.J.M., Stoelinga, P.J.W., Grace, K.L. et al. (1999). Long-term evaluation of patients with progressive condylar resorption following orthognathic surgery. *International Journal of Oral and Maxillofacial Surgery* 28(6): 411–418. doi: 10.1016/s0901-5027(99)80052-6.

Ingervall, B. (1968). Studies of mandibular positions in children. *Odontologisk Revy. Supplement* 15: 1–53.

Ji, Y.D., Resnick, C.M., and Peacock, Z.S. (2020). Idiopathic condylar resorption: A systematic review of etiology and management. *Oral Surgery, Oral Medicine, Oral Pathology, and Oral Radiology* 130(6): 632–639. doi: 10.1016/J.OOOO.2020.07.008.

John, M.T. (2020). Foundations of oral health-related quality of life. *Journal of Oral Rehabilitation, Jul.* 13. doi: 10.1111/JOOR.13040.

Jussila, P., Kiviahde, H., Näpänkangas, R. et al. (2017). Prevalence of temporomandibular disorders in the northern Finland birth cohort 1966. *Journal of Oral & Facial Pain and Headache* 31(2): 159–164. doi: 10.11607/OFPH.1773.

Kalaykova, S., Lobbezoo, F., and Naeije, M. (2010). Two-year natural course of anterior disc displacement with reduction. *Journal of Orofacial Pain* 24(4): 373–378.

Kalaykova, S.I., Lobbezoo, F., and Naeije, M. (2011). Risk factors for anterior disc displacement with reduction and intermittent locking in adolescents. *Journal of Orofacial Pain* 25(2): 153–160.

Kandasamy, S., Boeddinghaus, R., and Kruger, E. (2013). Condylar position assessed by magnetic resonance imaging after various bite position registrations. *American Journal of Orthodontics and Dentofacial Orthopedics* 144(4): 512–517. doi: 10.1016/J.AJODO.2013.06.014.

Kandasamy, S., Greene, C.S., and Obrez, A. (2018). An evidence-based evaluation of the concept of centric relation in the 21st century. *Quintessence International* 49(9): 755–760. doi: 10.3290/J.QI.A41011.

Kaneyama, K., Segami, N., and Hatta, T. (2008). Congenital deformities and developmental abnormalities of the mandibular condyle in the temporomandibular joint. *Congenital Anomalies* 48(3): 118–125. doi: 10.1111/J.1741-4520.2008.00191.X.

Khawaja, S.N., Crow, H., Mahmoud, R.F.G. et al. (2017). Is there an association between temporomandibular joint effusion and arthralgia? *Journal of Oral and Maxillofacial Surgery* 75(2): 268–275. doi: 10.1016/J.JOMS.2016.08.027.

Kircos, L.T., Ortendahl, D.A., Mark, A.S. et al. (1987). Magnetic resonance imaging of the TMJ disc in asymptomatic volunteers. *Journal of Oral and Maxillofacial Surgery* 45(10): 852–854. doi: 10.1016/0278-2391(87)90235-7.

Koolstra, J.H. (2002). Dynamics of the human masticatory system. *Critical Reviews in Oral Biology and Medicine* 13(4): 366–376. doi: 10.1177/154411130201300406.

Kurita, H., Uehara, S., Yokochi, M. et al. (2006). A long-term follow-up study of radiographically evident degenerative changes in the temporomandibular joint with different conditions of disk displacement. *International Journal of Oral and Maxillofacial Surgery* 35(1): 49–54. doi: 10.1016/J.IJOM.2005.04.004.

La Touche, R., Boo-Mallo, T., Zarzosa-Rodríguez, J. et al. (2020). Manual therapy and exercise in temporomandibular joint disc displacement without reduction. *A systematic review*. *Cranio* 40(5): 440–450. doi: 10.1080/08869634.2020.1776529.

Lee, S.K., Kim, Y.S., Oh, H.S. et al. (2001). Prenatal development of the human mandible. *Anatomical Record* 263(3): 314–325. doi: 10.1002/AR.1110.

Lelis, É.R., Guimarães Henriques, J.C., Tavares, M. et al. (2015). Cone-beam tomography assessment of the condylar position in asymptomatic and symptomatic young individuals. *Journal of Prosthetic Dentistry* 114(3): 420–425. doi: 10.1016/J.PROSDENT.2015.04.006.

Li, Y., Zheng, Y., Cai, H. et al. (2022). Standard orthodontic treatment after condylectomy for patients with active unilateral condylar hyperplasia. *American Journal of Orthodontics and Dentofacial Orthopedics* 161(3): 404–415.e1. doi: 10.1016/j.ajodo.2020.09.032.

Magnusson, T., Carlsson, G.E., and Egermark, I. (1994). Changes in clinical signs of craniomandibular disorders from the age of 15 to 25 years. *Journal of Orofacial Pain* 8(2): 207–215.

Mallya, S.M., Ahmad, M., Cohen, J.R. et al. (2022). Recommendations for imaging of the temporomandibular joint. Position statement from the American Academy of Oral and Maxillofacial Radiology and the American Academy of Orofacial Pain. *Oral Surgery, Oral Medicine, Oral Pathology, and Oral Radiology* 134(5): 639–648.

Manfredini, D., Lombardo, L., and Siciliani, G. (2017). Temporomandibular disorders and dental occlusion. A systematic review of association studies: End of an era? *Journal of Oral Rehabilitation* 44(11): 908–923. doi: 10.1111/joor.12531.

Marinho, L.H.M., and McLoughlin, P.M. (1994). Lateral open bite resulting from acute temporomandibular joint effusion. *British Journal of Oral and Maxillofacial Surgery* 32(2): 127–128. doi: 10.1016/0266-4356(94)90146-5.

Meazzini, M.C., Brusati, R., Caprioglio, A. et al. (2011). True hemifacial microsomia and hemimandibular hypoplasia with condylar-coronoid collapse: Diagnostic and prognostic differences. *American Journal of Orthodontics and Dentofacial Orthopedics* 139(5): e435–e447. doi: 10.1016/j.ajodo.2010.01.034.

Michelotti, A., and Iodice, G. (2010). The role of orthodontics in temporomandibular disorders. *Journal of Oral Rehabilitation* 37(6): 411–429. doi: 10.1111/j.1365-2842.2010.02087.x.

Michelotti, A., Farella, M., Vollaro, S. et al. (1997). Mandibular rest position and electrical activity of the masticatory muscles. *Journal of Prosthetic Dentistry 78*(1): 48–53. doi: 10.1016/S0022-3913(97)70087-8.

Naeije, M., te Veldhuis, A.H., te Veldhuis, E.C. et al. (2013). Disc displacement within the human temporomandibular joint: A systematic review of a "noisy annoyance." *Journal of Oral Rehabilitation* 40(2): 139–158. doi: 10.1111/JOOR.12016.

Niño-Sandoval, T.C., Maia, F.P.A., and Vasconcelos, B.C.E. (2019). Efficacy of proportional versus high condylectomy in active condylar hyperplasia – a systematic review. *Journal of Cranio-Maxillofacial Surgery* 47(8): 1222–1232. doi: 10.1016/j.jcms.2019.03.024.

Nitzan, D.W., Katsnelson, A., Bermanis, I. et al. (2008). The clinical characteristics of condylar hyperplasia: Experience with 61 patients. *Journal of Oral and Maxillofacial Surgery* 66(2): 312–318. doi: 10.1016/J.JOMS.2007.08.046.

Obwegeser, H.L., and Makek, M.S. (1986). Hemimandibular hyperplasia—hemimandibular elongation. *Journal of Maxillofacial Surgery* 14(4): 183–208. doi: 10.1016/S0301-0503(86)80290-9.

Okeson, J. (2013). *Management of Temporomandibular Disorders and Occlusion*, 7th ed. St. Louis, MO: Mosby.

Okeson, J.P., and Hayes, D.K. (1986). Long-term results of treatment for temporomandibular disorders: An evaluation by patients. *Journal of the American Dental Association* 112(4): 473–478. doi: 10.14219/JADA.ARCHIVE.1986.0047.

Olliver, S.J., Broadbent, J.M., Thomson, W.M. et al. (2020). Occlusal features and TMJ clicking: A 30-year evaluation from a cohort study. *Journal of Dental Research* 99(11): 1245–1251. doi: 10.1177/0022034520936235.

Owen, A.H. (1988). Unexpected TMJ responses to functional jaw orthopedic therapy. *American Journal of Orthodontics and Dentofacial Orthopedics* 94(4): 338–349. doi: 10.1016/0889-5406(88)90059-5.

Paknahad, M., Shahidi, S., Iranpour, S. et al. (2015). Cone-beam computed tomographic assessment of mandibular condylar position in patients with temporomandibular joint dysfunction and in healthy subjects. *International Journal of Dentistry* 2015: 301796. doi: 10.1155/2015/301796.

Peacock, Z.S., Lee, C.C.Y., Troulis, M.J. et al. (2019). Long-term stability of condylectomy and costochondral graft reconstruction for treatment of idiopathic condylar resorption. *Journal of Oral and Maxillofacial Surgery 77*(4): 792–802. doi: 10.1016/J.JOMS.2018.10.007.

Peck, C.C., Goulet, J.P., Lobbezoo, F. et al. (2014). Expanding the taxonomy of the diagnostic criteria for temporomandibular disorders. *Journal of Oral Rehabilitation* 41: 2–23. doi: 10.1111/joor.12132.

Pedersen, T.K., and Carlalberta, V. (2015). Functional and orthopedic treatment in developing dentofacial growth deviation in juvenile idiopathic arthritis. *Seminars in Orthodontics* 2(21): 134–139. doi: 10.1053/J.SODO.2015.02.010.

Perrotta, S., Bocchino, T., D'Antò, V. et al. (2020a). Pseudo hemifacial microsomia with condylar-coronoid collapse: New therapeutic approach in growing patients. *Journal of Craniofacial Surgery* 31(8): 2128–2131. doi: 10.1097/SCS.0000000000006812.

Perrotta, S., Lo Giudice, G., Bocchino, T. et al. (2020b). Orthodontics first in hemimandibular hyperplasia. "Mind the gap." *International Journal of Environmental Research and Public Health* 17(19): 1–9. doi: 10.3390/ijerph17197087.

Petty, R.E., Southwood, T.R., Manners, P. et al. (2004). International League of Associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. *Journal of Rheumatology* 31(2): 390–392.

Poluha, R.L., De La Torre Canales, G., Costa, Y.M. et al. (2019). Temporomandibular joint disc displacement with reduction: A review of mechanisms and clinical presentation. *Journal of Applied Oral Science: Revista FOB* 27: e20180433. doi: 10.1590/1678-7757-2018-0433.

Pullinger, A. (2013). Establishing better biological models to understand occlusion. I: TM joint anatomic relationships. *Journal of Oral Rehabilitation* 40(4): 296–318. doi: 10.1111/JOOR.12032.

Pullinger, A.G., Seligman, D.A., and Solberg, W.K. (1988). Temporomandibular disorders. Part II: Occlusal factors associated with temporomandibular joint tenderness and dysfunction. *Journal of Prosthetic Dentistry* 59(3): 363–367. doi: 10.1016/0022-3913(88)90191-6.

Rahimi, H., Twilt, M., Herlin, T. et al. (2018). Orofacial symptoms and oral health-related quality of life in juvenile idiopathic arthritis: A two-year prospective observational study. *Pediatric Rheumatology Online Journal* 16(1): 47. doi: 10.1186/s12969-018-0259-4.

Rasmussen, O.C. (1981). Clinical findings during the course of temporomandibular arthropathy. *Scandinavian Journal of Dental Research* 89(3): 283–288. doi: 10.1111/J.1600-0722.1981.TB01684.X.

Rauch, A., Schierz, O., Körner, A. et al. (2020). Prevalence of anamnestic symptoms and clinical signs of temporomandibular disorders in adolescents—results of the epidemiologic LIFE Child Study. *Journal of Oral Rehabilitation* 47(4): 425–431. doi: 10.1111/joor.12926.

Resnick, C.M., Frid, P., Norholt, S.E. et al. (2019). An algorithm for management of dentofacial deformity resulting from juvenile idiopathic arthritis: Results of a multinational consensus conference. *Journal of Oral and Maxillofacial Surgery 77*(6): 1152.e1–1152.e33. doi: 10.1016/J.JOMS.2019.02.014.

Rinchuse, D.J. (2021). The Roth-Rinchuse debate: It's been 25 years. *American Journal of Orthodontics and Dentofacial Orthopedics* 159(2): 141–146. doi: 10.1016/J.AJODO.2020.10.014.

Ringold, S., and Cron, R.Q. (2009). The temporomandibular joint in juvenile idiopathic arthritis: Frequently used and frequently arthritic. *Pediatric Rheumatology Online Journal* 7: 11. doi: 10.1186/1546-0096-7-11.

Rongo, R., Alstergren, P., Ammendola, L. et al. (2019). Temporomandibular joint damage in juvenile idiopathic arthritis: Diagnostic validity of diagnostic criteria for temporomandibular disorders. *Journal of Oral Rehabilitation* 46(5): 450–459. doi: 10.1111/joor.12769.

Roth, R.H. (1973). Temporomandibular pain-dysfunction and occlusal relationships. *Angle Orthodontist* 43(2): 136–153. doi: 10.1043/0003-3219(1973)043<0136:TPAOR>2.0.CO;2.

Roth, R.H. (1981a). Functional occlusion for the orthodontist. *Journal of Clinical Orthodontics* 15(1): 32–40.

Roth, R.H. (1981b). Functional occlusion for the orthodontist. *Part III*. *Journal of Clinical Orthodontics* 15(3): 174–179.

Roth, R.H., and Rolfs, D.A. (1981). Functional occlusion for the orthodontist. Part II. *Journal of Clinical Orthodontics* 15(2): 100–123.

Sadakah, A.A., Elshall, M.A., and Farhat, A.A. (2009). Bilateral intra-oral distraction osteogenesis for the management of severe congenital mandibular hypoplasia in early childhood. *Journal of Cranio-Maxillofacial Surgery* 37(4): 216–224. doi: 10.1016/j.jcms.2008.10.014.

Saridin, C.P., Raijmakers, P.G.H.M., Tuinzing, D.B. et al. (2011). Bone scintigraphy as a diagnostic method in unilateral hyperactivity of the mandibular condyles: A review and meta-analysis of the literature. *International Journal of Oral and Maxillofacial Surgery* 40(1): 11–17. doi: 10.1016/J.IJOM.2010.09.015.

Scheerlinck, J.P.O., Stoelinga, P.J.W., Blijdorp, P.A. et al. (1994). Sagittal split advancement osteotomies stabilized with miniplates. A 2-5-year follow-up. *International Journal of Oral and Maxillofacial Surgery* 23(3): 127–131. doi: 10.1016/S0901-5027(05)80285-1.

Schiffman, E., Ohrbach, R., Truelove, E. et al. (2014). Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) for clinical and research applications: Recommendations of the International RDC/TMD Consortium Network and Orofacial Pain Special Interest Group. *Journal of Oral & Facial Pain and Headache* 28(1): 6–27. doi: 10.11607/jop.1151.

Sharma, S., Breckons, M., Brönnimann Lambelet, B. et al. (2020). Challenges in the clinical implementation of a biopsychosocial model for assessment and management of orofacial pain. *Journal of Oral Rehabilitation* 47(1): 87–100. doi: 10.1111/joor.12871.

Sierwald, I., John, M.T., Schierz, O. et al. (2015). Association of temporomandibular disorder pain with awake and sleep bruxism in adults. *Journal of Orofacial Orthopedics* 76(4): 305–317. doi: 10.1007/S00056-015-0293-5.

Slade, G.D., Ohrbach, R., Greenspan, J.D. et al. (2016). Painful temporomandibular disorder: Decade of discovery from OPPERA studies. *Journal of Dental Research* 95(10): 1084–1092. doi: 10.1177/0022034516653743.

Stoustrup, P., Herlin, T., Spiegel, L. et al. (2020). Standardizing the clinical orofacial examination in juvenile idiopathic arthritis: An interdisciplinary, consensus-based, short screening protocol. *Journal of Rheumatology* 47(9): 1397–1404. doi: 10.3899/jrheum.190661.

Stoustrup, P., Kristensen, K.D., Küseler, A. et al. (2014). Management of temporomandibular joint arthritis-related orofacial symptoms in juvenile idiopathic arthritis by the use of a stabilization splint. *Scandinavian Journal of Rheumatology* 43(2): 137–145. doi: 10.3109/03009742.2013.830146.

Stoustrup, P., Kristensen, K.D., Verna, C. et al. (2012). Orofacial symptoms related to temporomandibular joint arthritis in juvenile idiopathic arthritis: Smallest detectable difference in self-reported pain intensity. *Journal of Rheumatology* 39(12): 2352–2358. doi: 10.3899/jrheum.120437.

Stoustrup, P., Pedersen, T.K., Nørholt, S.E. et al. (2021). Interdisciplinary management of dentofacial deformity in juvenile idiopathic arthritis. *Oral and Maxillofacial Surgery Clinics of North America* 11: 13142. doi: 10.1016/j.coms.2019.09.002.

Suvinen, T.I., Reade, P.C., Kemppainen, P. et al. (2005). Review of aetiological concepts of temporomandibular pain disorders: Towards a biopsychosocial model for integration of physical disorder factors with psychological and psychosocial illness impact factors. *European Journal of Pain* 9: 613–633. doi: 10.1016/j.ejpain.2005.01.012,

Talaat, W.M., Adel, O.I., and Al Bayatti, S. (2018). Prevalence of temporomandibular disorders discovered incidentally during routine dental examination using the Research Diagnostic Criteria for Temporomandibular Disorders. *Oral Surgery, Oral Medicine, Oral Pathology, and Oral Radiology* 125(3): 250–259. doi: 10.1016/J.OOOO.2017.11.012.

Tank, W., Wright, D., and Iizuka, T. (1998). Unilateral dysplasia of the mandibular condyle: Report of a case. *Journal of Oral and Maxillofacial Surgery* 56(6): 765–769. doi: 10.1016/S0278-2391(98)90816-3.

Tasaki, M.M., Westesson, P.L., Isberg, A.M. et al. (1996). Classification and prevalence of temporomandibular joint disk displacement in patients and symptom-free volunteers. *American Journal of Orthodontics and Dentofacial Orthopedics* 109(3): 249–262. doi: 10.1016/S0889-5406(96)70148-8.

Tatli, U., Benlidayi, M.E., Ekren, O. et al. (2017). Comparison of the effectiveness of three different treatment methods for temporomandibular joint disc displacement without reduction. *International Journal of Oral and Maxillofacial Surgery* 46(5): 603–609. doi: 10.1016/J.IJOM.2017.01.018.

Türp, J.C., Schlenker, A., Schröder, J. et al. (2016). Disk displacement, eccentric condylar position, osteoarthrosis – misnomers for variations of normality? Results and interpretations from an MRI study in two age cohorts. *BMC Oral Health* 16(1): 124. doi: 10.1186/S12903-016-0319-4.

Twilt, M., Arends, L.R., Ten Cate, R. et al. (2007). Incidence of temporomandibular involvement in juvenile idiopathic arthritis. *Scandinavian Journal of Rheumatology* 36(3): 184–188. doi: 10.1080/03009740601154368.

Twilt, M., Schulten, A.J.M., Nicolaas, P. et al. (2006). Facioskeletal changes in children with juvenile idiopathic arthritis. *Annals of the Rheumatic Diseases* 65(6): 823–825. doi: 10.1136/ard.2005.042671.

Ukra, A., Foster Page, L.A., Thomson, W.M. et al. (2017). Self-report of temporomandibular joint clicking and psychological factors: Is there an association? *Journal of Oral Rehabilitation* 44(7): 511–516. doi: 10.1111/JOOR.12514.

Wahlund, K., Nilsson, I.M., Carlsson, A.D. et al. (2021). Internet-based treatment for adolescents with symptomatic temporomandibular joint disc displacement with reduction. A randomized controlled clinical trial. *Acta Odontologica Scandinavica* 79(6): 473–481. doi: 10.1080/00016357.2021.1901983.

Walters, M., Claes, P., Kakulas, E. et al. (2013). Robust and regional 3D facial asymmetry assessment in hemimandibular hyperplasia and hemimandibular elongation anomalies. *International Journal of Oral and Maxillofacial Surgery* 42(1): 36–42. doi: 10.1016/J.IJOM.2012.05.021.

Wink, C., St Onge, M., and Zimny, M. (1992). Neural elements in the human temporomandibular articular disc. *Journal of Oral and Maxillofacial Surgery* 50: 334–337.

Wolford, L.M. (2001). Idiopathic condylar resorption of the temporomandibular joint in teenage girls (cheerleaders syndrome). *Proceedings (Baylor University. Medical Center)* 14(3): 246. doi: 10.1080/08998280.2001.11927772.

Xiao, J., Wu, Z., and Ye, W. (2022). Using 3D medical modeling to evaluate the accuracy of single-photon emission computed tomography (SPECT) bone scintigraphy in diagnosing condylar hyperplasia. *Journal of Oral and Maxillofacial Surgery* 80(2): 285.e1–285.e9. doi: 10.1016/J.JOMS.2021.09.005.

Xu, M., Chan, F.C., Jin, X. et al. (2014). Hemimandibular hyperplasia: Classification and treatment algorithm revisited. *Journal of Craniofacial Surgery* 25(2): 355–358. doi: 10.1097/01.SCS.0000436673.77122.00.

Yoda, T., Sakamoto, I., Imai, H. et al. (2003). A randomized controlled trial of therapeutic exercise for clicking due to disk anterior displacement with reduction in the temporomandibular joint. *Cranio* 21(1): 10–16. doi: 10.1080/08869634.2003.11746226.

Zonnenberg, A.J.J., Türp, J.C., and Greene, C.S. (2021). Centric relation critically revisited—what are the clinical implications? *Journal of Oral Rehabilitation* 48(9): 1050–1055. doi: 10.1111/joor.13215.

Part V
The Biomedical Orthodontist

22

The Role of Biomedical Engineers in the Design and Manufacture of Orthodontic Appliances

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Summary

Currently there are numerous opportunities for biomedical engineers to interact with orthodontists to produce customized appliances, such as shape-memory polymer wires, self-healing materials, smart brackets with force-moment sensors, biomimetic adhesives, and self-cleaning materials. These exciting new applications are discussed in the second part of this chapter. The first part summarizes extensive past work performed by investigators with a biomedical engineering orientation, and also reviews important complementary publications, to gain insight into orthodontic appliances and develop new appliances.

The broad scope of modern biomedical engineering (Box 22.1) is based on integration of engineering principles with biological sciences to develop devices, materials, and procedures that improve the health of people. To seek past examples of collaboration between biomedical engineers and orthodontists, a search of the biomedical literature using PubMed and the search terms “orthodontic appliances” and “biomedical engineering” was performed and revealed 99 publications since 1971 in the areas of archwire–bracket friction; archwires; force measurements, including degradation of

force-delivery modules; orthodontic appliances, including use of finite element analysis; and miscellaneous subjects, such as *Streptococcus mutans* and polymerase chain reaction (PCR), allergic reactions to materials, and mechanical behavior of the periodontal ligament. Examination of these publications revealed that the authors typically had biomedical engineering and other engineering affiliations, which accounted for the indexing of the articles by PubMed, although there was generally no specific mention in the articles about the applications of biomedical engineering principles. While these publications are only a small subset of the many published articles in these areas, they nonetheless provide excellent examples of how biomedical engineering principles have been applied in the past to orthodontic appliances. The first part of this chapter will summarize important past research activities involving collaborations between biomedical engineers and orthodontists, and the second part will describe current areas of research and potential future applications where there are highly promising new opportunities for such collaboration.

Past research activities

Archwire–bracket friction

The principal past research to understand the scientific basis of archwire–bracket friction and its applications to clinical orthodontic treatment was performed by the late Professor Robert Kusy and his group of graduate students. Kusy was jointly appointed to the Department of Biomedical Engineering of the School of Medicine and in the School of Dentistry at the University of North Carolina at Chapel Hill.

Kusy's initial study (Kusy et al., 1988) investigated the effects of surface roughness measured by laser specular reflectance (Figure 22.1) on the coefficients of static and dynamic friction in the dry state for model orthodontic systems that employed metallic archwires, lapped stainless steel, and as-received polycrystalline alumina surfaces to simulate brackets (Kusy and Whitley, 1990a). All–stainless steel couples of archwire and contacting surface had lower kinetic coefficients of friction than stainless steel–alumina couples,

and beta-titanium had the highest coefficient of friction among archwires, although nickel-titanium archwires had the roughest surfaces. Scanning electron microscope (SEM) observations using energy-dispersive x-ray analyses revealed adhesion of beta-titanium archwires to stainless steel flat surfaces and abrasion of beta-titanium archwires by flat alumina surfaces that were microscopically rough due to the sharp facets of the fine grains of the material.

Box 22.1 Examples of areas of modern biomedical engineering

- Biomaterials (hard tissues, soft tissues, and implants for in vivo applications).
- Biomechanics (e.g. implant and tissue mechanics, use of sensors, gait analyses, and analyses for trauma and stroke patients).
- Conventional biomedical devices (e.g. heart pacemakers and hemodialysis catheters).
- Microfabrication and nanofabrication of new devices (e.g. laboratory-on-a-chip concept).
- Biomedical imaging (scanning electron microscopy, atomic force microscopy, magnetic resonance, and ultrasound).Cell and tissue engineering (growth of replacement body parts for transplantation).

These pioneering studies with model systems were followed by an extensive series of investigations that evolved as new archwire and bracket products were introduced. Dry state friction was measured for archwires in stainless steel and polycrystalline alumina bracket slots by Kusy and Whitley (1990b). The resistance to sliding of self-ligating brackets and conventional stainless steel twin brackets for second-order angulation in the dry and wet (saliva) states was

studied by Thorstenson and Kusy (2001), followed by evaluation of the sliding resistance of stainless steel archwires in self-ligating brackets with passive slides and active clips (Thorstenson and Kusy, 2002a). Thorstenson and Kusy (2002b) then examined four designs of self-ligating brackets coupled with four different nickel-titanium archwires varying in size and nickel-titanium phase (Brantley, 2001). In subsequent studies, Thorstenson and Kusy (2003a) first compared the resistance to sliding for polycrystalline alumina brackets and polycarbonate brackets, with and without stainless steel inserts with control stainless steel brackets with stainless steel archwires, and then (Thorstenson and Kusy, 2003b, 2004) investigated the resistance to sliding for stainless steel archwires coupled to conventional stainless steel brackets and new bracket designs. Figures 22.2 and 22.3 (Rucker and Kusy, 2002a) illustrate the principles, schematic apparatus, and typical results for friction measurements. This study compared the resistance to sliding, in dry and wet (saliva) conditions, of multistrand stainless steel, single-strand stainless steel, and nickel-titanium archwires. The coefficients of binding were not affected by saliva but were proportional to wire stiffness, and differences in the kinetic coefficients of friction for stainless steel and nickel-titanium archwires became unimportant shortly after binding occurred.

In the final two studies of archwire–bracket friction from the Kusy laboratory, a more clinically oriented approach was employed to compare four conventional and four self-ligating brackets. Standardized archwires were drawn through quadrants of typodont models in dry and wet (saliva) states, and the drawing forces were measured for friction evaluation (Henao and Kusy, 2004). A small archwire simulated the earlier treatment stage, and two larger archwires simulated later stages; typodonts had quadrants with progressively increasing malocclusions. In their following study (Henao and Kusy, 2005) the same methodology was used to seek the optimal archwire–bracket system, using archwires and bracket designs from four manufacturers.

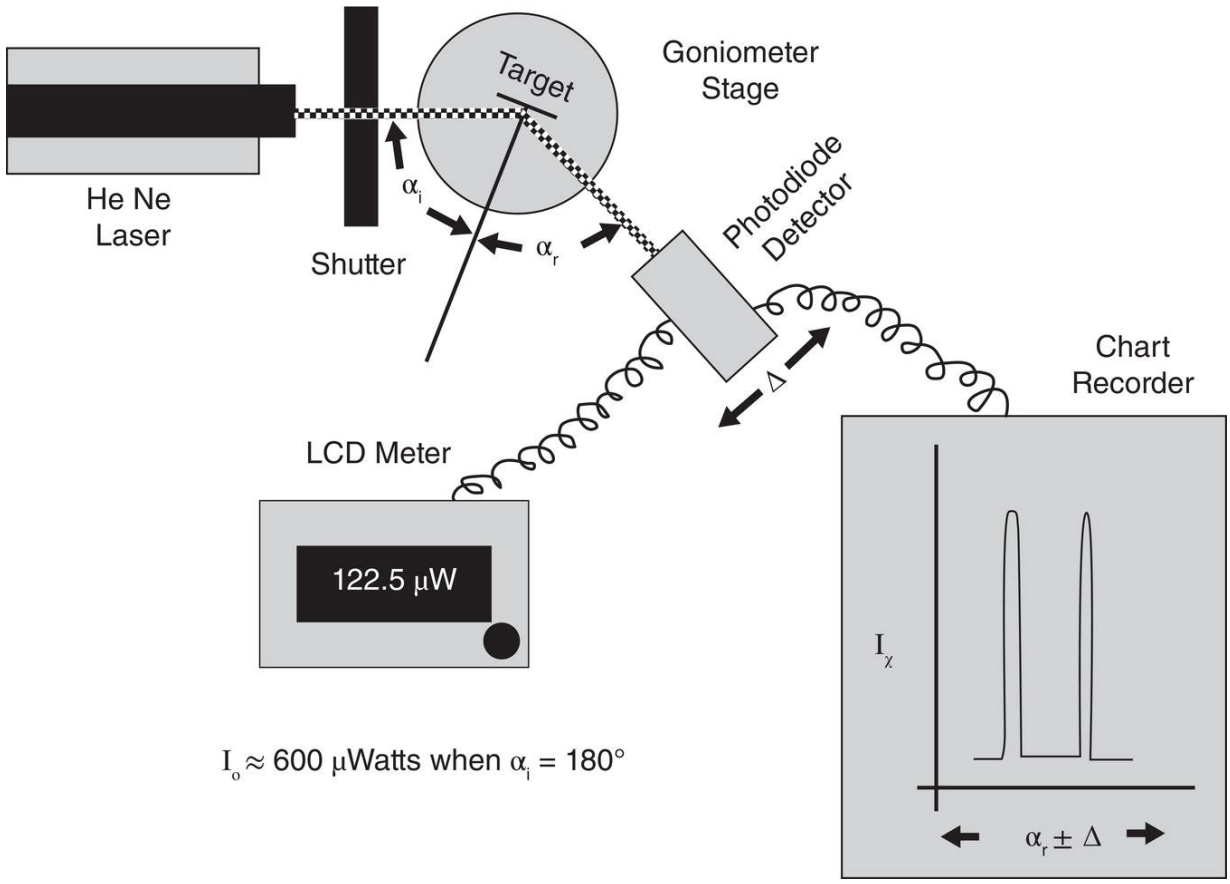


Figure 22.1 Schematic measurement of archwire surface roughness using laser reflectance spectroscopy.

Reproduced with permission from Kusy et al. (2004) / Elsevier.

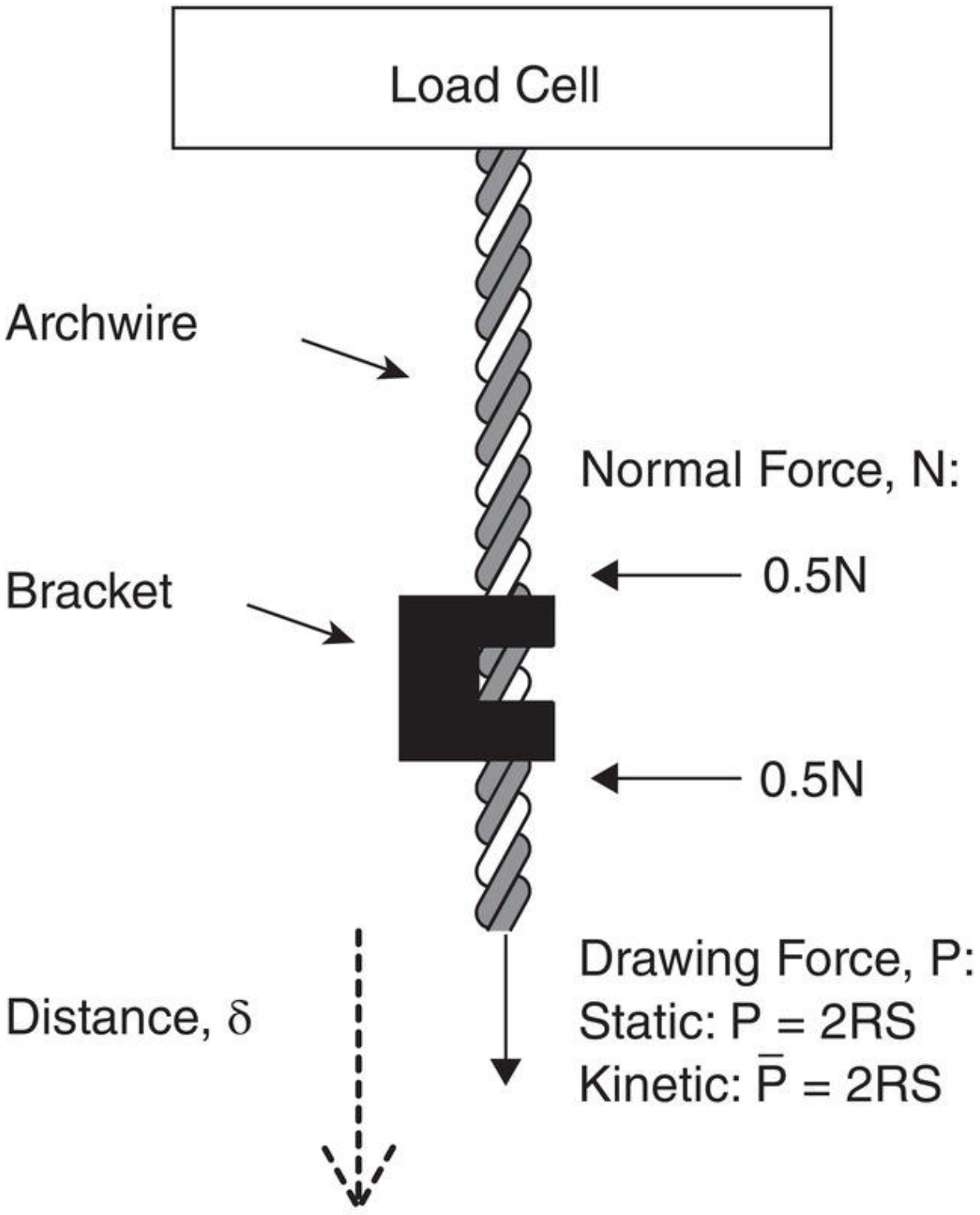

Load Cell
Archwire
Bracket
Normal Force, N:
0.5N
0.5N
Drawing Force, P:
Static: P = 2RS
Kinetic: $\bar{P}$ = 2RS
Distance, δ

Figure 22.2 Principles for measurement of archwire–bracket friction, showing normal force (N) applied to multistrand archwire, drawing force (P), distance of movement (δ), and relationships of static and kinetic force to resistance to sliding (RS).

Reproduced with permission from Rucker and Kusy (2002a) / Elsevier.

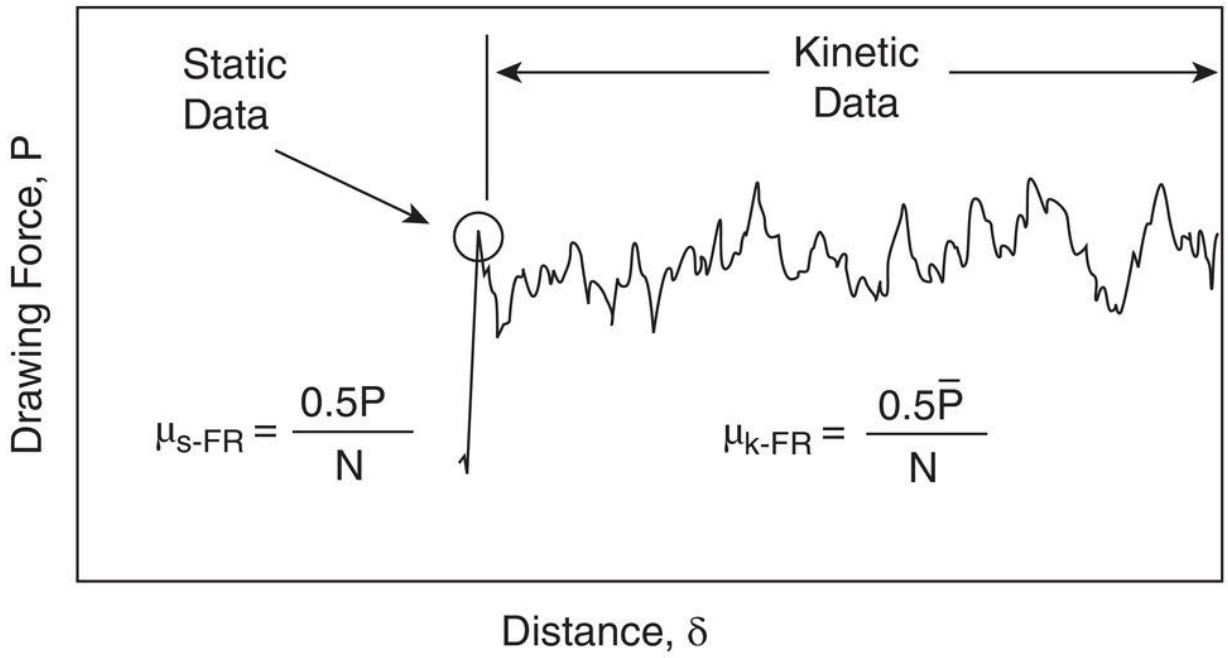


Figure 22.3 Schematic illustration of drawing force–distance data, showing determination of static and kinetic coefficients of friction ($\mu_{s\text{-}FR}$ and $\mu_{k\text{-}FR}$).

Reproduced with permission from Rucker and Kusy (2002a) / Elsevier.

The foregoing laboratory studies by the Kusy research group provided considerable fundamental understanding about the resistance to sliding for commercial archwires in commercial conventional and self-ligating brackets, along with the role of the critical angle for binding, the consequences of using inserts in brackets, the results from novel bracket designs, and use of different archwire materials and designs. Such information in principle provides the orthodontist with the ability to select the optimum archwires and brackets for a scientific approach to different patient treatment cases.

There is a prolific literature in this area in which biomedical engineers were not generally involved, with over 300 articles cited by

PubMed, beginning with Andreasen and colleagues in 1969. The articles by the Kusy research group were selected to illustrate past interactions between biomedical engineers and orthodontists in the investigation of archwire–bracket friction.

In a review article, Burrow (2009) comments that clinical studies indicate a minimal role for archwire–bracket sliding friction in bodily tooth movement, which instead involves successive steps of archwire binding by the bracket and its release. He also notes that clinical studies to date do not indicate that treatment time is reduced with self-ligating brackets because of lower friction. This important article stimulated several responses and replies in the Readers' Forum of the *American Journal of Orthodontics and Dentofacial Orthopedics* (July and December 2009). The reader is also directed to a classic article by Tidy (1989) on the *in vitro* measurement of frictional forces in fixed orthodontic appliances, and a later article by Loftus et al. (1999) presenting an *in vitro* dentoalveolar model for measurement of frictional forces. Reznikov et al. (2010) described a new system for measuring friction *in vitro* in a study that investigated stainless steel archwires and self-ligating brackets. These authors found that under certain clinical situations a firm passive bracket clip can adversely affect friction. However, none of these four pieces of research involved collaboration between orthodontists and biomedical engineers. New collaborations are needed for further progress in fundamental understanding of the sliding of different types of archwires in the wide variety of commercially available brackets, and how clinical treatment is affected by the complex archwire–bracket interactions that occur.

Fabrication and characterization of nonmetallic archwires

McKamey and Kusy (1999) created a polymer–polymer composite wire, designed for use as a ligature, by encasing ultra-high molecular weight polyethylene fibers in poly (n-butyl methacrylate) formulated from a polysol containing benzoin ethyl ether. Subsequently, Zufall and Kusy (2000a, 2000b) created poly(chloro-p-xylylene)-coated glass fiber–reinforced composite archwires made by photo-pultrusion from S2-glass and a polymer formed from bisphenol-A

diglycidyl methacrylate (Bis-GMA) and triethylene glycol dimethacrylate (TEGDMA), with benzoin ethyl ether as an ultraviolet light photoinitiator. Strength and force decay were measured for the polymer–polymer composite archwires, and the frictional and viscoelastic behavior of the fiber-reinforced polymer archwires was investigated extensively. Mathematical models were developed that described the *in vitro* behavior of the polymeric wires. Nonetheless, while laboratory results indicated that both polymeric wires would be suitable for their intended clinical applications, these wires were never introduced as commercial products, presumably because of the costs associated with developing the manufacturing techniques.

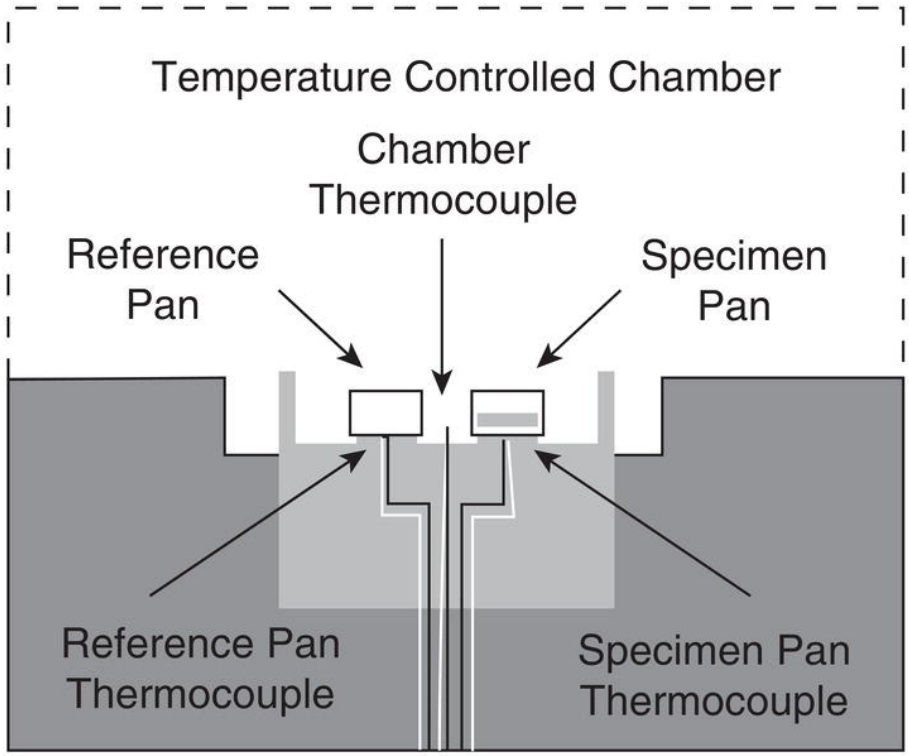
Besides the articles published by the Kusy research group that involved collaborations between biomedical engineers and orthodontists, other similar collaborative research on nonmetallic archwires has also been reported. Based on collaboration between the orthodontic faculty at the Hokkaido University School of Dentistry and an engineering faculty member at the Chiba Institute of Technology in Japan, Imai et al. (1998) reported a study of fiber-reinforced polymeric archwires containing $CaO–P_2O_5–SiO_2–Al_2O_3$ glass fibers that were longitudinally oriented in a polymethyl methacrylate matrix using a hot-drawing method. The glass fiber surfaces of these wires were treated by a silane coupling agent to improve bonding with the polymer matrix. Collaboration between engineering mechanics, bioengineering, and orthodontics faculty at Tongji University in China and the National University of Singapore resulted in an article by Huang et al. (2003) on a tube-shrinkage technique that was used to fabricate longitudinally oriented glass fibers (E-glass) in an epoxy resin matrix. These authors noted that this novel technique did not have the problem of fiber damage or the limitation of a straight cylindrical geometry associated with the pultrusion (drawing) technique that had been previously used to fabricate unidirectional fiber-oriented composite archwires.

It is important to acknowledge the extensive past research by Goldberg and Burstone, which also represented collaboration between a bioengineer and an orthodontist, on the development of fiber composites for a variety of dental applications, including orthodontic archwires. The publications from their past work can be

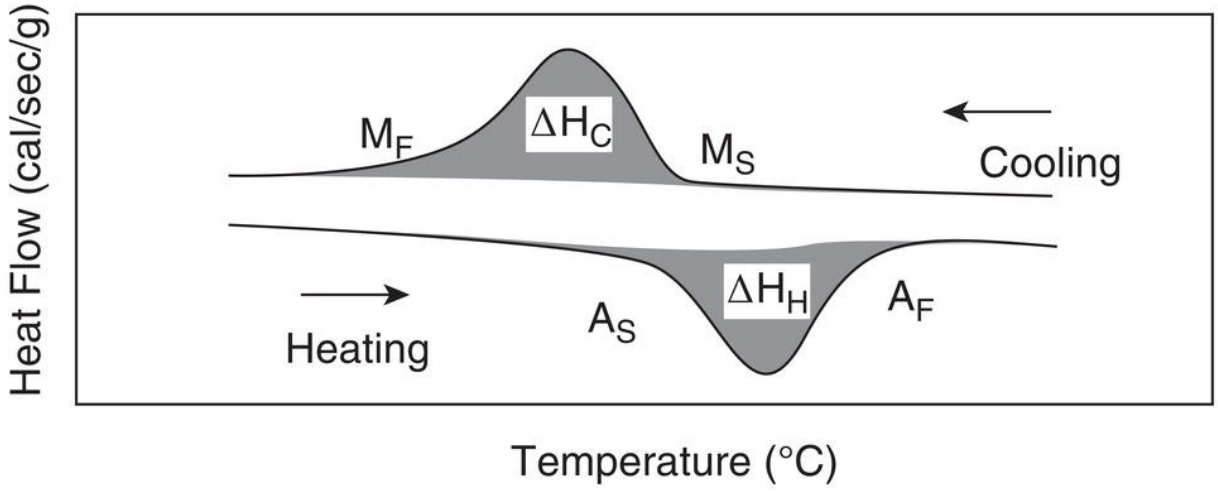
easily found on PubMed, and in 2011 an exciting publication (Burstone et al., 2011) on polyphenylene polymer archwires appeared in the *American Journal of Orthodontics and Dentofacial Orthopedics*.

Fundamental studies of metallic archwires

Two important laboratory techniques that have been employed to investigate the mechanical properties and structures of nickel-titanium orthodontic archwires, where these relationships have enormous clinical importance (Brantley, 2001), are differential scanning calorimetry (DSC; Lee et al., 1988; Khier et al., 1991) and dynamic mechanical analysis (DMA; Kusy and Wilson, 1990; Kusy and Whitley, 2007). Schematic illustrations of the experimental set-ups for conventional DSC and DMA, along with schematic plots of the results from both techniques, are provided in Figures 22.4 and 22.5.


Temperature Controlled Chamber
Chamber Thermocouple
Reference Pan
Specimen Pan
Reference Pan Thermocouple
Specimen Pan Thermocouple

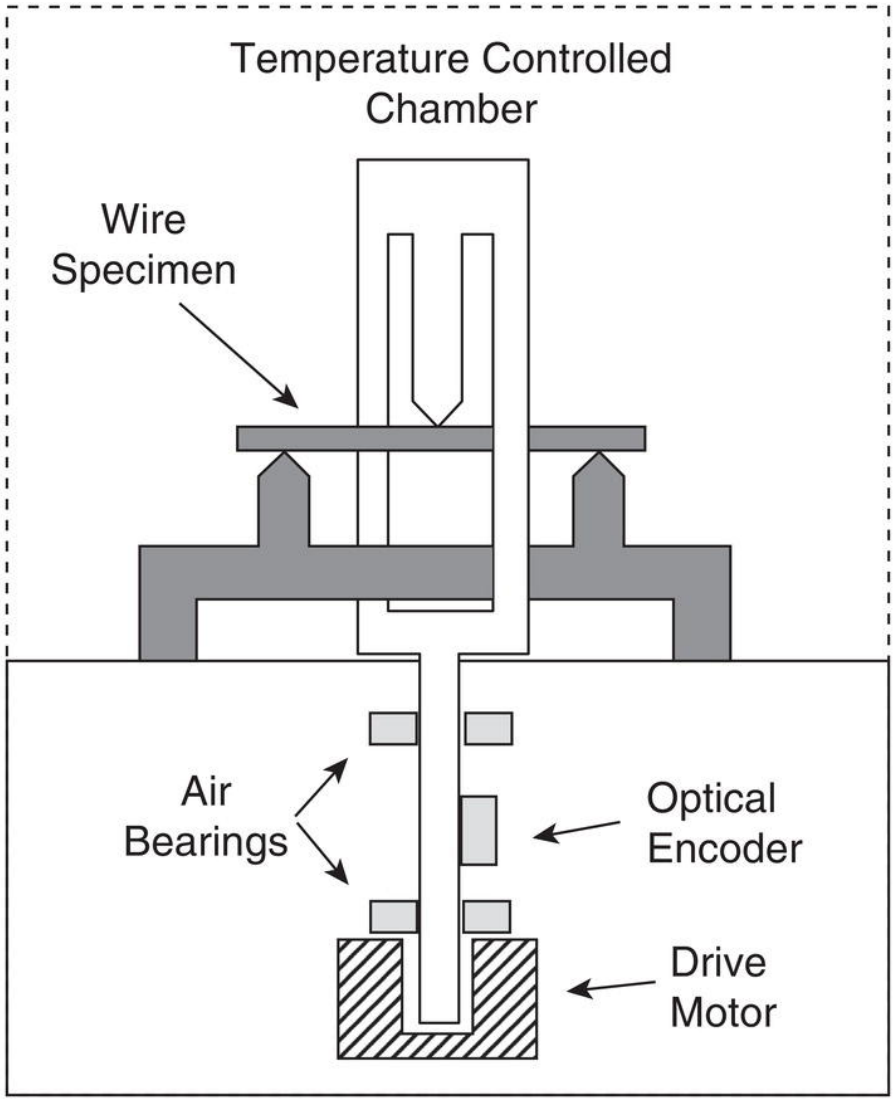
(a)


Heat Flow (cal/sec/g)
M_F
ΔH_C
M_S
Cooling
Heating
A_S
ΔH_H
A_F
Temperature (°C)

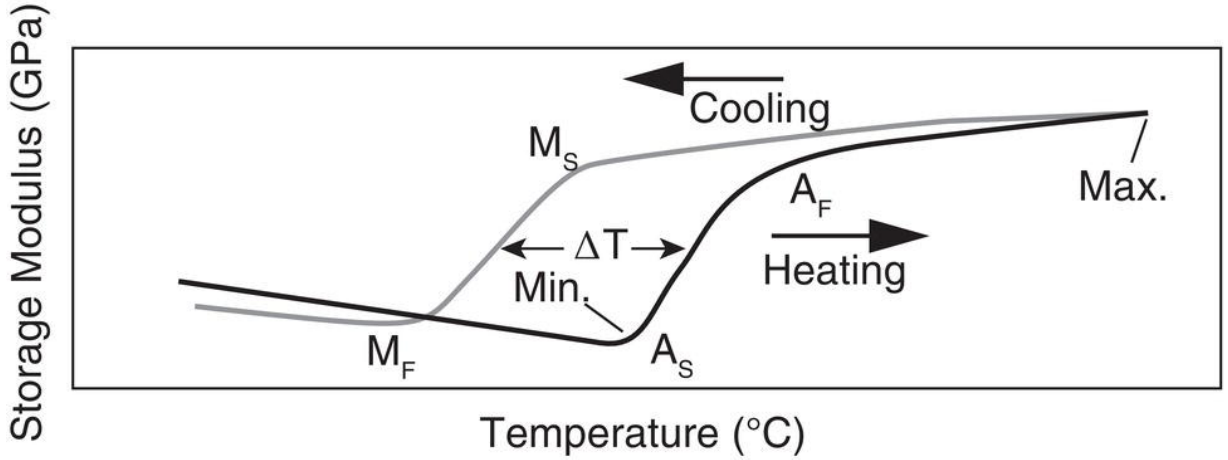
(b)

Figure 22.4 (a) Schematic experimental set-up for conventional differential scanning calorimetry (DSC). (b) Schematic DSC plot for nickel–titanium orthodontic wire, showing enthalpy changes for heating (ΔH_H) and cooling (ΔH_C), start (A_s) and finish (A_F) temperatures for transformation from martensite to austenite during heating, and start (M_S) and finish (M_F) temperatures for transformation from austenite to martensite on cooling.

Reproduced with permission from Kusy and Whitley (2007) / Elsevier.


Temperature Controlled
Chamber
Wire
Specimen
Air
Bearings
Optical
Encoder
Drive
Motor

(a)


Storage Modulus (GPa)
Cooling
M_S
A_F
Max.
ΔT
Heating
Min.
M_F
A_S
Temperature (°C)

(b)

Figure 22.5 (a) Schematic experimental set-up for dynamic mechanical analysis (DMA). (b) Schematic DMA plot of changes in storage modulus for nickel-titanium orthodontic wire, showing effects of transformation from martensite to austenite for heating and transformation from austenite to martensite for cooling, start and finish temperatures for both transformations, and temperature difference (hysteresis) between heating and cooling curves in transformation temperature range.

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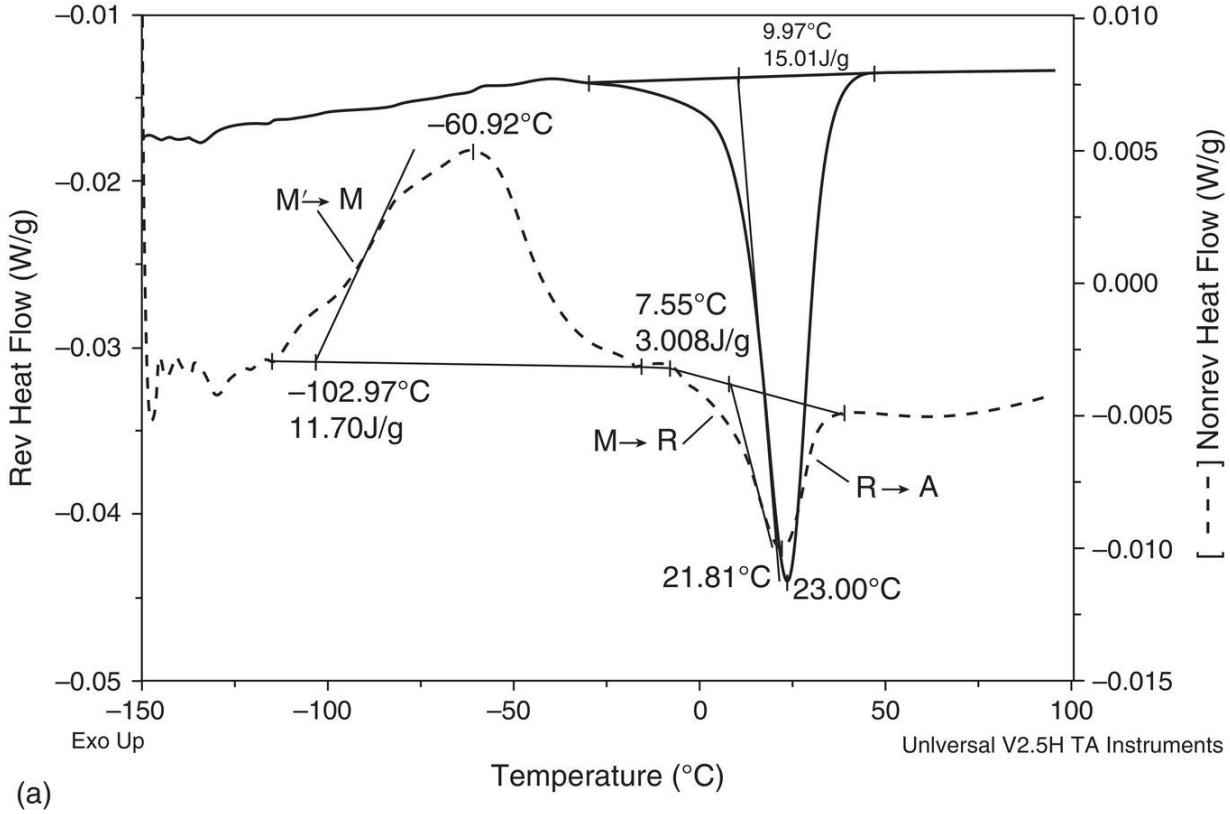
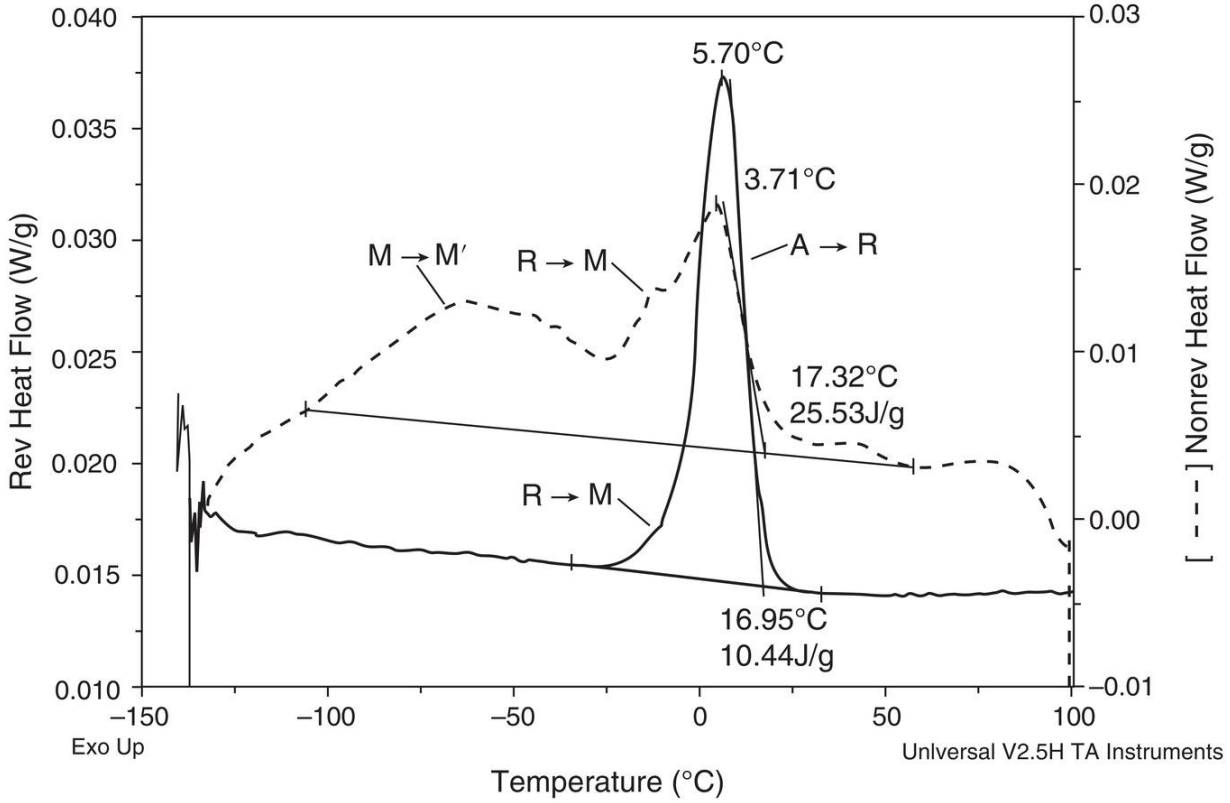
Conventional DSC provides information about temperatures for transformations between higher-temperature austenite and lower-temperature martensite phases, along with enthalpy changes (ΔH), and clearly differentiates among wires having true shape memory *in vivo* and the superelastic and nonsuperelastic wires (Khier et al., 1991). Temperature-modulated DSC (Brantley et al., 2003), where a small sinusoidal thermal oscillation is superimposed on the linear heating/cooling ramp of conventional DSC, provides additional insight into transformations of nickel-titanium wires (Figure 22.6), including occurrence of the intermediate R-phase and a low-temperature transformation within martensite, which was found to be twinning by transmission electron microscopy (Brantley et al., 2008).

With dynamic mechanical analysis, test specimens are subjected to an oscillating stress. Values are obtained for (i) storage modulus corresponding to the strain component in phase with stress (analogous to Young's modulus for tension or shear modulus for that loading mode); (ii) loss modulus for the strain component 90° out of phase with stress; and (iii) tangent delta (ratio of loss modulus and storage modulus), which indicates the level of viscoelastic (nonlinear elastic) behavior. While the dynamic mechanical properties of stainless steel and beta-titanium archwires did not vary over the DMA temperature range from −30 °C to 80 °C, differences in transformations observed by Kusy and Whitley (2007) for nonsuperelastic and superelastic archwires could have clinical significance. Values of transformation temperatures determined by DSC and DMA differ because the test specimens for the former

technique are not subjected to stress during analysis, in contrast to the sinusoidal stress for DMA.


9.97°C
15.01J/g
−60.92°C
M′→ M
7.55°C
3.008J/g
−102.97°C
11.70J/g
M→ R
R→ A
21.81°C
23.00°C
Rev Heat Flow (W/g)
[- - -] Nonrev Heat Flow (W/g)
Exo Up
Universal V2.5H TA Instruments
Temperature (°C)

(a)


5.70°C
3.71°C
M → M′
R → M
A → R
17.32°C
25.53J/g
R → M
16.95°C
10.44J/g
Rev Heat Flow (W/g)
[- - -] Nonrev Heat Flow (W/g)
Exo Up
Universal V2.5H TA Instruments
Temperature (°C)

(b)

Figure 22.6 Temperature-modulated DSC plots for (a) heating and (b) cooling of 35 °C Copper Ni-Ti. Transformations involving austenite (A), martensite (M), and R-phase (R) are designated by arrows. The R-phase transformation in many orthodontic wires is not detected by conventional DSC analysis.

Reproduced with permission from Brantley et al. (2003) / Elsevier.

The mechanical properties of stiffness (elastic modulus), strength (force or stress for elastic limit, or maximum moment for elastic deformation), and range (extent of elastic deformation) are fundamental for the clinical performance of archwires. The relationship between these elastic properties and their measurement (which can be performed in tension, bending, or torsion) are discussed by Brantley et al. (2001), where previous research on measuring these properties by the Kusy group is also presented.

Rucker and Kusy (2002b) compared stiffness, strength, and range for three-strand and six-strand stainless steel wires with single-strand stainless steel and nickel-titanium leveling wires, as well as measuring the properties of wire segments in tension. They concluded that fabrication of multistrand stainless steel wires using alloys with enhanced tensile yield strength would allow these wires to compete better against conventional nickel-titanium wires. Rucker and Kusy (2002c) used bending and tension tests to investigate the properties of noncoated single-strand stainless steel and superelastic nickel-titanium wires, nylon-coated single-strand and multistrand stainless steel wires, and noncoated multistrand stainless steel and nickel-titanium wires. An important conclusion of this research was that few superelastic nickel-titanium wires are activated sufficiently *in vivo* to exhibit superelastic behavior; that is, the superelastic plateau for unloading (Brantley, 2001).

In another important study, Kusy et al. (2004) investigated the composition, morphology, surface roughness, and sliding mechanics of six titanium-based archwires using an SEM with x-ray energy-dispersive analyses, laser specular reflectance, and a friction testing machine. Five wires were beta-titanium alloys with compositions similar to the original TMA (Ormco, Brea, CA, USA) product, and the sixth was an alpha–beta alloy containing 6 wt. % Al and 3 wt. % V.

Beta-titanium alloys are of particular clinical interest because of their biocompatibility due to the absence of nickel (Brantley, 2001). A variety of surface morphologies were observed, and specular reflectance and optical roughness measurements divided these wires into two groups. For values of angulation covering passive and active regions of sliding, coefficients of friction varied narrowly and were independent of surface roughness. Consequently, the authors suggested that from a clinical viewpoint, all six titanium-based archwire products were comparable.

A study by Walker et al. (2007), involving collaboration between an orthodontist, a dental biomaterials faculty member, and an engineering faculty member, employed the three-point bending test methodology in ANSI/ADA Specification No. 32. The elastic properties of 3M Unitek Beta III titanium and stainless steel archwires in distilled water, a neutral fluoride solution, and an acidulated phosphate fluoride solution were compared at 37 °C. The two fluoride solutions caused decreases in the clinically relevant unloading mechanical properties of both the beta-titanium and stainless steel archwires, as well as changes in surface topography from corrosive attack. The important result from this study was that use of these fluoride solutions by patients could extend the time for orthodontic treatment.

Other studies on metallic archwires with a biomedical engineering focus reported relationships between surface condition and electrochemical behavior of nickel-titanium wires and the use of diamond-like coatings. Clarke et al. (2006) prepared a series of wires with a variety of surface conditions. Wires with very thick oxides contained high nickel contents in the oxide layer, and untreated samples with thicker oxides showed lower pitting potential values and greater nickel release in both long- and short-term experiments. For long-term immersion tests in 0.9% NaCl solutions, breakdown potentials for the oxide layers increased. Results demonstrated that appropriate surface treatment of nickel-titanium wires is essential for optimum biomedical performance. Kobayashi et al. (2007) used an arc-discharge ion-plating process and deposited diamond-like coatings (DLC) on nickel-titanium orthodontic archwires. The wires were immersed in physiological saline at 37 °C for six months, and

the concentration of nickel ions released from DLC-coated wires was one-sixth that from noncoated wires. The growth rate of squamous carcinoma cells on DLC-coated wires was higher than that on noncoated wires. Wang and Zheng (2008) compared vacuum arc-melted, hot-rolled, quenched, and annealed plate specimens of a nickel-titanium alloy containing 2.8% cobalt and the equiatomic nickel-titanium alloy in deaerated artificial saliva. Potentiodynamic and potentiostatic test results showed that the corrosion behavior of the two alloys was similar, and that with increasing electrolyte pH, both the corrosion potential and the breakdown potential for pitting decreased. X-ray photoelectron spectroscopy (XPS) revealed that the outermost passive film for the nickel-titanium–cobalt alloy consisted mainly of TiO_2, as found for nickel-titanium. Inductively coupled plasma/optical emission spectroscopy (ICP/OES) indicated that nickel ion release from nickel-titanium–cobalt was very close to that from nickel-titanium, and neither titanium nor cobalt ions could be detected. This study emphasized the important *in vitro* relationship between corrosion behavior and pH underpinning the clinical use of nickel-titanium orthodontic wires.

Force measurements

With the recent improvements in technology, there has been much interest in orthodontic force measurements. Friedrich et al. (1999) described three-dimensional (3D) recording of orthodontic forces during treatment *in vivo* with fixed appliances, using brackets with a special design. Measurements were obtained by a six-axis force-torque sensor with strain gauge elements. Badawi et al. (2009) reported an *in vitro* method for 3D measurements and analyses of orthodontic force systems. Their orthodontic simulator was based on a single dental arch containing 14 teeth, to which brackets could be bonded and wires ligated. Using transducers, it was possible to measure simultaneously the force systems applied on all teeth in the arch by orthodontic appliances and generate 3D force displays. This article raised several controversies, with comments subsequently appearing in the Readers' Forum of the *American Journal of Orthodontics and Dentofacial Orthopedics* (January and April 2010). It is evident that further research is needed to evaluate the

biomechanics of conventional and self-ligating brackets and their clinical efficacy.

Other investigations have examined the behavior of polymeric force-producing modules. Stevenson and Kusy (1994) evaluated the effects of pre-stressing, environmental acidity, oxygen content, and temperature on polyurethane chains. Specimens were treated for 10 and 100 days, and mechanical properties were compared with untreated specimens using stress-relaxation tests. Conditioning treatments affected the residual load after relaxation, with the largest effect due to pre-stressing. An increase in temperature significantly affected the deterioration of mechanical properties, while the acidity and oxygen content of the environment had no significant effects. *In vitro* force decay was described by a Maxwell-Weichert model that assumed one mechanism was responsible for the rapid initial force loss and another mechanism was responsible for the slow force loss at longer times. While this model would ideally allow the orthodontist to predict the force supplied by these polyurethane chains at initial activation and any subsequent time during treatment, the *in vivo* environment to which the chains are exposed during clinical use causes complex degradation processes (Eliades et al., 2001a). The force decay of 3/16 in. latex elastics (3M Unitek, Monrovia, CA, USA) was evaluated by Wang et al. (2007). All specimen groups showed rapid force loss during the first hour, which had been reported previously. At later times of 24 and 48 hours, there was a highly significant force decrease *in vivo* and in artificial saliva, but no significant differences in a dry room. There was significantly more degradation for intermaxillary traction (where different times for wearing the elastics were important) than for intramaxillary traction, and for *in vivo* conditions compared with a dry room environment.

An earlier force measurement study was reported by Katona and Chen (1994), who performed an engineering analysis of a popular tensile bond strength testing methodology at that time for brackets bonded to enamel. They proposed that use of a long harness (wire loop) around the bracket constructed from thin ligature wire, pre-stressing the harness, and lubrication may reduce the effects of inevitable load–bracket misalignment. These authors and their colleagues subsequently conducted numerous other studies on

orthodontic force measurements and biomechanics, involving collaborations between orthodontics, biomechanics, and engineering faculty, and the corresponding publications can found on PubMed.

Orthodontic appliances and finite element analysis

Finite element analysis has been extensively employed in orthodontic research for three decades, with over 340 articles in PubMed. This technique, which has been utilized extensively by Katona, Chen and their colleagues, is a common procedure for solving biomedical engineering problems and is particularly useful for orthodontic biomechanics. Publications by this group (Viecilli et al., 2008, 2009; Meyer et al., 2010) illustrate the methodology and orthodontic applications.

Finite element analysis is a computational process that requires special software. A computer model of the system is initially subdivided into meshes. Using knowledge of elastic constants (Young's modulus and Poisson's ratio), computerized loading of the model causes deformation of the meshes, with displacements of their intersection points (nodes) that are converted to 3D strains and stresses using special finite element analysis software. Nonlinear elastic behavior can also be incorporated into finite element analyses.

An example of a model ceramic bracket with a network of meshes in shown in Figure 22.7. In an important earlier study, Ghosh et al. (1995) applied finite element analysis to several commercial ceramic brackets, observed the resulting stress distributions, and emphasized the value of this technique for investigating bracket design.

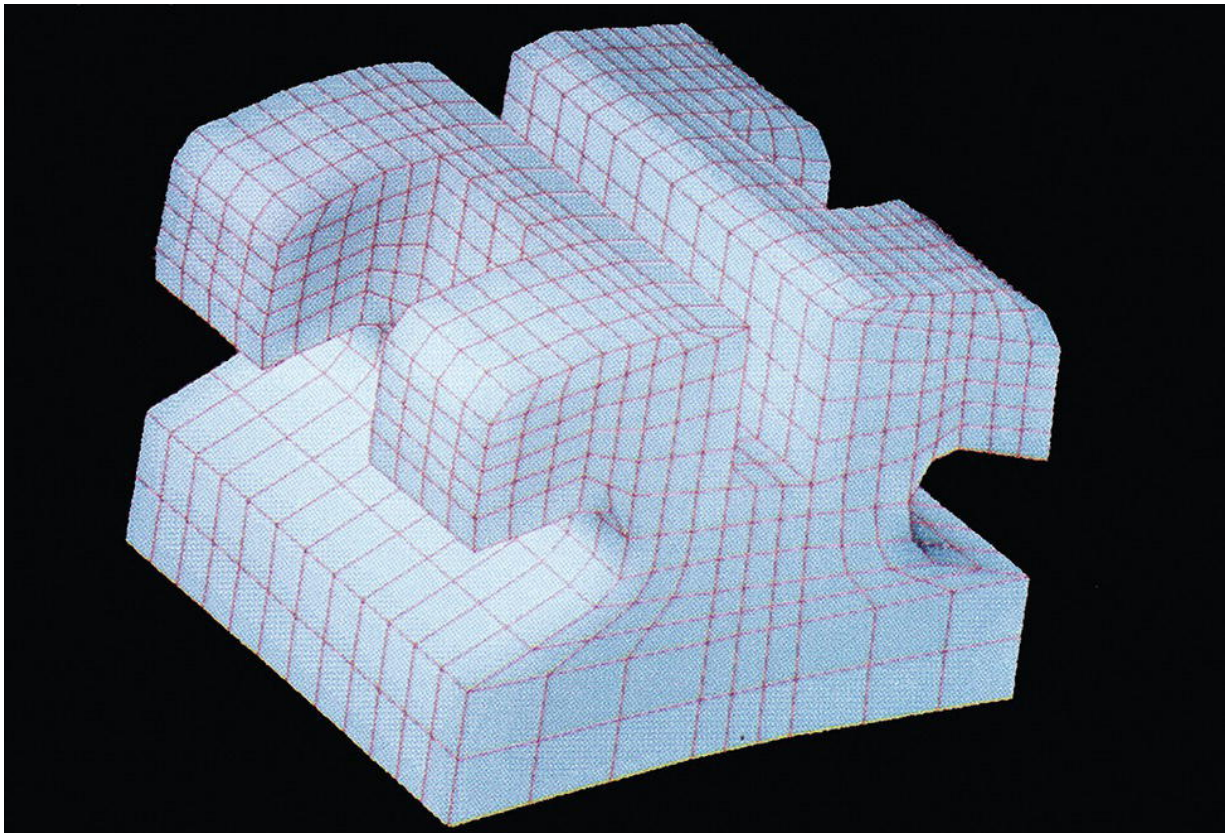


Figure 22.7 Example of bracket model with mesh pattern for finite element analyses of ceramic brackets.

Reproduced with permission from Ghosh et al. (1995) / Elsevier.

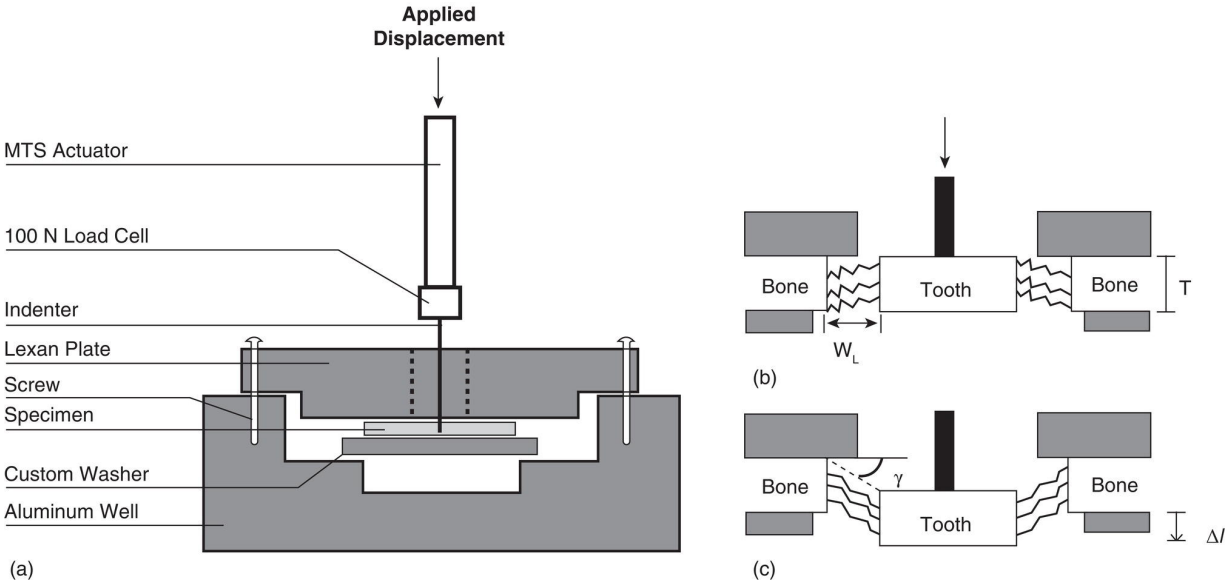


Figure 22.8 (a) Schematic experimental set-up used to investigate stress–strain behavior of periodontal ligament. Schematic illustrations of clamped specimen for loading in extrusion (b) before and (c) after application of load.

Reproduced with permission from Toms et al. (2002) / Elsevier.

Several miscellaneous articles on orthodontic appliances, involving finite element analysis and other sophisticated approaches in collaborations between biomedical engineers and orthodontists, were also retrieved using PubMed. Lewis et al. (1996) used finite element analysis to determine stresses in the adhesive layer of two-dimensional models of bonded brackets. Liu et al. (2004b) used strain tensor analysis to investigate effects of chin cup therapy on the mandible in Class III malocclusions. Lin et al. (2004) utilized finite element analyses to study the effect of retainer thickness on posterior resin-bonded prostheses. Pilliar et al. (2006) developed a finite element model to investigate crestal bone loss patterns around sintered porous-surface and machined-threaded implants produced for orthodontic anchorage that were used in an animal study. Qi et al. (2007) measured the transmission of forces for a cast-metal, fixed, twin-block appliance used to achieve rapid correction of Class II malocclusions. The very wide scope of these articles illustrates the range of research that can be performed in this area and should encourage future collaboration between biomedical engineers and orthodontists.

Miscellaneous areas of research

In the first of three diverse articles, Liu et al. (2004a) investigated the genotypic stability of *Streptococcus mutans* using plaque samples obtained from supragingival smooth surfaces of right maxillary teeth at four stages of orthodontic treatment. DNA was prepared from a large number of *S. mutans* strains, and strains were identified using PCR. PCR fingerprinting was applied to determine genotypes. The amount of *S. mutans* increased significantly after fixed appliances were bonded, and *S. mutans* clones were stable during orthodontic treatment.

In the second article, Kusy (2004) presented a theoretical bioengineering model that considered the influences of specific concentrations of allergens on their clinical effects, focusing on nickel and chromium for orthodontic patients. He noted clinical responses to these two allergens in a large number of patients. The practical application of his model involved a questionnaire, and in the patient reporting an allergy a skin patch test would be administered to establish whether alternative alloys not containing these elements should be used during treatment.

The third article was by Toms et al. (2002), who investigated the stress–strain behavior of the periodontal ligament (PDL) using tissues obtained from cadaveric specimens of young and elderly adults. The schematic experimental set-up is shown in Figure 22.8, and a representative stress–strain curve for the PDL is presented in Figure 22.9. The stress–strain curves for both intrusion and extrusion loading had nonlinear behavior with distinct low elastic modulus toe and higher elastic modulus linear regions. The loading behavior of the PDL was found to be dependent on age, location (cervical margin, apex region, and midroot region), and load direction (intrusion or extrusion). An important consequence from this study was the suggestion that computer simulations of orthodontic tooth movement should incorporate the nonlinear behavior of the PDL.

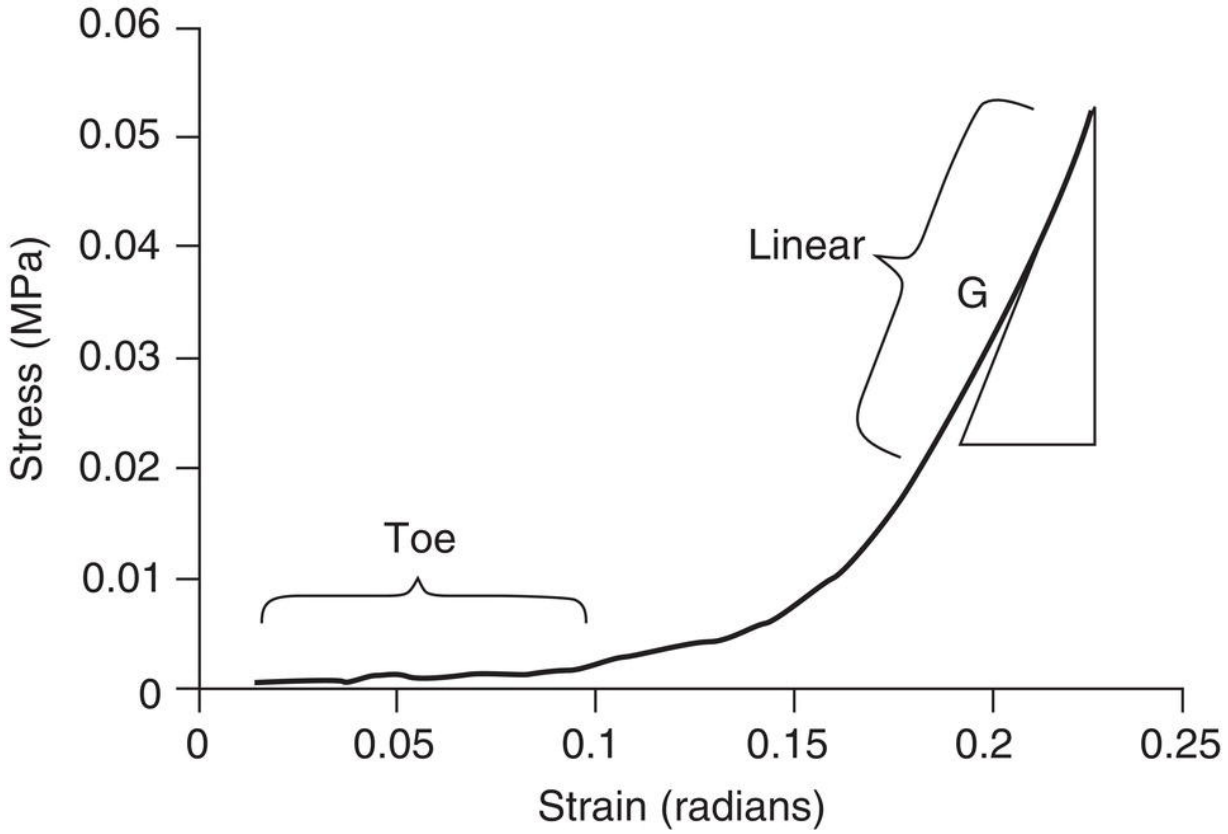


Figure 22.9 Nonlinear stress–strain curve for the periodontal ligament at low stress. Toe modulus was calculated for toe region, beginning at origin, and linear modulus was calculated in linear region shown. Modulus values were calculated for intrusion and extrusion.

Reproduced with permission from Toms et al. (2002) / Elsevier.

Current research activities and potential future applications

Advances in materials science and related fields have resulted in the introduction of materials and processes that create applications of unique properties in a wide range of biomedical disciplines. The purpose of this part of the chapter is to highlight advances (Box 22.2) that may have direct application to orthodontic materials from both the clinical and research perspectives. The majority of these advances have not yet been applied to orthodontic materials; in some areas preliminary data on experimental products have been

published, although without current translation into commercial availability.

Box 22.2 Recent advances in materials science and engineering areas with application to orthodontics

- Shape-memory polymers for archwires.
- Self-healing materials.
- Smart brackets with force–moment sensors.
- Biomimetic adhesives.
- Self-cleaning materials.

Shape-memory polymers – polymer wires

Shape-memory polymers are an emerging class of polymers with applications spanning various areas of everyday life. These polymers are dual-shape materials belonging to the group of "actively moving" polymers that can change from one shape to another, the first being a temporary shape obtained by mechanical deformation and the second obtained from subsequent fixation of that deformation (Behl and Lendlein, 2007).

For shape-memory polymers, heat, light, infrared radiation, electrical and magnetic fields, and immersion in water have been used to induce this property. The shape-memory effect depends on the molecular architecture and does not require a specific chemical structure in the repeating units. In essence, application of external stimuli to these materials introduces a departure from the as received shape to a new configuration that is reversible. This cycle of

programming and recovery can be repeated several times, with different temporary shapes in subsequent cycles. In comparison with metallic shape-memory alloys, the shape-memory "cycle" for these polymers can take place in a much shorter time and at a much higher deformation rate between shapes. An example of a biomedical application of shape-memory polymers is a laser-activated device for the mechanical removal of blood clots. The device is inserted by minimally invasive surgery into the blood vessel, and on laser activation the shape-memory polymer coils into its permanent shape, enabling the mechanical removal of the clot.

In orthodontics, the potential application of these materials involves the manufacturing of polymeric transparent wires with minimum stiffness, which could then be transformed into archwires of predetermined elastic modulus on exposure to a stimulus such as light or heat. Therefore, esthetics along with a preferable stiffness would be attained during intraoral application of these materials.

Polymers are largely being used in the specialty of orthodontics for manufacturing of aligners. In recent times, orthodontic research is slowly shifting its attention toward thermo-responsive shape-memory polyurethane-based thermoplastic material, which is claimed to have the ability to recover to its original thermoformed shape by a process of thermal activation at a specific temperature for a certain period of time. Due to the stepwise shape-changing property, this material might be used for the fabrication of orthodontic aligners and overcome the rate-limiting staging of conventional aligners and, consequently, reduce the number of aligners used per treatment (Elshazly et al., 2021).

Self-healing materials

The design and manufacturing of "smart" synthetic systems that can mimic the behavior of biological systems that heal themselves has been an objective of intense research during the past decade. Hybrid materials have been recently created where micrometer-scale conduits extend throughout the material and contain healing fluids or dissolved healing agents (Balazs, 2007). When a crack appears near the network, the fluid can flow to the damaged region and fill the fissure. The simplest form to achieve this behavior might be the

incorporation of bubbles of a material/substance/precursor in the raw material. This reservoir, on exposure to air, polymerizes as a result of crack formation and spontaneously closes the crack, thus maintaining the structural integrity of the material.

The orthodontic application of this concept may involve polymer brackets and archwires. The integration of nano-sized bubbles filled with auto-polymerized monomer in these materials may result in a reduction of wire and bracket breakages. Fracture of the bracket or wire would induce bursting of the nano-bubbles and exposure of the monomer to air, thereby resulting in polymerization and filling of the crack-induced gap.

Brackets with force–moment sensors

Estimation of force and moment magnitudes applied during standard mechanotherapeutic configurations in orthodontics has been the focus of many *in vitro* studies during the past two decades. These efforts have employed numerous devices and techniques, as described by Bourauel et al. (1992) and Badawi et al. (2009), to measure forces applied to teeth. Limitations of the *in vitro* environment, however, have imposed a substantial burden on the clinical relevance of the results.

A research perspective on this topic, which has been long sought in the orthodontic materials and biomechanics fields, has provided a breakthrough in developments in monitoring the variation of force applied to teeth *in vivo* under real-time conditions (Lapatki et al., 2007). These researchers, who are from Departments of Orthodontics and Microsystems Engineering at the University of Freiberg in Germany, have manufactured an orthodontic bracket with an integrated microelectronic chip equipped with multiple piezo-resistive stress sensors capable of quantitatively determining forces in three dimensions (Figure 22.10). A study assessing the accuracy of this sensor-integrated bracket demonstrated good agreement between measured and reference values, with standard deviations in the differences of 0.037 N for forces and 0.985 N·mm for moments. This bracket will be of major service to both the clinician and the researcher, allowing applications of low-force

bracket–wire configurations and providing the means to perform research on this subject in humans.

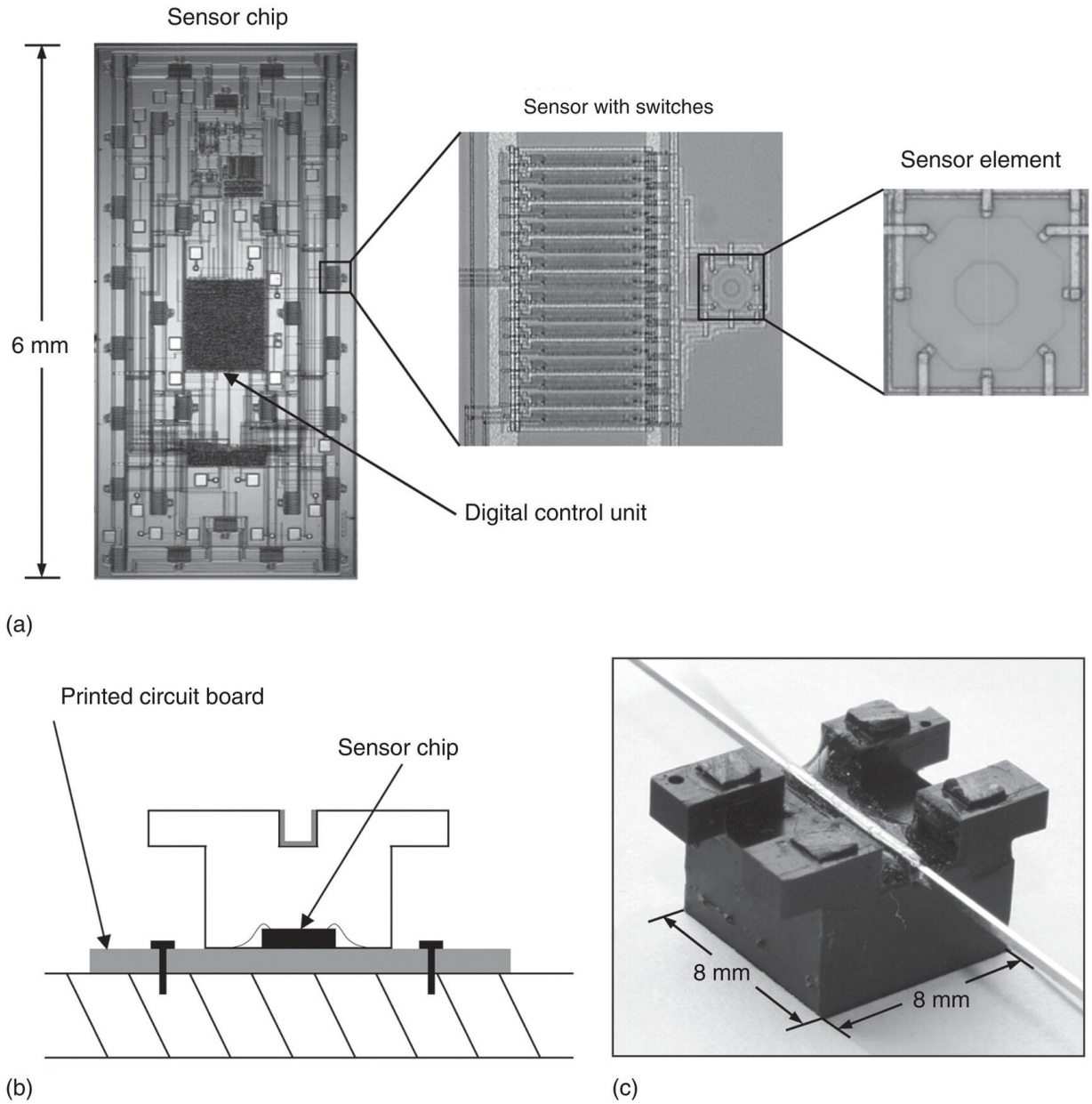


Figure 22.10 Smart bracket. (a) Micrograph of sensor chip, showing individual sensor with switches and sensor element. (b) Schematic cross-section of smart bracket model, with sensor chip wire-bonded to printed circuit board and encapsulated in plastic bracket. (c) Photograph of manufactured smart bracket with base of 8×8 mm^2 (approximate scale 2.5 : 1 compared with normal bracket).

Lapatki et al. (2007) / with permission from SAGE Publications.

Biomimetic adhesives

The issue of an enamel-friendly bonding mechanism for orthodontic appliances has been the subject of investigations since the introduction of the acid-etching technique. This intense interest derived from the description of alterations of enamel color and structure associated with acid-etched mediated bonding (Eliades et al., 2001b). Although glass-ionomer adhesives have offered an alternative, their applications remain limited, probably because of the higher failure rates.

The introduction during the past 15 years of a new class of materials that adopt the paradigms of nature has gradually established the category of biomimetic materials. This term derives from the Greek "bio" (living) and "mimetic" (imitating or resembling), and refers to how creatures ingenuously employ natural elements to solve problems in the environment (Lee et al., 2007; Hamming et al., 2008; Bilic et al., 2010).

For example, geckos are lizards that belong to the species of Gekkonidae and are characterized by a remarkable ability to sustain their weight while upside down. The strong but temporary adhesion employed by a gecko comes from a mechanical principle known as "contact splitting." The foot of a gecko has a flat pad that is densely packed with very fine hairs that are split at the ends, resulting in a greater number of contact points than if the hairs were not split. More contact points between these hairs and a surface result in a significant increase in adhesion. Researchers have discovered that the special nature of the foot pads allows the gecko to stick to surfaces through the formation of localized van der Waals forces. This mechanism has been employed for high-friction microfibers or carbon nanotubes, which are sprayed on a surface. Because of their enormous number per unit area, the physical forces developed mimic the ability of a gecko to attach firmly to surfaces without the use of a chemical substance.

While this mode of bonding may be suitable for dry environments, it fails to provide reliable performance with wet surfaces (Lee et al., 2007). This problem inspired researchers to adopt another natural example of bonding: that of mussels. Combining the important

elements of gecko and mussel adhesion, the new adhesive material, called “geckel,” functions like a sticky note and exhibits strong yet reversible adhesion in both air and water. Mussel-mimetic polymers have an amino acid called L-3,4-dihydroxyphenylalanine (DOPA) found in high concentrations in the “glue” proteins of mussels (Hamming et al., 2008). Analogous to the gecko-based approach, pillar arrays (400–600 nm in diameter and length) coated with the mussel-mimetic polymer improved wet adhesion by 15-fold over uncoated pillar arrays. One of the first applications of this new material has involved fetal membrane defects, which pose a serious risk for leakage of amniotic fluid that can result in premature birth or termination of pregnancy. A sealant inspired by the ability of mussels to stick to surfaces under wet conditions has shown promise for repairing defects in human fetal membranes (Bilic et al., 2010).

There is vast scope for orthodontic application of this innovation. Brackets having bases with pads mimicking the gecko foot and covered with a layer of DOPA would provide adequate bond strength to sound enamel without prior enamel conditioning and with minimal color and structural alterations to the enamel. To the best of our knowledge, the use of this type of biomimetic adhesive has not yet been adopted by manufacturers of orthodontic brackets.

Self-cleaning materials

The issue of plaque retention on brackets and microbial attachment onto these calcified biofilms has been a major concern from an enamel prophylactic perspective. The development of a material that could clean itself of not only inorganic (mainly) but also organic precipitations is an attractive prospect in the materials science areas involving biomedical, industrial, and aeronautical applications. Early research in this field adopted the paradigm of microscopic bumps on a lotus leaf, which transform its waxy surface into an extremely water-repellent, or superhydrophobic, material (Forbes, 2008). Synthetic self-cleaning materials have been developed, some of which are based on this “lotus effect,” whereas others employ the opposite property of “superhydrophilicity” as well as catalytic chemical reactions.

The use of titanium oxide nanocoatings has been found to increase the safety of aircraft by preventing the build-up of ice and other contaminants. This process creates self-cleaning “superhydrophobic” surfaces, and involves the application of a hydrofluoric acid coating on the titanium alloy substrate. A substantially self-cleaning superhydrophobic surface is created when exposure to ultraviolet light causes the titanium oxide layer to undergo photocatalytic reaction with oxygen to oxidize any organic contaminants that may be present. Since superhydrophobic surfaces resist soiling by water-borne contaminants, they are easily cleaned and useful in directing flow in microfluidic devices.

Polyoxometalates (POM) have rich and promising photochemical behavior. On illumination corresponding to the OMCT (oxygen-metal-charge transfer) band (i.e. in the ultraviolet and near-visible areas), POM become powerful oxidizing reagents able to oxidize a wide variety of organic compounds (Papaconstantinou et al., 2003). In the process, the POM undergo stepwise reduction, accumulating electrons that can be subsequently delivered via thermal reactions to different oxidants. In this way a wide variety of organic compounds are oxidized and mineralized to carbon dioxide, water, and inorganic anions. Several organic and inorganic compounds can be reduced via a photocatalytic process in which the POM serve as electron relays. Thus, in principle, POM can serve as decontamination photocatalysts of aquatic media, removing both organic pollutants and metal ions.

Photocatalytic activity from the reaction of titanium oxide with ultraviolet light has recently gained attention in orthodontic materials (Horiuchi et al., 2007). In particular, there is scientific interest in inducing photocatalytic reactions on the nickel–titanium archwire alloy. By thickening the titanium oxide film with electrolytic treatment and then applying heat treatment, the surface film on nickel–titanium was modified from an amorphous structure to crystalline rutile (TiO_2).

Other smart biomaterials

Other “smart biomaterials” are described in an article by Anderson et al. (2004). For example, some polymeric biomimetic materials that

utilize nanofibers formed from peptides and proteins have the ability to self-assemble into 3D structures. Such materials may be able to control cellular behavior and enable the production of multiple lineages from a single stem cell type. Hydrogels containing matrix metalloproteinase (MMP)-degradable sites and growth factors such as bone morphogenetic proteins (BMP) may find application for healing of bony defects. Implant biomaterials are being developed that can be converted from the liquid state to the solid state at desired sites *in vivo*, using light, temperature, or pH changes. Other biomaterials with "smart surfaces" are being developed that can reversibly switch between a hydrophilic and hydrophobic nature with the application of an electrical potential, and such coatings would enable the production of devices with digitally responsive surfaces. All of these materials might potentially find applications in orthodontics, provided that continued laboratory developments are successful and these innovations are communicated to orthodontists and biomedical engineers. This exciting new field of smart biomaterials lies at the intersection of cell biology, tissue engineering, and materials science, which are major domain areas for modern biomedical engineering.

Conclusions

These are exciting times for the development of customized orthodontic materials and appliances, and interactions with biomedical engineers will accelerate the pace of improvements. Smart biocompatible materials and brackets will become part of the armamentarium in the future. Important domains of biomedical engineering, particularly use of nanotechnology for device fabrication, continued development of nanostructured and biomimetic materials, and application of tissue engineering principles for hard and soft tissues, should be prominent areas of forthcoming research.

Based on our experience, orthodontic faculties in research-oriented institutions need to approach faculty in biomedical engineering or bioengineering departments and point out the opportunities that are available for collaboration. While such collaborations have occurred in a few universities in the past, there is a critical need for much

greater mutual interaction, which can be fostered by joint departmental appointments. Innovative research that translates into fruitful relationships between *in vitro* laboratory studies and the *in vivo* clinical environment will require considerable dialog between researchers with disparate orthodontic and biomedical engineering viewpoints to frame the appropriate protocols. In the United States, novel research proposals on the applications of biomimetic materials and smart materials, and the interaction between biomechanical and biological processes for orthodontics, may be considered favorably for support by the National Institutes of Health.

References

Anderson, D.G., Burdick, J.A., and Langer, R. (2004). Smart biomaterials. *Science* 305: 1923–1924.

Andreasen, G., and Quevedo, F. (1969). Evaluation of friction forces in the .022 by .028 by edgewise bracket in vitro. *American Journal of Orthodontics* 55(2): 201. doi: 10.1016/0002-9416(69)90137-7.

Badawi, H.M., Toogood, R.W., Carey, J.P. et al. (2009). Three-dimensional orthodontic force measurements. *American Journal of Orthodontics and Dentofacial Orthopedics* 136: 518–528.

Balazs, A.C. (2007). Modeling self-healing materials. *Materials Today* 10: 18–23.

Behl, M., and Lendlein, A. (2007). Shape-memory polymers. *Materials Today* 4: 20–28.

Bilic, G., Brubaker, C., Messersmith, P.B. et al. (2010). Injectable candidate sealants for fetal membrane repair: Bonding and toxicity in vitro. *American Journal of Obstetrics and Gynecology* 202: 85.e1–9.

Bourauel, C., Drescher, D., and Thier, M. (1992). An experimental apparatus for the simulation of three-dimensional movements in orthodontics. *Journal of Biomedical Engineering* 14: 371–378.

Brantley, W.A. (2001). Orthodontic wires. In: W.A. Brantley and T. Eliades (eds.), *Orthodontic Materials: Scientific and Clinical Aspects*. Stuttgart: Thieme, pp. 79–97.

Brantley, W.A., Eliades, T., and Litsky, A.S. (2001). Mechanics and mechanical testing of orthodontic materials. In: W.A. Brantley and T. Eliades (eds.), *Orthodontic Materials: Scientific and Clinical Aspects*. Stuttgart: Thieme, pp. 33–36.

Brantley, W.A., Guo, W., Clark, W.A.T. et al. (2008). Microstructural studies of 35°C copper Ni–Ti orthodontic wire and TEM confirmation of low-temperature martensite transformation. *Dental Materials* 24: 204–210.

Brantley, W.A., Iijima, M., and Grentzer, T.H. (2003). Temperature-modulated DSC provides new insight about nickel-titanium wire transformations. *American Journal of Orthodontics and Dentofacial Orthopedics* 124: 387–394.

Burrow, S.J. (2009). Friction and resistance to sliding in orthodontics: A critical review. *American Journal of Orthodontics and Dentofacial Orthopedics* 135: 442–447.

Burstone, C.J., Liebler, S.A.H., and Goldberg, A.J. (2011). Polyphenylene polymers as esthetic orthodontic archwires. *American Journal of Orthodontics and Dentofacial Orthopedics* 139: e391–e398.

Clarke, B., Carroll, W., Rochev, Y. et al. (2006). Influence of Nitinol wire surface treatment on oxide thickness and composition and its subsequent effect on corrosion resistance and nickel ion release. *Journal of Biomedical Materials Research A* 79: 61–70.

Eliades, T., Eliades, G., Watts, D.C. et al. (2001a). Elastomeric ligatures and chains. In: W.A. Brantley and T. Eliades (eds.), *Orthodontic Materials: Scientific and Clinical Aspects*. Stuttgart: Thieme, pp. 173–187.

Eliades, T., Kakaboura, A., Eliades, G. et al. (2001b). Comparison of enamel color changes associated with orthodontic bonding using

two different adhesives. *European Journal of Orthodontics* 1: 85–90.

Elshazly, T. M., Keilig, L., Alkabani, Y. et al. (2021). Primary evaluation of shape recovery of orthodontic aligners fabricated from shape memory polymer (a typodont study). *Dentistry Journal* 9(3): 31.

Forbes, P. (2008) Self-cleaning materials. *Scientific American* 299: 88–95.

Friedrich, D., Rosarius, N., Rau, G. et al. (1999). Measuring system for in vivo recording of force systems in orthodontic treatment—concept and analysis of accuracy. *Journal of Biomechanics* 32: 81–85.

Ghosh, J., Nanda, R.S., Duncanson, M.G., Jr. et al. (1995). Ceramic bracket design: An analysis using the finite element method. *American Journal of Orthodontics and Dentofacial Orthopedics* 108: 575–582.

Hamming, L.M., Fan, X.W., Messersmith, P.B. et al. (2008). Mimicking mussel adhesion to improve interfacial properties in composites. *Composite Scientific Technology* 68: 2042–2048.

Henao, S.P., and Kusy, R.P. (2004). Evaluation of the frictional resistance of conventional and self-ligating bracket designs using standardized archwires and dental typodonts. *Angle Orthodontist* 74: 202–211.

Henao, S.P., and Kusy, R.P. (2005). Frictional evaluations of dental typodont models using four self-ligating designs and a conventional design. *Angle Orthodontist* 75: 75–85.

Horiuchi, Y., Horiuchi, M., Hawana, T. et al. (2007). Effect of surface modification on the photocatalysis of Ti-Ni alloy in orthodontics. *Dental Materials Journal* 26: 924–929.

Huang, Z.M., Gopal, R., Fujihara, K. et al. (2003). Fabrication of a new composite orthodontic archwire and validation by a bridging micromechanics model. *Biomaterials* 24: 2941–2953.

Imai, T., Watari, F., Yamagata, S. et al. (1998). Mechanical properties and aesthetics of FRP orthodontic wire fabricated by hot drawing. *Biomaterials* 19: 2195–2200.

Katona, T.R., and Chen, J. (1994). Engineering and experimental analyses of the tensile loads applied during strength testing of direct bonded orthodontic brackets. *American Journal of Orthodontics and Dentofacial Orthopedics* 106: 167–174.

Khier, S.E., Brantley, W.A., and Fournelle, R.A. (1991). Bending properties of superelastic and nonsuperelastic nickel-titanium orthodontic wires. *American Journal of Orthodontics and Dentofacial Orthopedics* 99: 310–318.

Kobayashi, S., Ohgoe, Y., Ozeki, K. et al. (2007). Dissolution effect and cytotoxicity of diamond-like carbon coatings on orthodontic archwires. *Journal of Materials Science: Materials in Medicine* 18: 2263–2268.

Kusy, R.P. (2004). Clinical response to allergies in patients. *American Journal of Orthodontics and Dentofacial Orthopedics* 125: 544–547.

Kusy, R.P., and Whitley, J.Q. (1990a). Effects of surface roughness on the coefficients of friction in model orthodontic systems. *Journal of Biomechanics* 23: 913–925.

Kusy, R.P., and Whitley, J.Q. (1990b). Coefficients of friction for arch wires in stainless steel and polycrystalline alumina bracket slots. I. The dry state. *American Journal of Orthodontics and Dentofacial Orthopedics* 98: 300–312. Erratum (1993) in *American Journal of Orthodontics and Dentofacial Orthopedics* 104: 26.

Kusy, R.P., and Whitley, J.Q. (2007). Thermal and mechanical characteristics of stainless steel, titanium-molybdenum, and nickel-titanium archwires. *American Journal of Orthodontics and Dentofacial Orthopedics* 131: 229–237.

Kusy, R.P., Whitley, J.Q., and de Araújo Gurgel, J. (2004). Comparisons of surface roughnesses and sliding resistances of 6

titanium-based or TMA-type archwires. *American Journal of Orthodontics and Dentofacial Orthopedics* 126: 589–603.

Kusy, R.P., Whitley, J.Q., Mayhew, M.J. et al. (1988). Surface roughness of orthodontic archwires via laser spectroscopy. *Angle Orthodontist* 58: 33–45.

Kusy, R.P., and Wilson, T.W. (1990). Dynamic mechanical properties of straight titanium alloy arch wires. *Dental Materials* 6: 228–236.

Lapatki, B.G., Bartholomeyczik, J., Ruther, P. et al. (2007). Smart bracket for multi-dimensional force and moment measurement. *Journal of Dental Research* 86: 73–78.

Lee, H., Lee, B.P., and Messersmith, P.B. (2007). A reversible wet/dry adhesive inspired by mussels and geckos. *Nature* 448: 338–341.

Lee, J.H., Park, J.B., Andreasen, G.F. et al. (1988). Thermomechanical study of Ni-Ti alloys. *Journal of Biomedical Materials Research* 22: 573–588.

Lewis, G., Manickam, S., and Wharton, D. (1996). Effect of debonding forces on bonded orthodontic brackets: Finite element study. *Biomedical Materials Engineering* 6: 113–121.

Lin, T.S., Lin, C.L., Wang, C.H. et al. (2004). The effect of retainer thickness on posterior resin-banded prostheses: A finite element study. *Journal of Oral Rehabilitation* 31: 1123–1129.

Liu, J., Bian, Z., Fan, M. et al. (2004a). Typing of mutans streptococci by arbitrarily primed PCR in patients undergoing orthodontic treatment. *Caries Research* 38: 523–529.

Liu, P.H., Chang, C.H., Chang, H.P. et al. (2004b). Treatment effects of chin cup appliance on mandible in Class III malocclusion: Strain tensor analysis. *A pilot study*. *Quintessence International* 35: 621–629.

Loftus, B.P., Årtun, J., Nicholls, J.I. et al. (1999). Evaluation of friction during sliding tooth movement in various bracket-arch

wire combinations. *American Journal of Orthodontics and Dentofacial Orthopedics* 116: 336–345.

McKamey, R.P., and Kusy, R.P. (1999). Stress-relaxing composite ligature wires: Formulations and characteristics. *Angle Orthodontist* 69: 441–449.

Meyer, B.N., Chen, J., and Katona, T.R. (2010). Does the center of resistance depend on the direction of tooth movement? *American Journal of Orthodontics and Dentofacial Orthopedics* 137: 354–361.

Papaconstantinou, E., Hiskia, A., and Troupis, A. (2003). Photocatalytic processes with tungsten oxygen anion clusters. *Frontiers in Bioscience* 8: s813–s825.

Pilliar, R.M., Sagals, G., Meguid, S.A. et al. (2006). Threaded versus porous-surfaced implants as anchorage units for orthodontic treatment: Three-dimensional finite element analysis of peri-implant bone tissue stresses. *International Journal of Oral and Maxillofacial Implants* 21: 879–889.

Qi, J., Tan, Z.R., He, H. et al. (2007). A preliminary report of a new design of cast metal fixed twin-block appliance. *Journal of Orthodontics* 34: 213–219.

Reznikov, N., Har-Zion, G., Barkana, I. et al. (2010). Measurement of friction forces between stainless steel wires and “reduced-friction” self-ligating brackets. *American Journal of Orthodontics and Dentofacial Orthopedics* 138: 330–338.

Rucker, B.K., and Kusy, R.P. (2002a). Resistance to sliding of stainless steel multistranded archwires and comparison with single-stranded leveling wires. *American Journal of Orthodontics and Dentofacial Orthopedics* 122: 73–83.

Rucker, B.K., and Kusy, R.P. (2002b). Elastic flexural properties of multistranded stainless steel versus conventional nickel titanium archwires. *Angle Orthodontist* 72: 302–309.

Rucker, B.K., and Kusy, R.P. (2002c). Elastic properties of alternative versus single-stranded leveling archwires. *American Journal of Orthodontics and Dentofacial Orthopedics* 122: 528–541.

Stevenson, J.S., and Kusy, R.P. (1994). Force application and decay characteristics of untreated and treated polyurethane elastomeric chains. *Angle Orthodontist* 64: 455–464; discussion 465–467.

Thorstenson, G.A., and Kusy, R.P. (2001). Resistance to sliding of self-ligating brackets versus conventional stainless steel twin brackets with second-order angulation in the dry and wet (saliva) states. *American Journal of Orthodontics and Dentofacial Orthopedics* 120: 361–370.

Thorstenson, G.A., and Kusy, R.P. (2002a). Comparison of resistance to sliding between different self-ligating brackets with second-order angulation in the dry and saliva states. *American Journal of Orthodontics and Dentofacial Orthopedics* 121: 472–482.

Thorstenson, G.A., and Kusy, R.P. (2002b). Effect of archwire size and material on the resistance to sliding of self-ligating brackets with second-order angulation in the dry state. *American Journal of Orthodontics and Dentofacial Orthopedics* 122: 295–305.

Thorstenson, G.A., and Kusy, R. (2003a). Influence of stainless steel inserts on the resistance to sliding of esthetic brackets with second-order angulation in the dry and wet states. *Angle Orthodontist* 73: 167–175.

Thorstenson, G.A., and Kusy, R.P. (2003b). Effects of ligation type and method on the resistance to sliding of novel orthodontic brackets with second-order angulation in the dry and wet states. *Angle Orthodontist* 73: 418–430.

Thorstenson, G.A., and Kusy, R.P. (2004). Resistance to sliding of orthodontic brackets with bumps in the slot floors and walls: Effects of second-order angulation. *Dental Materials* 20: 881–892.

Tidy, D.C. (1989). Frictional forces in fixed appliances. *American Journal of Orthodontics and Dentofacial Orthopedics* 96: 249–254.

Toms, S.R., Lemons, J.E., Bartolucci, A.A. et al. (2002). Nonlinear stress-strain behavior of periodontal ligament under orthodontic loading. *American Journal of Orthodontics and Dentofacial Orthopedics* 122: 174–179.

Viecilli, R.F., Katona, T.R., Chen, J. et al. (2008). Three-dimensional mechanical environment of orthodontic tooth movement and root resorption. *American Journal of Orthodontics and Dentofacial Orthopedics* 133: 791.e11–26.

Viecilli, R.F., Katona, T.R., Chen, J. et al. (2009). Orthodontic mechanotransduction and the role of the P2X7 receptor. *American Journal of Orthodontics and Dentofacial Orthopedics* 135: 694.e1–16.

Walker, M.P., Ries, D., Kula, K. et al. (2007). Mechanical properties and surface characterization of beta titanium and stainless steel orthodontic wire following topical fluoride treatment. *Angle Orthodontist* 77: 342–348.

Wang, Q.Y., and Zheng, Y.F. (2008). The electrochemical behavior and surface analysis of $Ti_{50}Ni_{47.2}Co_{2.8}$ alloy for orthodontic use. *Dental Materials* 24: 1207–1211.

Wang, T., Zhou, G., Tan, X. et al. (2007). Evaluation of force degradation characteristics of orthodontic latex elastics in vitro and in vivo. *Angle Orthodontist* 77(4): 688–693.

Zufall, S.W., and Kusy, R.P. (2000a). Sliding mechanics of coated composite wires and the development of an engineering model for binding. *Angle Orthodontist* 70: 34–47.

Zufall, S.W., and Kusy, R.P. (2000b). Stress relaxation and recovery behaviour of composite orthodontic archwires in bending. *European Journal of Orthodontics* 22: 1–12.

23
Designing and Manufacturing Customized Orthodontic Appliances

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Summary

Digital technology has changed many aspects of our daily life. Orthodontics could not have been an exception to this change. The inclusion of surface and volume scanners, computer-aided design (CAD) software, three-dimensional (3D) printers, and printing resins in the armamentarium of the orthodontic profession enabled the evolution of orthodontic appliance customization. The ability to install a small laboratory in the orthodontic office, consisting of the majority of such units and materials, developed the concept of in-house design and manufacture of customized orthodontic appliances. The core of a digital office is the orthodontic imaging and analysis software, which can hold all the digital data obtained by digital units and by the clinical examination. Metal printing can only be performed in special laboratories, enabling the manufacture of various metallic appliances. Thermoformed aligners and lately printed aligners are appliances that can be manufactured in the orthodontic office. Novel software called Ubrackets enables the orthodontist to design and print customized lingual and labial orthodontic brackets using special hybrid ceramic resins or zirconia slurry. In-house manufacturing seems to shift company-dependent orthodontic offices to self-sufficient ones. Nevertheless, protocols have to be created around the inclusion of laboratories in orthodontic offices that will protect both patients and personnel from hazards. Artificial intelligence (AI) is a form of technology that is been used in orthodontics over the last few years. While AI will never replace the orthodontist, it will assist in achieving better orthodontic treatment results.

Orthodontics is a specialty that combines the biology of tooth movement with the science of engineering. Orthodontic therapy is based on the interaction between mechanics and biology (Davidovitch and Krishnan, 2009). Thus, the term biomechanics entails aspects of orthodontic treatment, biology, and mechanics.

In recent years digital technology has caused a tremendous evolution of engineering, which has changed many aspects of our daily life.

Orthodontics was no exception and we are witnessing transformation of the profession from an analog to an almost completely digital one. Surface scanning (intraoral), volume scanning (cone beam computerized tomography, CBCT), computer-aided design (CAD) software for three-dimensional (3D) design of appliances, artificial intelligence (AI) machines, additive manufacturing (3D printing), resins for 3D printing, archwire bending robots, and lately zirconia printers are already in the armamentarium of the orthodontist to perform treatment using customized orthodontic appliances. Moreover, as digital technology progresses, it allows inclusion of such technological advances within the space of the orthodontic office where 3D design and printing can be performed. In that sense, an orthodontic office can incorporate within its space a small laboratory without the need for traditional machines and materials, but instead with the presence of computers, software, 3D printers, and other post-printing units. Nevertheless, including all units and materials in the orthodontic office entails health hazards that cannot be overlooked (Panayi and Eliades, 2022).

A fully digital orthodontic office instead of an analog one essentially includes software that manages all the digital input taken by CBCT (or a digital cephalometric and panoramic x-ray machine), an intraoral scan, and a face scan. Intraoral and face examinations are also recorded in the software to create the so-called virtual patient (Panayi, 2021; Retrouvey and Abdallah, 2021). This software is the core of a digital office that helps the clinician make the diagnosis, set the treatment goals and treatment options, and finally create the treatment plan. The software can be useful for presenting the treatment options and the treatment plan to the patient. Another essential digital tool in a digital orthodontic office is CAD software, which enables the orthodontist to design and print orthodontic appliances. During the last few years new CAD software has appeared on the market that helps to design clear thermoformed or printed aligners, metallic appliances like rapid palate expanders (RPEs), lingual arches, molar distalizers combined with temporary anchorage devices, surgical splints, and so on. Very recently new CAD software has been released for the in-house design and printing of customized orthodontic brackets (Panayi and Tsolakis, 2021). In

the armamentarium of a digital office are 3D printers, while lately retainer wire bending machines and archwire bending robots have started to show up. At this point, metal printing using bed powder fusion printers can only be performed in laboratories due to the machines' size and the workflow that demands special post-printing units.

Orthodontic imaging and analysis software

As already mentioned, the core of a digital office is the software that gathers all the digital and nondigital data from surface and volume scanners and intraoral–extraoral examinations. An example of such software is that from Dolphin Imaging (Chatsworth, CA, USA). As the company states, this imaging and management software enables the orthodontist to superimpose a CBCT scan with a face and intraoral scan, perform digital measurements, analyze a cephalogram, and helps to diagnose the patient's orthodontic problem, set the treatment goals, make treatment simulations, and finally define a treatment plan. In addition, the orthodontist can present to the patient the treatment plan and the possible outcome at the end of treatment. In orthognathic surgery cases, the patient can visualize the predicted bony and soft tissue changes to their face after treatment. At the same time, surgical splints can be designed and sent for 3D printing. During the course of and at the end of treatment, digital records can be imported into the software to evaluate the treatment process.

Recently, new software has appeared on the market that allows for online evaluation and analysis of cephalometric, panoramic x-rays, and CBCTs. Most of these services use AI software to automatically trace cephalograms, segment CBCTs, and up to a point diagnose dental or orthodontic problems. CephX (Orca, Las Vegas, NV, USA; Borohovitz et al., 2021) is an example of an online service offering cephalogram analysis and CBCT segmentation, while Diagnocat (Tel-Aviv, Israel) is another company that offers panoramic analysis and diagnosis using AI.

Surface and volume scanning

Surface scanning is a general term for intraoral, desktop, or face scanning. A surface scanner can scan the outer surface of an object in 3D. A volume scanner (CBCT) scans the whole volume of an object and not only its surface, using x-rays. A CBCT is not always essential in a digital orthodontic office, although its presence helps a lot in diagnosis, treatment planning, and designing certain orthodontic appliances. Due to the high radiation emitted, a tomograph should be taken with caution and only when it is justified by the ALARA (as low as reasonably achievable) rule (Yeung, 2019).

On the other hand, surface scanning is harmless and can be used as many times as desired. Intraoral scanners are extensively used in orthodontics, giving an accurate digital impression of the oral cavity. Intraoral scanners can be also used to evaluate the progress of orthodontic treatment by superimposing dental scans of the patient. Desktop scanners, although more accurate compared to intraoral ones (Su and Sun, 2015), are mainly installed in laboratories for dental model or impression scanning. A 3D scanner projects light onto the scanning object, which then is reflected and recorded as separate images or videos (Kravitz et al., 2014; Martin et al., 2015). The most common file format for a 3D object acquired by a scanner is the STL (Standard Tessellation Language) format.

A surface scanner can also be used to acquire a 3D image of a patient's face. Some CBCT machines include a face scanner that acquires 3D face images together with or without volume scanning. Stand-alone facial scanners can also be found in the market and are used mostly for nonorthodontic purposes. Companies that manufacture CBCT, intraoral, and face scanners use a common software interface, enabling superimposition of all the images in a single 3D file allowing a global visualization of the bony, soft tissue, and intraoral structures, thus helping to create a virtual patient. The whole process of transforming a real object into a 3D digital one is called digitization, while the process of transforming a 3D digital object into a real object is called undigitization (Panayi, 2021).

Orthodontic computer-aided design software

CAD software has been on the market for over 50 years, mainly for aerospace and engineering. The purpose of CAD software is to create, modify, analyze, and optimize a design. At the same time, it helps the designer improve the design quality and create a database for manufacturing. The first CAD software in dentistry appeared on the market in 1985 when Mőrmann and Brandestini introduced the Chairside Economical Restoration of Esthetic Ceramics (CEREC®) system, which uses software (CAD and computer-aided manufacturing, CAM) and computer-controlled machinery to automate a manufacturing process (Mörmann et al., 1985). Manufacturing is performed using subtractive technology (milling) or additive technology (3D printing). During the last few years, orthodontic CAD software like Maestro (Age Solutions, Pisa, Italy), Onyxceph (Image Instruments, Chemnitz, Germany), Ortho System (3Shape, Copenhagen, Denmark), and Deltaface (Coruo, Limoges, France) has been introduced mainly for the design of clear aligners (thermoformed or printed), orthodontic appliances like RPEs, lingual arches, bands, and so on. The first CAD software for 3D design and printing of customized brackets, called Deltaface Ubrackets (Panayi and Tsolakis, 2021).

Three-dimensional manufacturing

The general term 3D manufacturing includes subtractive and additive manufacturing. Subtractive manufacturing (milling) is removing material from an object to create a 3D model according to a 3D object that was designed in CAD software. Additive manufacturing (3D printing) is creating 3D objects by laying down successive layers of material until the object is created (Shahrubudin et al., 2019). Subtractive manufacturing is mainly used in dentistry for creating crowns, bridges, and so on. Due to the excessive loss of material and the geometrical complexity of orthodontic appliances, subtractive manufacturing is not used in orthodontics. Another important reason why milling is not used in orthodontics is that the 20 mm thick discs used are not enough to manufacture orthodontic appliances.

On the other hand, 3D printing is a process that is used exclusively in orthodontic appliance manufacturing. It was invented in 1980 by Hideo Kodama of Nagoya Municipal Industrial Research Institute, Japan, who first presented the process for creating 3D plastic parts by photo-hardening polymers with ultraviolet (UV) light exposure (Kodama, 1981a, 1981b). In 1983, Charles (Chuck) Hull developed a system referred to as stereolithography (SLA), in which layers were added by curing photopolymers with UV lasers (Hull, 2012). In 1986, Hull co-founded 3D Systems (Rock Hill, SC, USA) to introduce the technology to the market, while the first ever 3D printer, the SLA-1®, was introduced in 1987.

In 2009, the American Society for Testing and Materials (ASTM) created the F42 Technical Committee to develop the first additive manufacturing standards. Those standards established 3D printing as an industrial manufacturing technology (Lee et al, 2019). According to the ISO/ASTM 52900 standard, seven general types of 3D printing were defined:

- *Vat polymerization*, which uses UV light to cure liquid photopolymer in a vat.
- *Powder bed fusion*, which uses a high-energy source to fuse material powder particles.
- *Material extrusion*, which selectively dispenses material through a nozzle to create the 3D object.
- *Binder jetting*, which selectively binds powder using a liquid bonding agent.
- *Material jetting*, which deposits and cures droplets of material.
- *Direct energy deposition*, which uses a high-energy source to fuse material as it is deposited.
- *Sheet lamination*, which bonds and forms sheets of material layer by layer.

The types that are mainly used in orthodontics are vat polymerization, powder bed fusion, and material extrusion. Vat polymerization, also known as stereolithography, utilizes photopolymer resins to create dental models, splints, indirect

bonding trays, surgical splints, directly printed aligners, and lately customized orthodontic brackets. The 3D printers that belong to the vat polymerization category are SLA printers that use a laser beam to polymerize the resin, DLP (direct light processing) that uses a UV light projector to cure the resin, and more recently MSLA (masked stereolithography) that uses a liquid crystal display (LCD) panel to cure the resin (Gibson et al., 2010; Gupta et al., 2019).

Many resins can be found on the market for all printing purposes: model, splint, indirect bonding trays and casting resins, permanent and temporary crown resins, denture resins, and lately a directly printed aligner resin called TC-85DAC (Graphy, Seoul, Korea; Can et al., 2021). A forthcoming new material currently under study and construction is bracket resin.

Customized orthodontic appliances

Many of the traditionally made orthodontic appliances could be called customized. For instance, a lingual arch or an RPE is an appliance manufactured for a specific patient and cannot be used for another one. Nevertheless, a few parts of those appliances, like bands or wires, are universal, and they are chosen and bent to fit each different patient. Aligners or positioners are also tailor-made the traditional way using plaster set-ups. In contrast to the conventional customization method, digitally designed customized orthodontic appliances are designed and manufactured differently. The most important difference between traditional appliances and digitally designed appliances is the design and manufacturing environment. Traditional appliance manufacturing is performed in an orthodontic laboratory using plaster, bands, wires, soldering material, and so on. In contrast, the modern 3D digital design process is mostly performed on a computer, using CAD software, and a 3D printer is used to manufacture the orthodontic appliances (Figure 23.1). In fact, the ability to design all appliances on a computer together with the ease of appliance manufacturing using 3D printers has moved part of the laboratory work into the space of the orthodontic office, although it is important to be aware that not all appliances can be 3D printed in an orthodontic office.

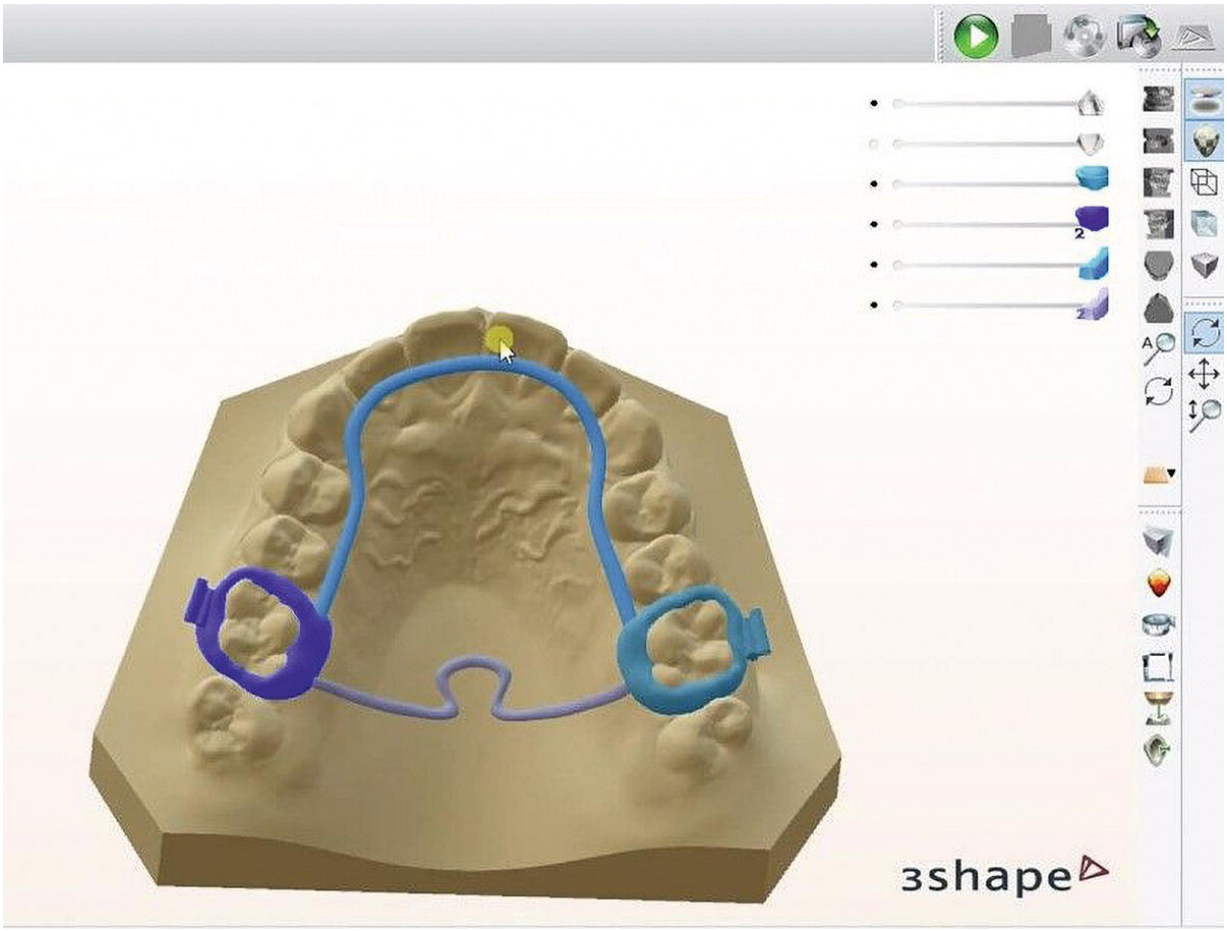


Figure 23.1 Virtual appliance design using 3 Shape appliance design software.

In recent years more and more orthodontists have begun to include all the necessary equipment to design and print orthodontic appliances in their offices. Nevertheless, installation of such equipment does not necessarily follow a protocol regarding the safety of personnel and patients, and many hazards derived from the various materials and equipment used may be overlooked. Beyond the excitement about 3D technology, it is important to set some guidelines that must be followed before the orthodontist decides to include this technology and equipment in the orthodontic office (Panayi and Eliades, 2022). For instance, printers, washing machines, and UV curing units should be placed in special rooms away from the clinic and patient reception. Most of the materials used for printing, such as resins, are toxic and can cause allergies. In addition, they emit bad and irritating odors, while isopropyl alcohol, which is used in washing machines to clean and remove the uncured

excess resin, is very irritating to humans, potentially toxic and allergic, and extremely flammable. The laboratory has to be well ventilated and the machines and materials must be away from electricity. Furthermore, most of the resins are not biocompatible. For this reason, printed objects cannot be cleaned in the same washing machine using the same isopropyl alcohol liquid. Either the alcohol has to be changed every time a different 3D object is cleaned or several washing machines should be installed.

Clear aligners

Clear aligners are generally known from the late 1990s when Align Technology (San Jose, CA, USA) introduced its aligners called Invisalign. Nevertheless, the technique was originated by Kesling much earlier (Kesling, 1945) and evolved by Sheridan, who invented the Essix® appliance (Sheridan et al., 1993).

During the last few years, many orthodontic CAD programs have appeared on the market, allowing the in-house design of clear aligners. The workflow is typically the same for all kinds of software: import of dental 3D scans, segmentation of the teeth, root positioning, and finally set-up. The software calculates the amount of movement and creates dental models corresponding to the movement each aligner can perform in three dimensions (rotation, tipping, translation, extrusion, intrusion, etc.). The dental models are printed and a thermoforming procedure follows, using a positive- or negative-pressure thermoforming machine together with special plastic foils to create the aligners. The aligners can be used in conjunction with or without composite attachments, while other miscellaneous accessories (buttons, temporary anchorage devices, etc.) can be simultaneously used.

Graphy's TC-85DAC resin can be used to directly print aligners. The workflow is different to that for thermoforming. Designing the aligners is done in the CAD software. After set-up, the orthodontist has to design the aligner on the virtual model (in the same way as an indirect bonding [IDB] tray) and set the thickness of the aligner, which most of the time lies between 0.3 and 0.4 mm (Figure 23.2). Recently Graphy has proposed using 0.4-0.5 mm of aligner thickness

when the aligners are to be changed every week, or 0.7 mm if the aligners are going to be changed every 10 days. Other companies also manufacture aligner resins that probably have different mechanical properties, giving more options to the orthodontist, for instance OD-Clear TF LTP (3Dresyns, Barcelona, Spain), Luxalign (Luxcreo, Belmont, CA, USA) and Clear-A (Senertek, Ismir, Turkey). The software automatically calculates the number of printed aligners that will have to be used and creates the STL files of the aligners to be exported for printing. Aligner printing can be performed on various 3D printers (SLA, DLP, MSLA) using the aligner resin (Figure 23.3). The next step is to remove the excess resin that was not cured. Instead of using isopropyl alcohol to clean the aligners, a centrifugation machine has to be used for some minutes.

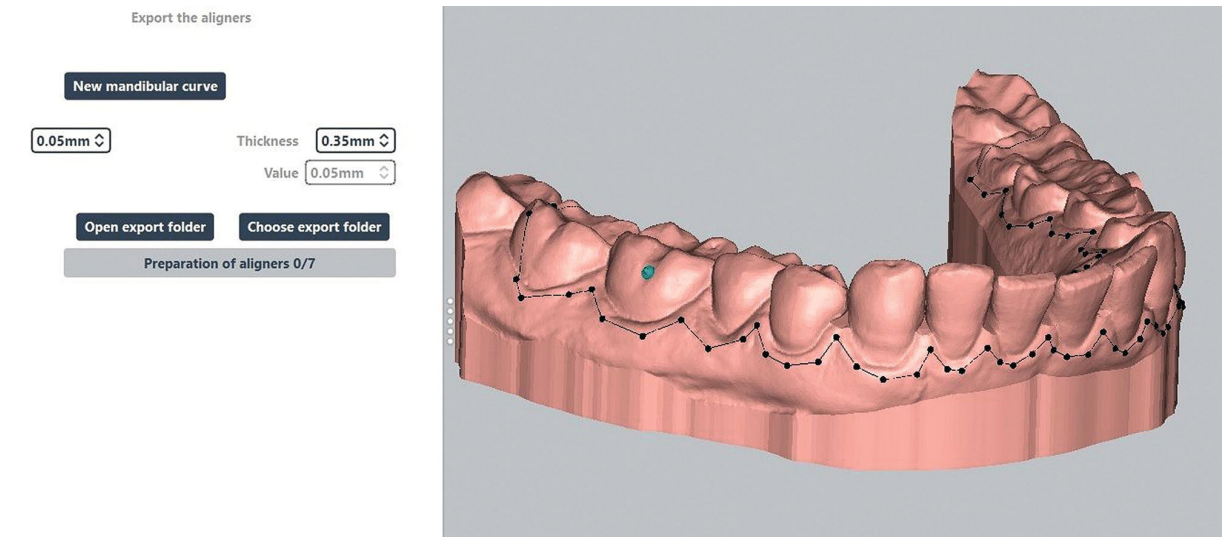


Figure 23.2 Virtual design of a series of printed aligners using Deltaface software. Note the option for different aligner thicknesses.

Figure 23.3 Printed aligners on the printer's platform.

The next stage may be one of the most important parts of the aligner printing workflow, in which the 3D printer polymerizes the resin by using UV light. Polymerization in 3D printing is incomplete due to the inability of UV light to penetrate the whole volume of the object and due to the relatively low intensity of the UV light. For this reason, a UV curing unit is needed. The market offers many UV

curing units with different degrees of UV power and ways of curing 3D objects. Printed aligners are by definition active appliances that exert force for teeth movement, while all other 3D printed orthodontic appliances or objects are passive appliances (models, splints, IDB trays, etc.). For this reason, the curing unit must be made for curing printed aligners, giving the aligner the best possible mechanical properties, transparency, and biocompatibility. Graphy initially created the Cure M UV curing unit, which was specially made for printed aligners. Nevertheless, oxygen prevents complete polymerization of the aligners, which has impacts on their transparency, especially during the last days of aligner wear (Gauthier et al., 2005). In addition, it seems that polymerization in the absence of oxygen might enhance the mechanical properties of the aligners, although in a recent study where printed aligners were used for one week in patients, according to Graphy's old protocol, their mechanical properties were maintained to a very high level (Can et al., 2021). In a similar study by the same research group, Invisalign lost almost half of its properties in one week of patient wear (Papadopoulou et al., 2019). For this reason, Graphy created a new curing unit with a nitrogen generator called the Tera Harz. This unit compresses air and generates nitrogen, which is supplied to the unit chamber where curing is performed, while at the same time oxygen is automatically removed. Removing the supports using a handpiece is the next step and the aligners are then delivered to the patient.

It can be seen that 3D printing is a multistage procedure where each step can influence other steps. It is also a sensitive procedure, all steps of which must be performed accurately to reach a satisfactory outcome. Especially in the case of printed aligners and brackets, strictly following the protocols is essential. Designing the aligners in the CAD software can lead to excellent and high-resolution STL aligner files, but also corrupted or low-resolution files. For this reason, the software must design high-resolution STL files with no defects. The printer should also be able to accurately and consistently print the aligners according to the aligner resin settings defined by Graphy. One study showed that different printers print aligners with different mechanical properties (Zinelis et al., 2022b). It can thus be concluded that not every design and print workflow

configuration will lead to the same aligners in terms of mechanical properties. This finding is very important, as printed aligners are active appliances and their mechanical properties will affect the way they behave in the mouth. As mentioned before, UV curing is maybe the most important part of the whole workflow. Due to its complex, multistage workflow, aligner printing technology should be investigated fully to help the technology to advance for the sake of both patients and orthodontists.

Selective laser sintering and metallic orthodontic appliances

Selective laser sintering (SLS) is a relatively new technology in dentistry and orthodontics. The technology mainly used for metal printing is called powder bed fusion, in which metallic or plastic powder is melted, solidified, or joined, usually by the use of a laser or electron beam, to create the 3D object (Deckard, 1989). Powder bed fusion has been advanced through the years by many companies, giving different names to the technology like direct metal laser sintering (DMLS), selective laser melting (SLM), electron beam melting (EBM), and so on.

The next step after printing is debinding, sintering, and polishing of the appliances. It is a procedure that cannot take place in an office due to the big volume of the printers, the post-printing procedure, and the hazards derived from the materials used. Nowadays, cobalt–chrome (CoCr) alloys are mostly used for printing bands, various appliances like RPEs, lingual arches, molar distalizers, and so on (Figure 23.4). Although metal printing can be used to print stainless steel and titanium, orthodontics does not make extensive use of these materials. An attempt was made to print orthodontic brackets using CoCr, but this seems to be difficult due to the printing and postprinting workflow and the inability to accurately print important parts of the bracket like the slot (Panayi, 2021). Regarding the behavior of the alloy in the mouth, a study was conducted by studying CoCr-made appliances removed after six months in the patient's mouth. It was concluded that the intraoral conditions do not influence the mechanical properties of the appliance. Nevertheless, the intraorally aged group showed degradation in

breakdown potential of the protective oxide layer, which is against pitting corrosion (Zinelis et al., 2022a).

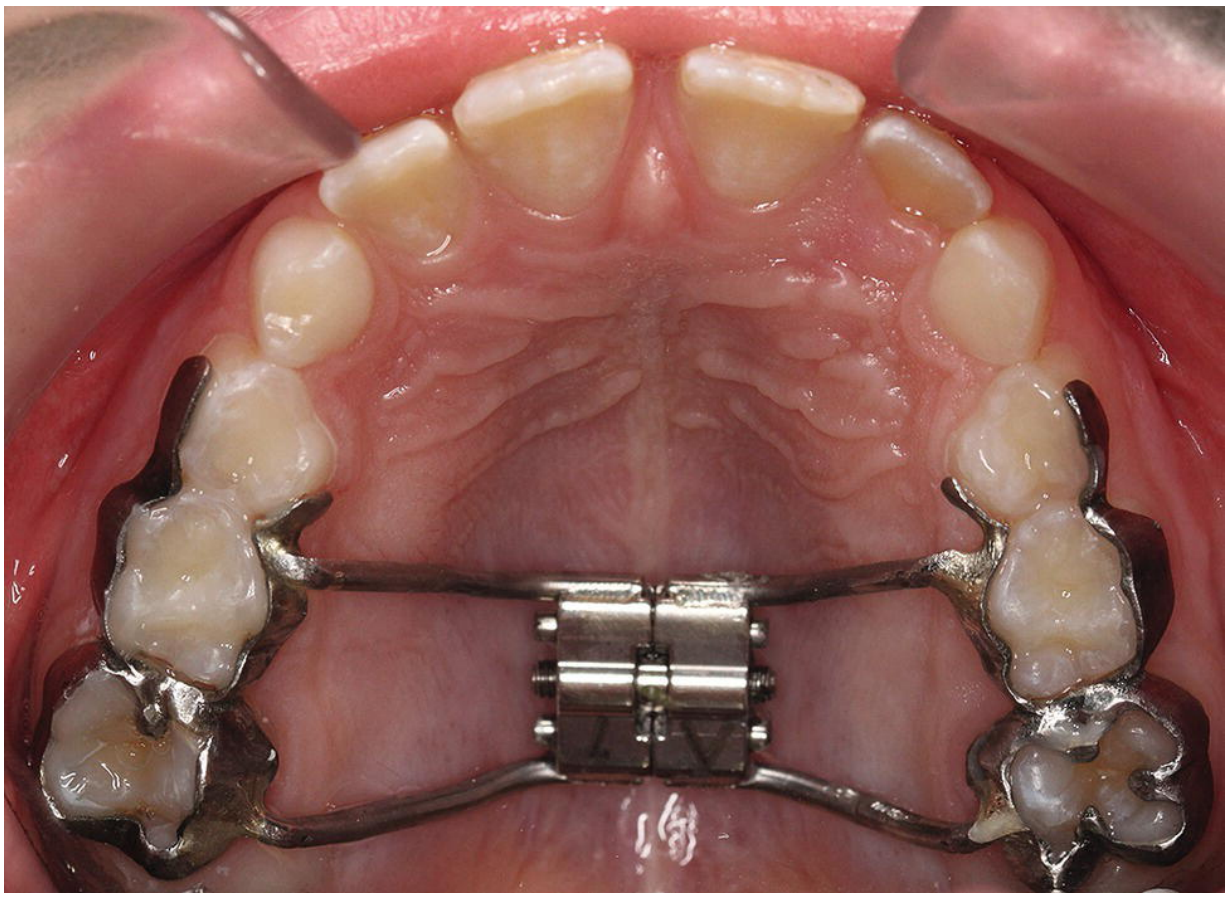


Figure 23.4 Customized rapid palate expander printed in cobalt–chrome alloy using Meshmixer computer-aided design freeware.

The 3D technology brings design and manufacturing to a different level, allowing the design of more complicated appliances using software and computers. A disadvantage of CoCr alloy printing is that the appliances are rigid and lack flexibility. For this reason, they cannot be used to exert force as a spring can. In addition, compared to the commercially available bands they cannot be placed below the maximum circumference of the tooth, which probably creates retention problems with more band failures.

Customized orthodontic brackets

E.H. Angle, the father of modern orthodontics, created the edgewise appliance through developmental stages derived from his experience

with his earlier devices like the E-arch, pin and tube, and ribbon-arch appliances (Angle, 1928, 1929). It was not until the early 1970s that Andrews refined the edgewise appliance by introducing preadjusted brackets, which had compensations for the dental morphology of each tooth, in what was called the “straight-wire appliance.” In reality, this was the first attempt to create customized orthodontic brackets that could match most people's teeth in three dimensions (Andrews, 1975). During the next few years invisible orthodontic treatment was in high demand, especially among adults. Fujita in 1979 invented lingual orthodontic brackets in order to provide a more aesthetic alternative to buccal fixed appliances for patients (Andrews, 1975). With the introduction of digital technology in the late 1990s, Wiechmann introduced the first customized lingual orthodontic bracket system, called Incognito (3M, Monrovia, CA, USA, Wiechmann, 2001, Wiechmann et al., 2003). From that point, other companies started introducing mainly customized lingual brackets.

Through all those years of the use of lingual customized brackets, the advantages of customized brackets were appreciated, resulting in the inclusion of this technology in the manufacturing of customized labial brackets. Insignia (Ormco, Orange, CA, USA) and LightForce (LightForce Orthodontics, Burlington, MA, USA) are customized brackets that were recently introduced to the market. In both systems, the orthodontist digitizes the patient’s dental arches by scanning and sends the 3D files to the company. Through an online set-up, the company creates customized brackets made of ceramic or metallic material (Insignia). Another system called Braces On Demand (Hicksville, NY, USA) was introduced to allow the printing of noncustomized brackets and other auxiliaries using a denture teeth resin (used for printing denture teeth) made by Formlabs (Somerville, MA, USA).

During the last few years the concept of appliance design and printing in the orthodontic office has been introduced, mainly for clear aligners. Software for aligner design in the office is available, while printers and curing units are easy to purchase at relatively low prices. Webinars on this topic are easy to find on the internet, which is spreading the in-house concept to more orthodontists worldwide. However, in-house customized bracket design and printing did not

become available due to the absence of CAD software for design and the lack of proper bracket resins. An attempt to design and metal print customized brackets was made using freeware called Meshmixer and an SLS printer (Panayi, 2021). The idea of creating software that the orthodontist could use to create a set-up of the patient's malocclusion and then design customized brackets was the next step. Software called Ubrackets, included in the Deltaface software, was developed to design customized brackets (Figure 23.5) (Panayi et al., 2021). The software is similar to aligner design software up to the point of set-up. From that point, the orthodontist can choose between labial and lingual brackets, fully customized and printable brackets, or semi-customized brackets by adding composite at the base of commercial brackets already included in the software library. A tool is used to automatically place the full set of 0.018 × 0.025 in. brackets and tubes aligned on a flat 0.018 × 0.025 in. archwire to the teeth. The final archwire after set-up finalization serves as the prototype archwire, which will be used from the beginning until the end of the treatment in various diameters, cross-section shapes, and materials (superelastic, stainless steel, etc.). The brackets can be moved mesially or distally, lingually or labially using a manipulator, while the brackets can rotate on a perpendicular axis (Figure 23.6). The whole brackets–archwire system can also be moved in a vertical direction and rotated in whatever direction the operator likes. The brackets prescription is defined according to the set-up the orthodontist has performed.

One advantage of the in-house concept is that in cases where overcorrections or teeth compensations are needed, those could be included in the design of the brackets. For example, in a case where first premolars have to be extracted, the canine bracket should be positioned in such a way as to counteract the rotation and tipping while canine distalization takes place. In addition, the operator can include narrower or wider brackets according to the teeth's position relative to the adjacent ones (Papageorgiou et al., 2022). According to the resin (hybrid ceramic material) or slurry (printed zirconia) that will be used, the appropriate series of printable brackets should be used that are found in the software library. A significant advantage of the software is that the company can design and import a series of brackets to satisfy specific needs at any time. Other

auxiliaries can be added that are automatically positioned by the software. Tools for detecting collisions between brackets and opposing teeth are also available.

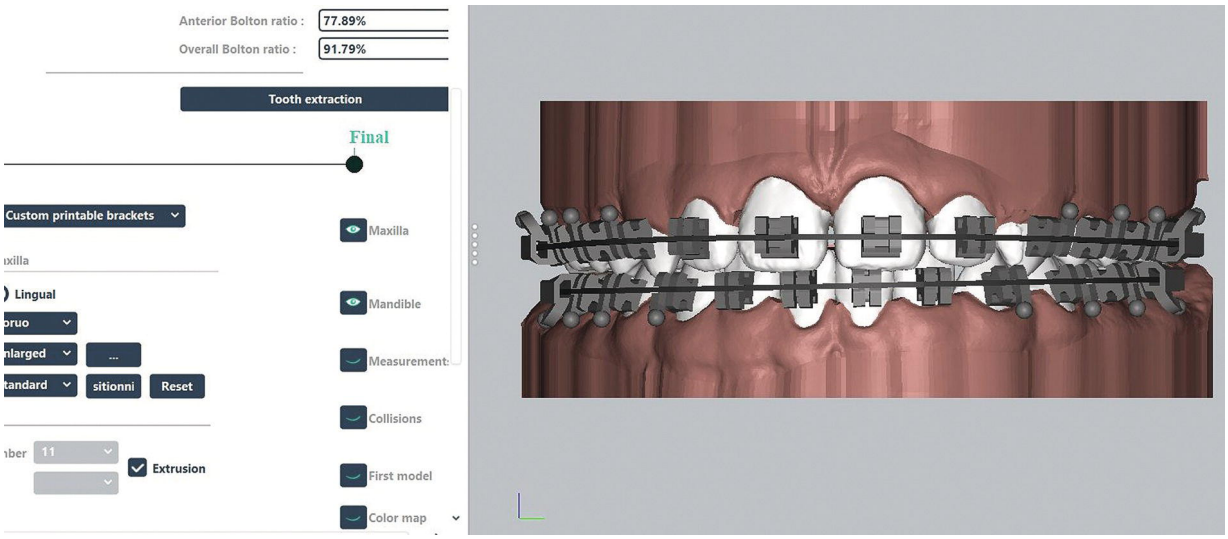


Figure 23.5 In-house customized brackets designing using Ubrackets software.

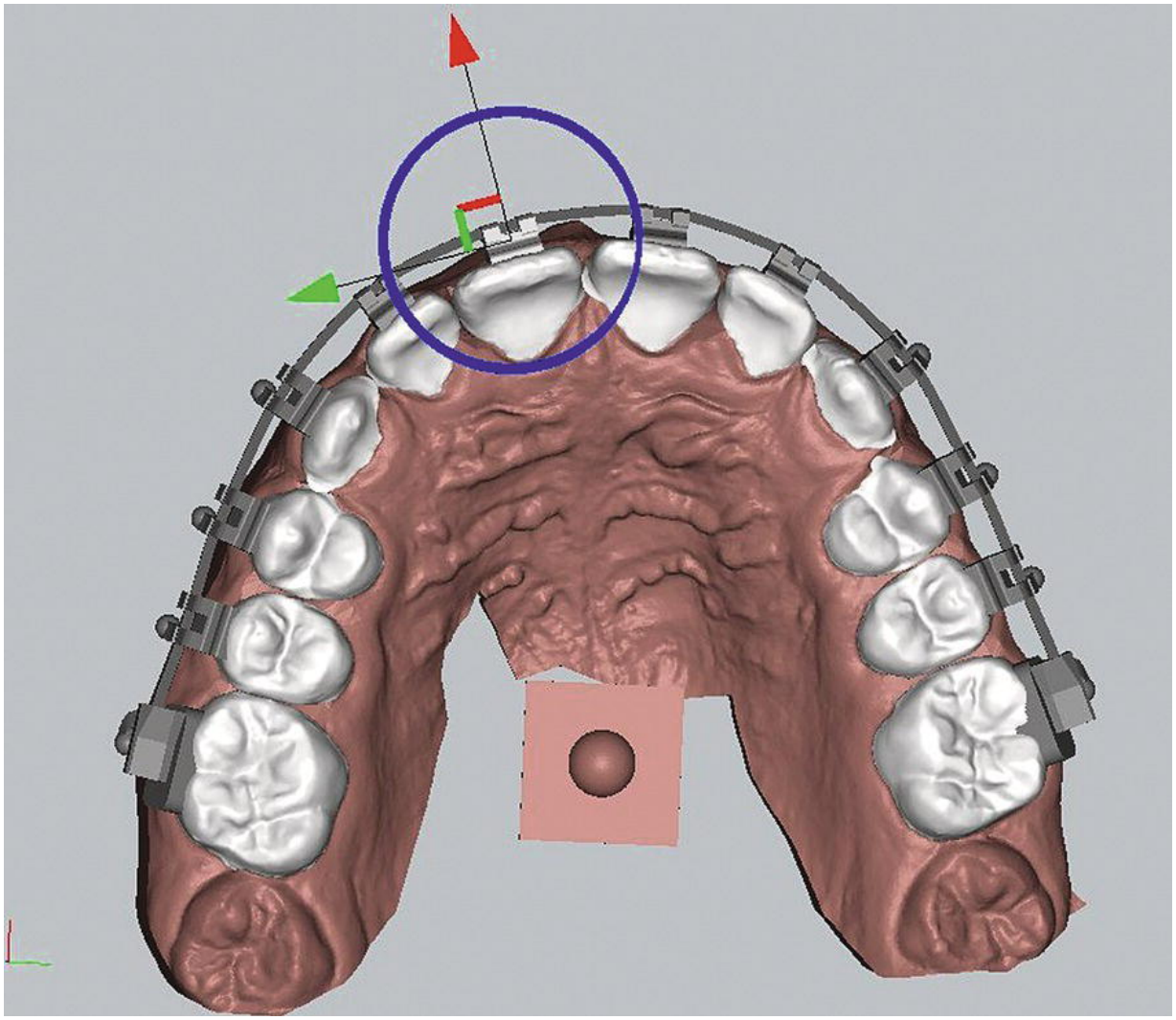


Figure 23.6 A manipulator is used to move the customized brackets in mesial, distal, lingual, and buccal directions. The brackets can be also rotated along their perpendicular axis. The circle and the arrow are parts of the manipulator for moving the bracket. The circle enables the rotation of the bracket and the arrow its buccal or lingual movement.

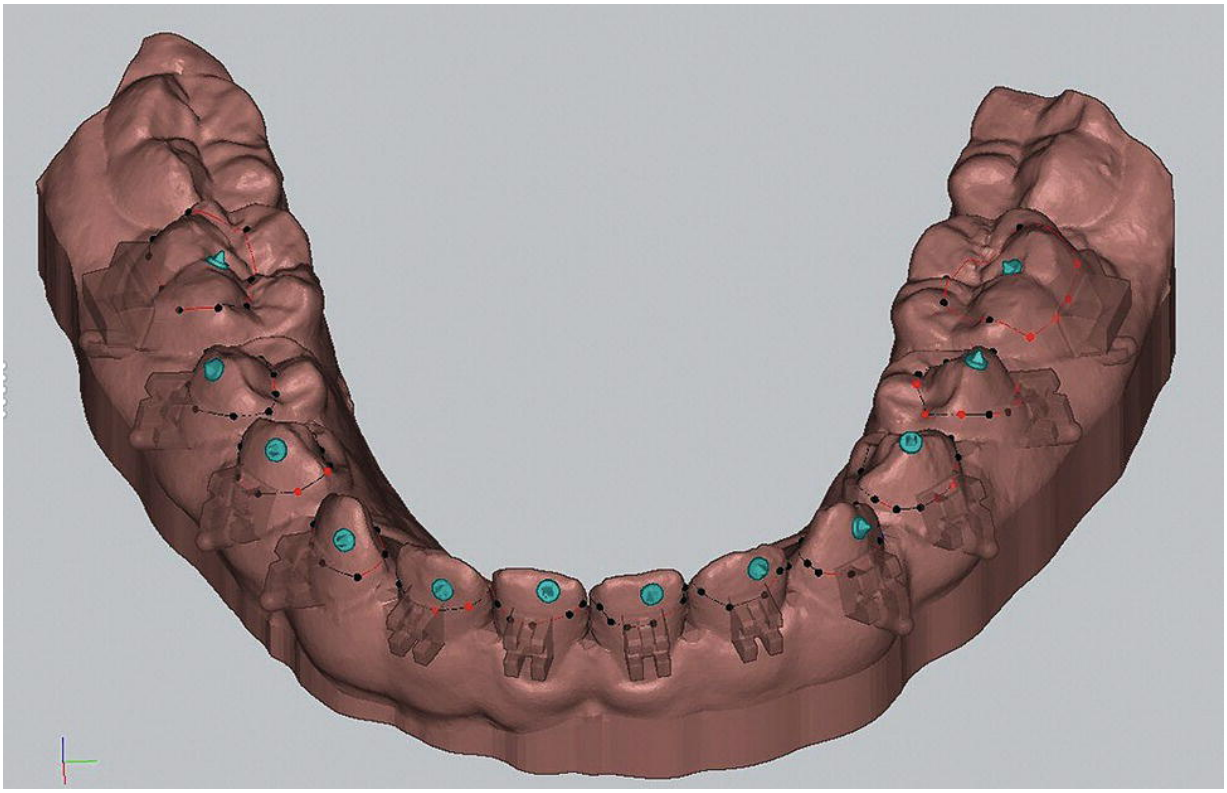


Figure 23.7 Virtual design of the positioning keys for accurate direct bonding of printed customized brackets.

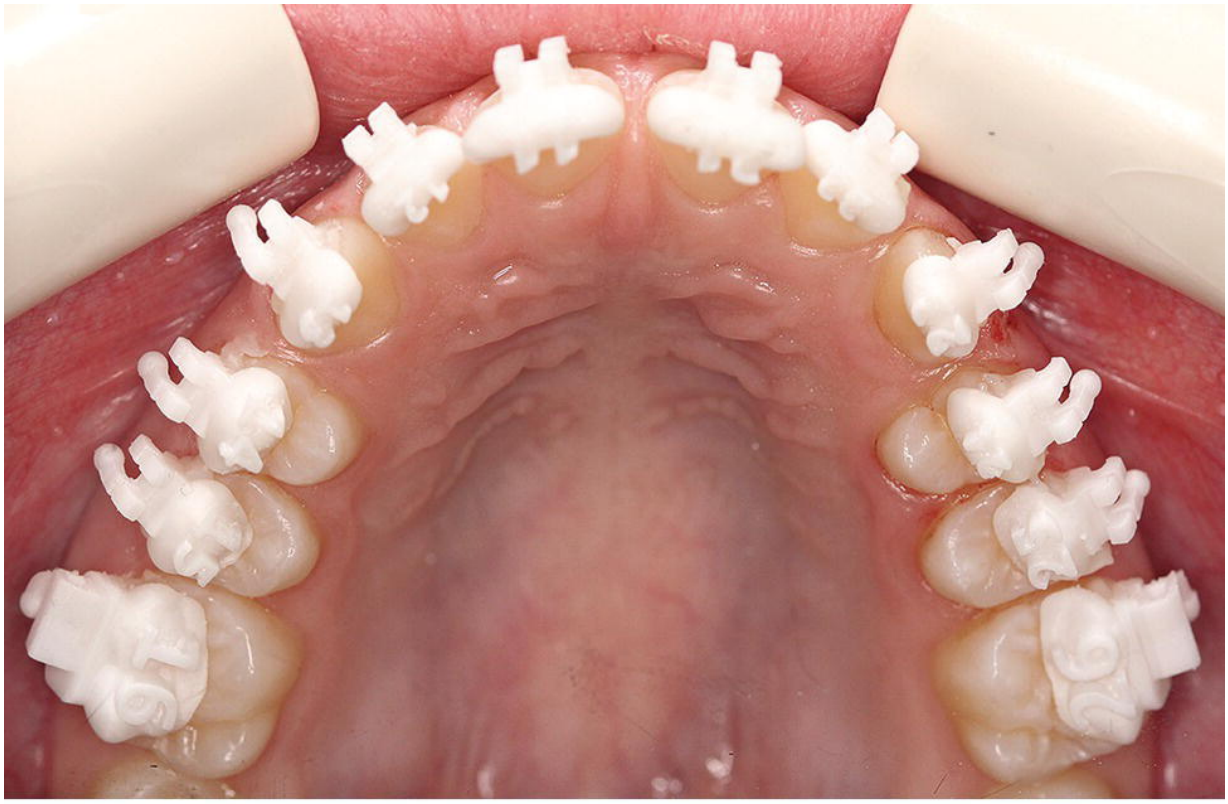
The next step after finalizing the position of the brackets is to design the IDB tray or design positioning keys that are used to accurately bond the brackets to the teeth without needing an IDB tray (Figure 23.7). Those keys are easily removed after bracket bonding. The files that are exported from the Ubrackets software are the 3D customized brackets files, the 3D file of the prototype archwire, the initial and final 3D files of the dental models with and without the brackets positioned, the IDB tray, and a drawing of the archwire in a 1 : 1 ratio in a pdf file for manual archwire bending using pliers. The brackets can be printed using various materials. As a proof of concept, the author used a permanent crown resin (hybrid ceramic) supplied by

Formlabs in a Formlabs 3B printer to print customized brackets designed in Ubrackets (Figure 23.8; (Panayi and Tsolakis, 2021). The first article comparing a permanent and a temporary crown resin by Formlabs for bracket printing was recently published (Papageorgiou et al., 2022). The study compared the mechanical properties of the two resins. The results showed no difference between them in terms of hardness, modulus of elasticity, and brittleness. Nevertheless, although hardness was relatively low, it was almost double compared to commercial plastic brackets according to a similar study by Eliades et al. (2004). Elastic moduli were also found to be relatively low. Ideal printed brackets should have high hardness, elastic modulus, and fracture toughness.

Figure 23.8 Customized brackets printed using permanent hybrid ceramic crown resin bonded with the help of the positioning keys. The keys are removed after bonding using a high-speed handpiece. A customized archwire is inserted.

During the last year a zirconia printer called Zirpo (AON, Seoul,

Korea) was released for crown and bridge printing. The printer uses DLP printing technology, while printed objects pass through a sintering procedure according to the company's instructions. The author used this technology to print customized zirconia brackets (Figure 23.9). The color of the slurry is currently A1, which could be changed by zirconia painting using all color shades according to the patient's teeth color. Nevertheless, AON plans to create slurries with all possible shades of white to give the orthodontist the ability to print zirconia brackets according to the color of the patient's teeth. Printing was successful in offering another option to the orthodontist for zirconia bracket manufacturing. As the company states, the final 3D-printed and sintered objects undergo 10–20% shrinkage. This has to be compensated for by enlarging the series of brackets to be designed and printed by 20%. A further study performed by the author and the universities of Zurich and Athens has shown promising results in increasing the fracture toughness of zirconia brackets through 3D printing, thereby reducing the brittleness compared with standard commercial alumina ceramic brackets and other outsourced printed brackets (Polychronis et al., 2023). The study presented significantly better fracture toughness (which is the weak point of ceramic brackets) of the zirconia brackets compared to Clarity (3M) and LightForce. This conclusion is proof that in-house design and printing of customized brackets using zirconia slurry could be the next big step in orthodontics, allowing the use of brackets that have better mechanical properties compared to other commercial or outsourced printed brackets.



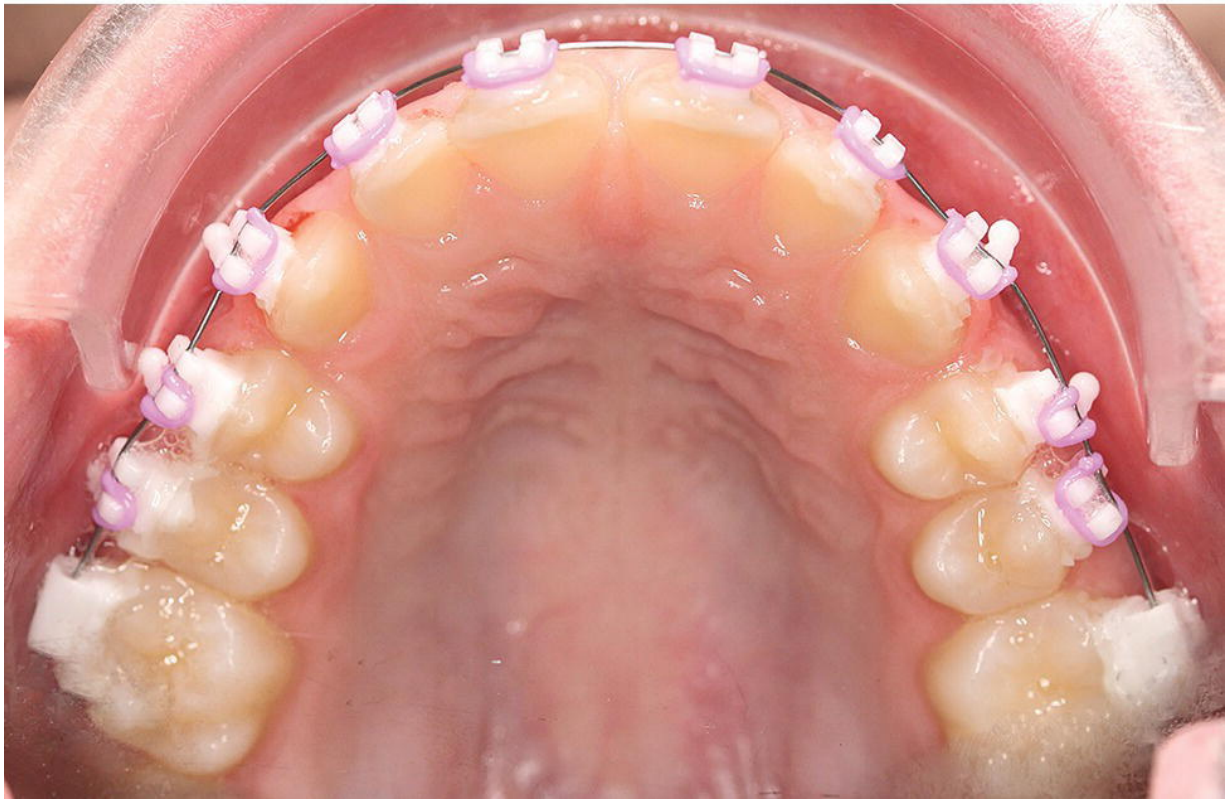


Figure 23.9 Customized brackets printed using zirconia slurry in A1 color using positioning keys that are removed after bonding. The color can be changed by a special zirconia paint or by the new zirconia slurries that have available all the shades of white. Note the tooth number on each bracket key.

The in-house concept and workflow of designing and printing customized brackets consists of many steps that determine the outcome in terms of bracket manufacturing accuracy and mechanical properties. The software designs the brackets to be used and exports them as STL format files. From that point, the printer plays a significant role in creating the brackets. The printer has to have high printing resolution in the X and Y axes in order to accurately print the slot with its exact dimensions. The Z axis plays also a critical role in printing (Shahrubudin et al., 2019). Most of the new printers have high resolution and can be used for bracket printing. The orientation of the bracket relative to the printing platform also has significance when it comes to accurate slot printing, while supports should be placed away from important parts like the slot or the bracket base. The resin (or slurry for zirconia) to be used may be the most important part of the workflow. The resin should have properties that allow the printing of brackets with similar mechanical properties to brackets that are already available in the market. The resin temperature and homogeneity are other important parts of printing. Low resin temperature or inhomogeneous resin can lead to failures. The next important part is isopropyl alcohol bracket washing to remove the excess resin. Excess resin, especially in the slot area, could decrease the slot dimension. UV curing is crucial for the brackets because it gives them their final mechanical properties. Generally, higher curing intensity and increased curing time up to a point increase the object's hardness (Kim et al., 2020). Oxygen, as a rule, inhibits proper polymerization (Gauthier et al., 2005). Graphy's Tera Harz curing unit is suitable for better and more complete UV curing. As mentioned before, the unit includes a nitrogen generator to import nitrogen into the unit's chamber.

Considering all this, it is obvious that the characteristics of the printed brackets depend on many factors in various steps that alter the final product. For this reason, each in-house design and print workflow configuration is different. For instance, comparing two

different print configurations with the same CAD software, the same bracket resin, and the same UV curing unit but with different printers could affect the printed bracket's characteristics. Commercial noncustomized brackets are made differently with fewer steps (i.e. direct injection molding), resulting in more consistent outcomes. An essential part of the concept of customized bracket design and printing is the manufacturing of customized archwires; thus the complete package should include customized brackets with their customized archwires. A forthcoming unit that will be able to bend the customized archwires exported by the Ubrackets software will be an in-house archwire bending robot (Panayi, 2021).

In conclusion, in-house bracket manufacturing should include CAD software for customized bracket design, a suitable high-resolution 3D printer, bracket resin, a washing machine, a UV curing unit, and an archwire bending robot. In the case of zirconia printing, a furnace that will sinter the printed brackets is used instead of a washing machine and UV curing unit.

Conclusion

Digital technology advances are steadily changing many aspects of orthodontic treatment that we were taught during our postgraduate studies. The present generation of orthodontists will be at the core of those changes. Laboratories will be included in our offices, while the orthodontist will be in charge of the orthodontic treatment and the whole manufacturing process. Offices will be self-sufficient, and data from many orthodontic offices will be shared and gathered to be used by AI software, which will process them and give feedback to orthodontists for better orthodontic treatment for the benefit of the patient, the orthodontists, and our profession. Nevertheless, machines, software, and AI will never replace the orthodontist, but will serve as assistants for better, more efficient, faster, and safer orthodontic treatment.

References

Andrews, L.F. (1975) *The Straight-Wire Appliance: Syllabus of Philosophy and Techniques*, rev. ed. San Diego, CA: Lawrence F.

Andrews.

Angle, E.H. (1928). The latest and best in orthodontic mechanism. *Dental Cosmos* 70: 1143–1156.

Angle, E.H. (1929). The latest and best in orthodontic mechanism. *Dental Cosmos* 71: 164–174.

Borohovitz, C.L., Abraham, Z., and Redmond, W.R. (2021). The diagnostic advantage of a CBCT-derived segmented STL rendition of the teeth and jaws using an AI algorithm. *Journal of Clinical Orthodontics* 55(6): 361–369.

Can, E., Panayi, N., Polychronis, G. et al. (2021). In-house 3D-printed aligners: Effect of in vivo ageing on mechanical properties. *European Journal of Orthodontics* 44(1): 51–55. doi: 10.1093/ejo/cjab022.

Davidovitch, Z., and Krishnan, V. (2009). Role of basic biological sciences in clinical orthodontics: A case series. *American Journal of Orthodontics and Dentofacial Orthopedics* 135(2): 222–231. doi: 10.1016/j.ajodo.2007.03.028.

Deckard, C. (1989). Method and apparatus for producing parts by selective sintering. U.S. Patent 4,863,538, filed October 17, 1986.

Eliades, T., Gioka, C., Zinelis, S. et al. (2004). Plastic brackets: Hardness and associated clinical implications. *World Journal of Orthodontics* 5: 62–66.

Fujita, K. (1979). New orthodontic treatment with lingual bracket mushroom arch wire appliance. *American Journal of Orthodontics* 76(6): 657–675. doi: 10.1016/0002-9416(79)90211-2.

Gauthier, M., Stangel, I., Ellis, T. et al. (2005). Oxygen inhibition in dental resins. *Journal of Dental Research* 84(8): 725–729. doi: 10.1177/154405910508400808.

Gibson, I., Rosen, D., and Stucker, B. (2010). *Additive Manufacturing Technologies*. New York: Springer.

Gupta, V., Nesterenko, P., and Paull, B. (2019). An introduction to 3D printing. In: V. Gupta, P. Nesterenko, and B. Paull, *3D Printing in Chemical Sciences*. London: Royal Society of Chemistry, pp. 1–21.

Hull, C. (2012). On stereolithography. *Virtual and Physical Prototyping* 7(3): 177. doi: 10.1080/17452759.2012.723409.

Kesling, H. (1945). The philosophy of the tooth positioning appliance. *American Journal of Orthodontics and Oral Surgery* 31(6): 297–304. doi: 10.1016/0096-6347(45)90101-3.

Kim, D., Shim, J., Lee, D. et al. (2020). Effects of post-curing time on the mechanical and color properties of three-dimensional printed crown and bridge materials. *Polymers* 12(11): 2762. doi: 10.3390/polym12112762.

Kodama, H. (1981a). A scheme for three-dimensional display by automatic fabrication of three-dimensional model. *IEICE Transactions on Electronics Apr*: 237–241.

Kodama, H. (1981b). Automatic method for fabricating a three-dimensional plastic model with photo-hardening polymer. *Review of Scientific Instruments* 52(11): 1770–1773. doi: 10.1063/1.1136492.

Kravitz, N.D., Groth, C., Jones, P.E. et al. (2014). Intraoral digital scanners. *Journal of Clinical Orthodontics* 48(6): 337–347.

Lee, B., Pei, E., and Um, J. (2019). An overview of information technology standardization activities related to additive manufacturing. *Progress in Additive Manufacturing* 4(3): 345–354. doi: 10.1007/s40964-019-00087-5.

Martin, C.B., Chalmers, E.V., McIntyre, G.T. et al. (2015). Orthodontic scanners: What's available? *Journal of Orthodontics* 42(2): 136–143.

Mörmann, W., Brandestini, M., Ferru, A. et al. (1985). [Marginal adaptation of adhesive porcelain inlays in vitro]. *Schweiz Monatsschrift Zahnmed* 95(12): 1118–1129.

Panayi, N. (2021). *DIY Orthodontics: Design It Yourself*. Chicago, IL: Quintessence Publishing.

Panayi, N., and Eliades, T. (2022). In-office 3-dimensional-printing: Does the hype obscure the hazards for the operator? *American Journal of Orthodontics and Dentofacial Orthopedics* 161(6): 757–759. doi: 10.1016/j.ajodo.2022.02.002.

Panayi, N., and Tsolakis, A. (2021). In-house computer-aided design and 3-dimensional printing of customized orthodontic brackets using hybrid ceramic resin: Is it the time for the orthodontist to take over? *AJO-DO Clinical Companion* 1(3): 187–193. doi: 10.1016/j.xaor.2021.07.001.

Papadopoulou, A., Cantele, A., Polychronis, G. et al. (2019). Changes in roughness and mechanical properties of Invisalign® appliances after one- and two-weeks use. *Materials* 12(15): 2406. doi: 10.3390/ma12152406.

Papageorgiou, S., Polychronis, G., Panayi, N. et al. (2022). New aesthetic in-house 3D-printed brackets: Proof of concept and fundamental mechanical properties. *Progress in Orthodontics* 23(1): 6. doi: 10.1186/s40510-022-00400-z.

Polychronis, G., Papageorgiou, S., Panayi, N. et al. (2023). Fracture toughness and hardness of in-office, 3D-printed ceramic brackets. *Orthodontics & Craniofacial Research* Jan 17. doi: 10.1111/ocr.12632.

Retrouvey, J.-M., and Abdallah, M.-N. (2021). *3D diagnosis and Treatment Planning in Orthodontics: An Atlas for the Clinician*. New York: Springer.

Shahrubudin, N., Lee, T., and Ramlan, R. (2019). An overview on 3D printing technology: Technological, materials, and applications. *Procedia Manufacturing* 35: 1286–1296. doi: 10.1016/j.promfg.2019.06.089.

Sheridan, J.J., LeDoux, W., and McMinn, R. (1993). Essix retainers: Fabrication and supervision for permanent retention. *Journal of Clinical Orthodontics* 27(1): 37–45.

Su, T., and Sun, J. (2015). Comparison of repeatability between intraoral digital scanner and extraoral digital scanner: An in-vitro study. *Journal of Prosthodontic Research* 59(4): 236–242. doi: 10.1016/j.jpor.2015.06.002.

Wiechmann, D. (2001). Modulus-driven lingual orthodontics. *Clinical Impressions* 10(1): 2–7.

Wiechmann, D., Rummel, V., Thalheim, A. et al. (2003). Customized brackets and archwires for lingual orthodontic treatment. *American Journal of Orthodontics and Dentofacial Orthopedics* 124(5): 593–599. doi: 10.1016/j.ajodo.2003.08.008.

Yeung, A. (2019). The “as low as reasonably achievable” (ALARA) principle: A brief historical overview and a bibliometric analysis of the most cited publications. *Radioprotection* 54(2): 103–109. doi: 10.1051/radiopro/2019016.

Zinelis, S., Georgios, P., Papadopoulos, F. et al. (2022a). Mechanical and electrochemical characterization of 3D printed orthodontic metallic appliances after in vivo ageing. *Dental Materials* 38(11): 1721–1727.

Zinelis, S., Panayi, N., Polychronis, G. et al. (2022b). Comparative analysis of mechanical properties of orthodontic aligners produced by different contemporary 3D printers. *Orthodontics and Craniofacial Research* 25(3): 336–341. doi: 10.1111/ocr.12537.

24
Regenerative Medicine in Orthodontic Therapy

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Summary

The impact of regenerative medicine on orthodontics is clearly visible in experimental studies, but it only represents the beginning of a process. Advances in the regeneration of anatomically correct teeth and periodontal ligament/bone are among examples of biological regeneration in the field of orthodontics. Regenerative therapies are already being utilized in the clinic, including enamel matrix extracts and platelet-derived growth factors for periodontal regeneration. Clinical orthodontics provides ample opportunities for tissue engineering, including segmental tooth movement, cleft lip and palate, orofacial deformities, temporomandibular joint regeneration, and congenital craniofacial anomalies. Regeneration of multiple dental, oral, and craniofacial tissues by bioscaffolds, bioactive factors, tissue engineering, and/or stem cells offers unprecedented challenges and opportunities for orthodontics.

Orthodontics and dentofacial orthopedics (ODO) form "the branch of dentistry that specializes in the diagnosis, prevention and treatment of dental and facial irregularities. The practice of orthodontics requires professional skills in the design, application and control of corrective appliances to bring teeth, lips and jaws into proper alignment and to achieve facial balance" (American Association of Orthodontists, https://aaoinfo.org). Contemporary orthodontics is widely considered to have originated in the early years of the twentieth century, when Edward Hartley Angle began to practice fixed appliance treatment, by dragging and/or pushing malaligned teeth into esthetic positions with metallic bands and brackets cemented to the teeth. Over the past century, orthodontics, or the field later named orthodontics and dentofacial orthopedics, has witnessed few fundamental innovations, although many diagnostic and therapeutic refinements have been instituted (Mao et al., 2010).

Regenerative medicine is defined as the process of replacing or "regenerating" human cells, tissues, or organs to restore or establish normal function. This field holds the promise of regenerating damaged tissues and organs in the body by replacing damaged tissue or by stimulating the body's own repair mechanisms to heal tissues or organs. Regenerative medicine also enables scientists to grow tissues and organs in the laboratory and safely implant them when the body is unable to heal itself. Orthodontics and regenerative medicine are two separate fields of study, and yet with a multitude of

unrealized common threads. Both ODO and tissue engineering strive to improve tissue functions. Regenerative medicine is a much younger field in comparison with orthodontics, but has nonetheless witnessed robust growth in the fields of tissue healing and organ defects that are currently deemed incurable by contemporary medicine. The classic regenerative medicine paradigm involved the combination of living cells with a natural, synthetic, or bioartificial support to develop a biological substitute or a three-dimensional (3D) living construct that is structurally, mechanically, and functionally equal to a tissue. Currently, researchers have gained high expertise in cell manipulation, materials science, and bioengineering for the design of highly complex biomimetic tissue substitutes for reparative/regenerative purposes, leading to the development of 3D engineered models designed to recapitulate the particular conditions that are intended to be mimicked. (Figure 24.1; Caddeo et al., 2017). ODO is considered to be at a pivotal point of transformation, with digital technology–assisted treatment planning and execution, more incorporation of skeletal anchorage systems in treatment, and conducting more and more research on regenerative medicine methods. This chapter attempts to identify potential interactions between ODO and regenerative medicine, including situations in which ODO may generate translational and clinical motivations for tissue engineering.

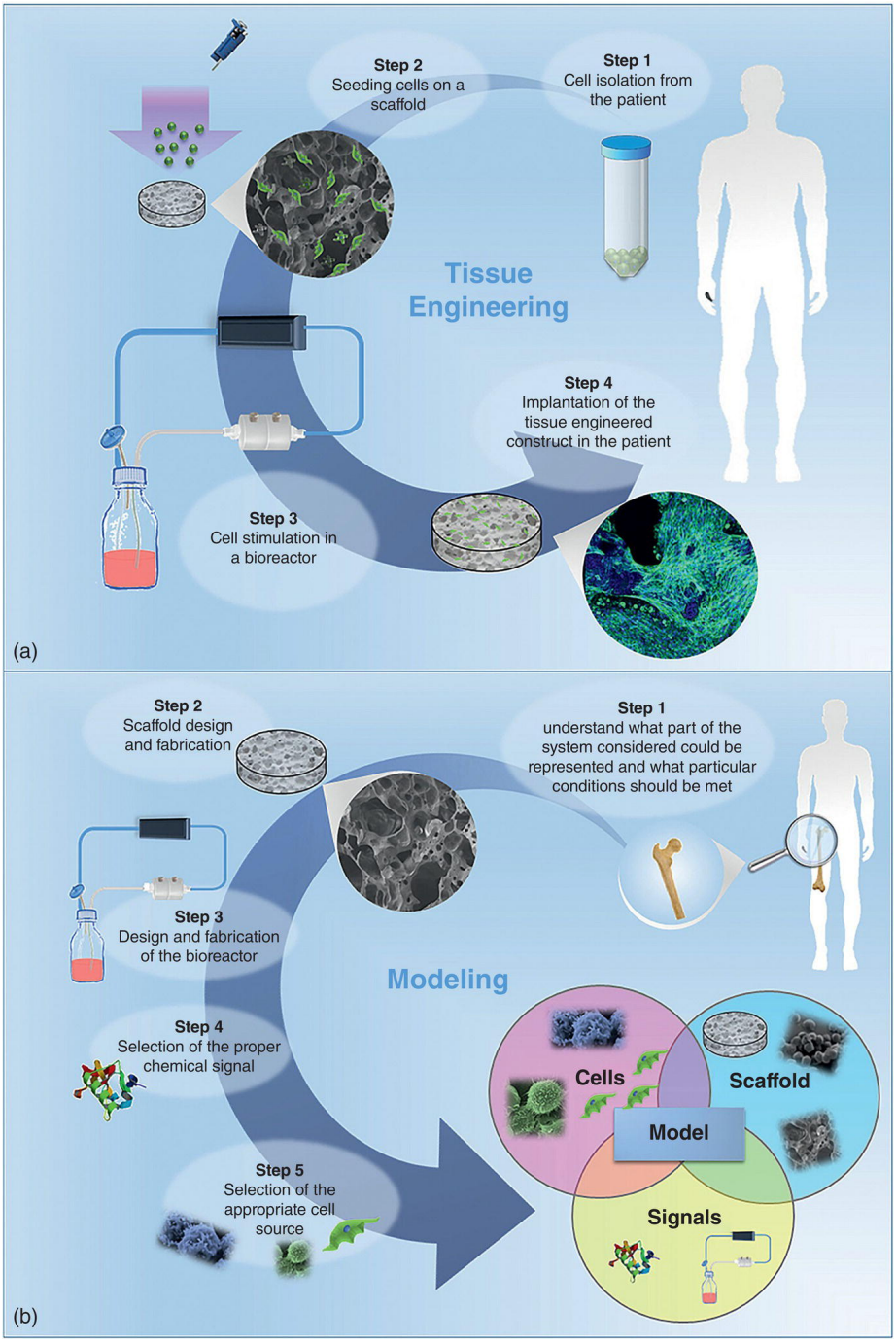
Step 2
Seeding cells on a scaffold
Step 1
Cell isolation from the patient
Tissue Engineering
Step 4
Implantation of the tissue engineered construct in the patient
Step 3
Cell stimulation in a bioreactor
(a)
Step 2
Scaffold design and fabrication
Step 1
understand what part of the system considered could be represented and what particular conditions should be met
Step 3
Design and fabrication of the bioreactor
Modeling
Step 4
Selection of the proper chemical signal
Cells
Scaffold
Model
Signals
Step 5
Selection of the appropriate cell source
(b)

Figure 24.1 (a) The classic tissue engineering paradigm consists in the isolation of primary cells from the patient and further seeding on a three-dimensional (3D) porous scaffold, specifically designed to induce cell proliferation and differentiation. The bioartificial system is developed in a specific environment, where the metabolic, mechanical, and electrical stimuli are provided by a bioreactor. In this tissue-specific designed system, cells start to produce extracellular matrix, leading to in vitro tissue maturation. The tissue-engineered construct is then implanted in the patient, undergoing to a remodeling process in vivo, which allows tissue restoration. (b) The tissue engineering approach for the development of in vitro models. The first step is to understand what part of the system considered should be represented and which specific conditions should be met. The second step is the design of the appropriate scaffold, i.e. the design of a 3D porous construct recapitulating the architecture and the mechanical and surface properties of the tissue/organ to be modeled. The third step is the selection of the cells to be seeded in the designed scaffold. The subsequent steps should be the design and fabrication of a bioreactor and the selection of the appropriate chemical signals (e.g. cocktail of growth factors) to be included in the model. Once a model is successfully developed, it can be improved by increasing its complexity, by introducing an additional cell type or chemical factor, or coupling different mechanical stimuli. The final step is validation, aiming to demonstrate the relevance of the model for the intended purpose. The validation procedure is fundamental and this step should be carefully designed.

Source: Caddeo et al. (2017) / from Frontiers Media S.A., CC BY 4.0.

Principles of tissue regeneration

Tissue engineering is the construction of bioartificial tissues *in vitro* and/or the *in vivo* alteration of cell growth and function via implantation of suitable cells isolated from donor tissue and biocompatible scaffold materials. The basic tenets of tissue engineering have been to incorporate cells and scaffold and signaling molecules into *in vitro* analogs of tissues that are to functionally replace diseased or lost tissues (Figure 24.2; Langer and Vacanti, 1993; Rahaman and Mao, 2005; Scheller et al., 2009; Caddeo et al., 2017). Combinations of cells and materials can reorganize themselves based on the strength of adhesion between cells and substrate and among the various cell types present in the tissue construct. It is essential for the biomaterials used for tissue engineering to have controlled surface chemistry, porosity, and biodegradability so that optimal cell adhesion, migration, and deposition of endogenous extracellular matrix materials by the cells are promoted. The tissue constructs created should be able to intimately integrate into the host's vascular system in order to provide efficient nutrient supply and waste removal. For tissue engineering to be successful, one must understand the structure and function of the tissue to be regenerated, and then apply this knowledge in the design of tissue engineering strategies.

Many challenges remain for tissue engineering of dental, oral, and craniofacial structures. Considerations such as high demand for esthetics, appropriate vascularization, the complex environment, and the need for accommodating multiple tissue phenotypes should be taken into account when dental, oral, and craniofacial tissues are candidates for tissue engineering. A number of approaches have been explored to determine and accommodate the need for regenerating craniofacial tissues.

Stem cell basics

In postnatal life, stem cells are generally those rare cells with the potential to differentiate into multiple cell types. Usually, stem cells are quiescent in the body and serve as reserve cells. Under physiological conditions, stem cells periodically replenish themselves in a process known as cycling or self-renewal, to maintain a renewable stem cell pool (Watt and Hogan, 2000; Verfaillie, 2002). Self-renewal is fundamental for biological tissues, not only to replace dead or aged cells, but also to repair pathological defects or trauma (National Institutes of Health, 2009). With the great deal of interest in the regeneration of dental, oral, and craniofacial tissues, one should not overlook the role of stem cells in maintaining tissue homeostasis. Tissue turnover is exemplified most obviously by epithelial cells of the skin and by bone cells. Skin and bone, as well as many other tissues, undergo physiologically necessary turnover throughout life.

Stem cell characteristics

Stem cells are unspecialized cells and are important tools owing to their capacity to differentiate into a large number of cells according to the stimuli provided. These require the correct medium containing the factor that will provide the desired stimulation to guided differentiation along the macroenvironment with adequate temperature, pH, gas rate (such as a bioreactor), and a 3D structure to provide the right microenvironment for cell proliferation, growth, and differentiation (scaffold; Tonelli et al., 2017). For example, mesenchymal stem cells are capable of differentiating into cells such as osteoblasts, fibroblasts, chondrocytes, and myocytes (Figure 24.3) and can give rise to bone, cartilage, bone marrow stroma, interstitial fibrous tissue, skeletal muscle, tendons, ligaments, as well as adipose tissue (Jiang et al., 2002; Mezey et al., 2003; Alhadlaq et al., 2005; Sonoyama et al., 2005; Marion and Mao, 2006; Stosich and Mao, 2007; Lee et al., 2010a). Stem cells can be classified as follows (Zakrzewski et al., 2019):

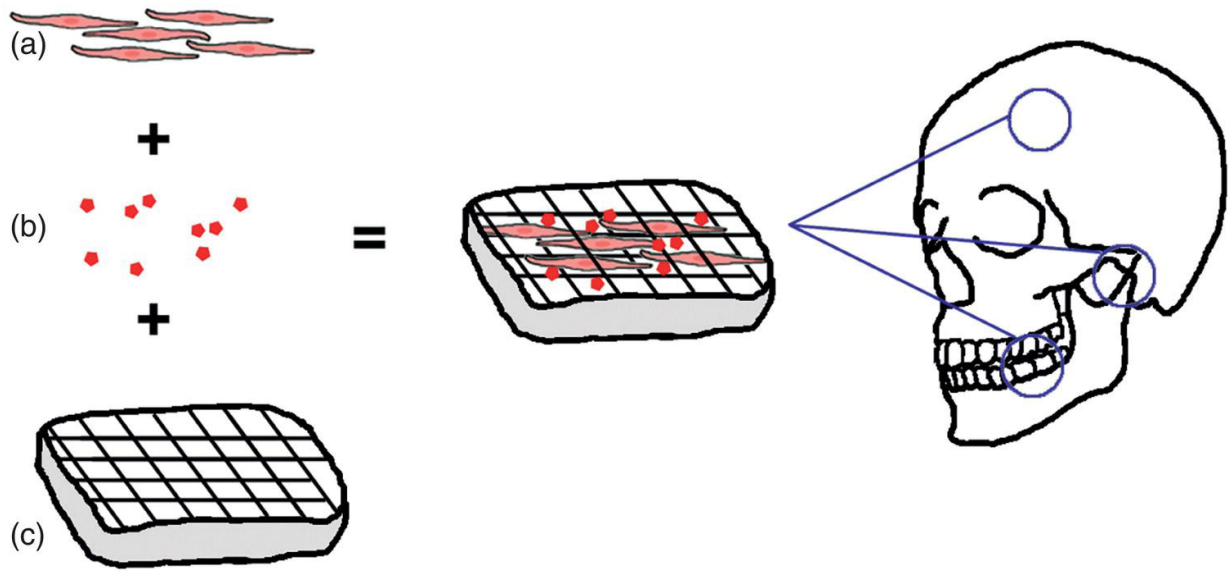

Figure 24.2 Traditional application of tissue engineering. Appropriate cells such as (a) stem cells, (b) bioactive molecules, and (c) a compatible scaffold are mixed together for the correct tissue formation of the craniofacial area, such as teeth, periodontium, temporomandibular joints, and calvarial bone.

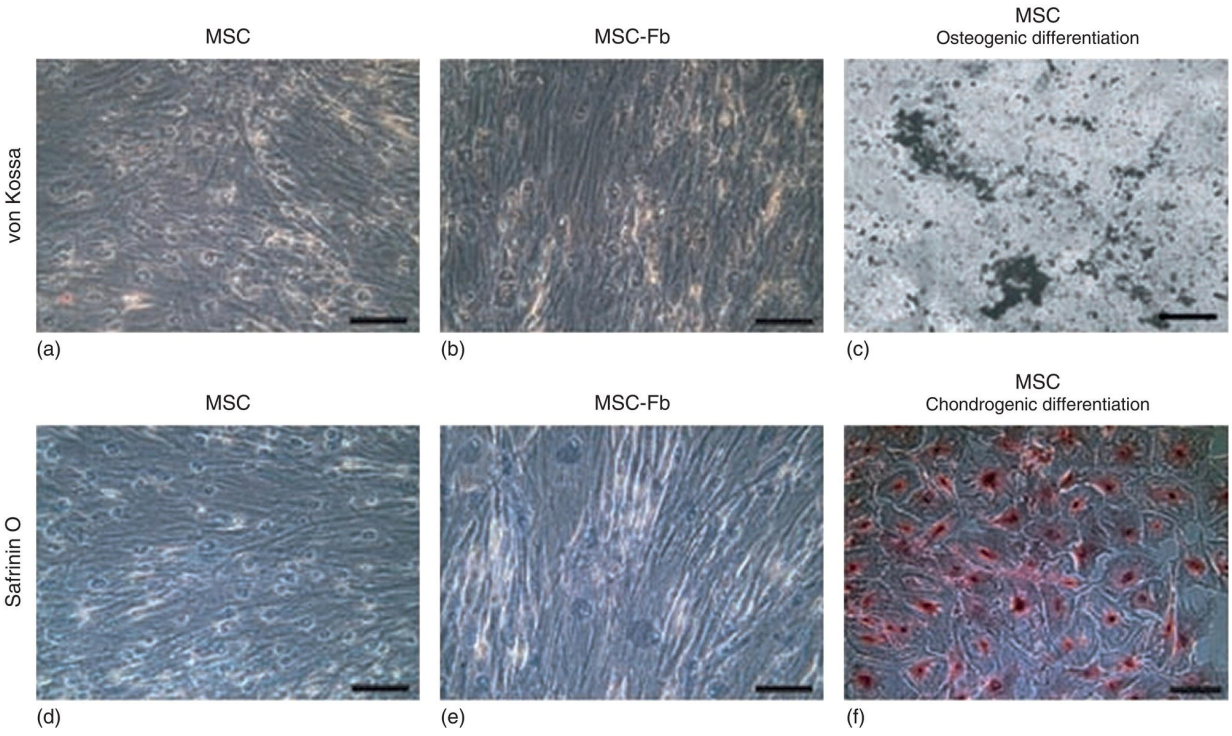

Figure 24.3 (a, b) Mesenchymal stem cells (MSCs). (c) MSCs subjected to osteogenic stimulation readily differentiated into osteogenic cells that elaborated minerals. (d, e) Safranin O staining is negative in connective tissue growth factor (CTGF)-treated MSCs (e), as in MSCs without CTGF treatment (d). (f) In contrast, MSCs subjected to chondrogenic stimulation readily differentiated into Safranin O positive chondrogenic cells. MSC-Fb, MSC differentiated into fibroblasts. Scale bars: 100 μm.

Source: Lee et al. (2010) / courtesy of the American Society for Clinical Investigation.

- *Totipotent stem cells*. Totipotency has the highest differentiation potential and allows cells to form both embryonic and extraembryonic structures. The zygote, which is formed after a sperm fertilizes an egg, is the classic example of a totipotent stem cell. These stem cells can later either develop into any of the three germ layers or form a placenta. After approximately four days, the blastocyst's inner cell mass is the source of pluripotent cells called embryonic stem cells (ESCs).
- *Pluripotent stem cells* (PSCs) form cells of all germ layers, but not extraembryonic structures such as the placenta. ESCs derived from the inner cell mass of preimplantation embryos are a typical example. Another example is induced pluripotent stem cells (iPSCs) derived from the epiblast layer of implanted embryos. Their pluripotency is a continuum, starting from completely pluripotent cells such as ESCs and iPSCs and ending as representatives with less potency: multi-, oligo-, or unipotent cells. Their culturing and utilization seem to be very promising in regenerative medicine.
- *Multipotent stem cells* have a narrower spectrum of differentiation than PSCs, but they can specialize in discrete cells of specific cell lineages. One example is a hematopoietic stem cell, which can develop into several types of blood cells. After differentiation, a hematopoietic stem cell becomes an oligopotent cell. Its differentiation abilities are then restricted to cells of its lineage.
- *Oligopotent stem cells* can differentiate into several cell types. A myeloid stem cell is an example that can divide into white blood cells but not red blood cells.
- *Unipotent stem cells* are characterized by the narrowest differentiation capabilities and a special property of dividing repeatedly. This latter feature makes them a promising candidate for therapeutic use in regenerative medicine. These cells are only able to form one cell type.

A detailed description of ESCs (totipotent and pluripotent), adult stem cells (multipotent, oligopotent, and unipotent), and iPSCs follows.

Embryonic stem cells

ESCs are found in the inner cell mass of the human blastocyst. In normal embryonic development, they disappear after the seventh day in order to form the three embryonic tissue layers. The blastocysts formed after the fusion of sperm and ovum fertilization are composed of two distinct cell types: the inner cell mass (ICM), which develops into epiblasts and induces the development of a fetus, and the trophectoderm. As the trophectoderm begins to form a specialized support structure, such as the placenta, the ICM cells remain undifferentiated, fully pluripotent, and proliferative,

allowing them to form any cell of the organism. Human embryonic stem cells (hESCs), derived from the ICM, form aggregations called germ layers during the process of embryogenesis to endoderm, ectoderm, and mesoderm (Figure 24.4). After ESCs differentiate into one of the germ layers, they become multipotent stem cells, whose potency is limited to only the cells of the germ layer. After that, PSCs occur all over the organism as undifferentiated cells, and their key abilities are proliferation by the formation of the next generation of stem cells and differentiation into specialized cells under certain physiological conditions.

In 1998 hESCs were successfully grown in the laboratory for the first time (Thomson et al., 1998). Undifferentiated ESCs extracted from the inner cell mass during the blastocyst stage can be cultured in the laboratory and under the right conditions will proliferate indefinitely and retain the potential to differentiate into cells of all three embryonic tissue layers. Research involving hESCs is at the center of the ethical debate about stem cell use and potential in regenerative medicine (National Research Council (US) and Institute of Medicine (US) Committee on the Biological and Biomedical Applications of Stem Cell Research, 2002).

Adult stem cells

Somatic or adult stem cells are undifferentiated and found among differentiated cells in the whole body after development. The adult stem cells have the capacity to self-renew themselves into a limited number of mature cell types and help in maintaining tissue homeostasis. They are usually maintained in a quiescent state, but on the loss of cells or injury to the tissue they can be activated to proliferate and differentiate into the required type of cells (Watt and Hogan, 2000; National Institutes of Health, 2009). Among many types, there are the following (Zakrzewski et al., 2019):

- Mesenchymal stem cells (MSCs) are present in many tissues. In bone marrow, these cells differentiate mainly into bone, cartilage, and fat cells. As stem cells, they are an exception because they act pluripotently and can specialize in the cells of any germ layer.
- Neural cells give rise to nerve cells and their supporting cells: oligodendrocytes and astrocytes.
- Hematopoietic stem cells (HSCs) form all kinds of blood cells: red, white, and platelets.
- Skin stem cells form, for example, keratinocytes, which create a protective layer of skin.

Bone marrow is the source of at least three stem cell populations: MSCs, HSCs, and proangiogenic progenitor cells (CD34+ and CD133+). Isolation of MSCs from bone marrow was first described by Friedenstein and collaborators (1974). MSCs isolated by adherence to culture plates are heterogeneous. Only a fraction of cells among typical MSC preparations are stem cells (Lee et al., 2010b). Through employing suitable media and growth supplements that initiate lineage differentiation, human MSCs (hMSCs) have the capacity to differentiate into all the three lineages; that is, ectoderm (neuronal cells and dental-derived MSCs are one source of generating these cells), mesoderm (adipocytes, osteocytes, and chondrocytes) and endoderm (hepatocytes and pancreocytes; Zakrzewski et al., 2019). Several studies have explored the potential of

MSCs in the regeneration of craniofacial tissues, such as alveolar bone, periodontium, and even ectomesenchymal-based tooth structures (Kawaguchi et al., 2004; Maria et al., 2007; Kim et al., 2010a; Kim et al., 2010b).

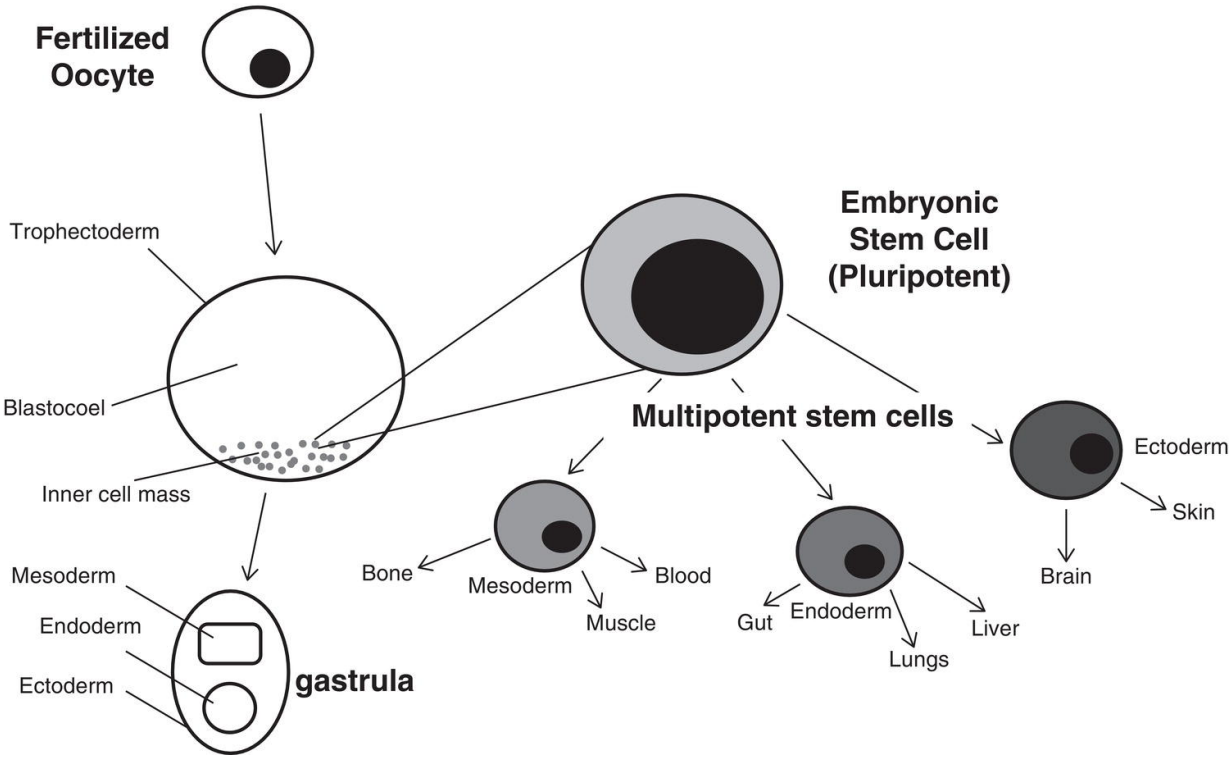

Figure 24.4 Oocyte development and formation of stem cells. The blastocoel, which is formed from oocytes, consists of embryonic stem cells that later differentiate into mesodermal, ectodermal, or endodermal cells. Blastocoel develops into the gastrula.

Source: Zakrzewski et al. (2019) / Springer Nature / CC BY-4.0.

HSCs are important because they are by far the most thoroughly characterized tissue-specific stem cell. HSCs are coinhabitants of bone marrow with MSCs, and MSCs and osteoblasts serve as stromal cells for HSCs. HSCs are responsible for the generation of all functional hematopoietic lineages in blood, including erythrocytes, leukocytes, and platelets. HSC transplantation solves problems that are caused by inappropriate functioning of the hematopoietic system, which includes diseases such as leukemia and anemia (Zakrzewski et al., 2019). The osteoclasts, the bone-resorbing cells during bone turnover and orthodontic tooth movement, derive from this hematopoietic lineage (Kyba, 2005).

Induced pluripotent stem cells

iPSCs are adult somatic cells that have been genetically reprogrammed to an ESC-like state through the forced expression of genes and factors important for maintaining the defining properties of ESCs. It was Yamanaka's laboratory at Kyoto University that developed mouse iPSCs from mouse fibroblasts in 2006. Human iPSCs were first independently produced by Yamanaka's and Thomson's groups from human fibroblasts in late 2007. Human iPSCs have been successfully generated from adipocyte-derived stem cells, amniocytes, peripheral blood, cord blood, dental pulp

cells, oral mucosa, and skin fibroblasts. Various growth factors and chemical compounds have recently been found to improve the induction efficiency of iPSCs. Nakagawa et al. (2008) have shown that iPSCs can be generated from fibroblasts by viral integration of Oct4/Sox2/Klf4. This suggests that endogenous expression of transcription factors, which maintain stemness, have a role in the reprogramming process of pluripotency. Even though retroviruses are being extensively used to reprogram somatic cells into iPSCs, retroviral vectors may have significant risks that could limit their use in patients (Ye et al., 2013). In the current state, a better understanding of epigenetic alterations and transcriptional activity associated with the induction of pluripotency and following differentiation is required for the efficient generation of therapeutic cells. Long-term safety data must be obtained to use human iPSC-based cell therapy for the treatment of diseases.

Dental tissues as a source of stem cells

Cranial neural crest cells are essential for the development of craniofacial structures. The head is formed through an interaction between mesodermal and cranial neural crest cells. The neural crest arises from the ectoderm-derived neural tube during prenatal development at approximately day 20 in the human embryo (Bhattacherjee et al., 2007). These cells migrate to the presumptive face, and possess the ability to self-renew and differentiate into multiple cell types for the genesis of teeth, bone, and cartilage. How neural crest cells differentiate into craniofacial tissues is only partially understood. The cranial neural crest cells migrate into the pharyngeal arches, disperse throughout this region, and give rise to the ectomesenchyme, which will interact with its surroundings to form the diverse tissues already mentioned as well as other tissues such as the neurons and glia of cranial ganglia (Chai et al., 2000; Graham and Smith, 2001; Le Douarin et al., 2008). Craniofacial bones are further developed by intramembranous ossification or deposition of bone matrix by osteoblasts. Tooth morphogenesis occurs via a series of complex signaling interactions between the oral epithelium (dental lamina) and the underlying ectomesenchyme (Olsen et al., 2000; Tucker and Sharpe, 2004). In comparison, the bones of the rest of the body form by mesoderm-derived mesenchymal cells, through endochondral ossification where there is a chondrogenic template, before bone matrix is laid down (Vaglia and Hall, 1999; Olsen et al., 2000; Noden and Trainor, 2005).

Neural crest cells differentiate into ectomesenchymal progenitor cells in the cap stage of the dental follicle. The dental follicle surrounds the dental papilla and dental epithelium, and gives rise to cementum, periodontal ligament, and alveolar bone. Specifically, interactions between Hertwig's epithelial root sheath and dental follicle lead to the differentiation of cementoblasts, osteoblasts, and fibroblasts. Important regulators of alveolar bone development include Runx2, Dlx 5/6, and Msx1 (Saito et al., 2009; Fleischmannova et al., 2010).

On completion of tooth morphogenesis, stem cells have been identified in several dental and periodontal structures, including the dental pulp of both deciduous and permanent teeth, papillae, periodontal ligament, dental follicles, and dental-derived epithelial stem cells (Gronthos et al., 2000; Miura et al., 2003; Seo et al., 2004; Honda et al., 2007; Sonoyama et al., 2008; Yao et al., 2008). It should come as no surprise when stem cells are discovered in any biological tissues, given the fundamental roles of

stem cells to maintain tissue homeostasis and participate in tissue repair following trauma or pathological insults.

The various sources of dental progenitor cells include the dental pulp stem cells (DPSCs; Gronthos et al., 2000), stem cells from human exfoliated deciduous teeth (SHED; Miura et al., 2003), periodontal ligament stem cells (PDLSCs; Seo et al., 2004), dental follicle stem cells (DFSCs; Morsczeck et al., 2005), stem cells from apical papilla (SCAP; Sonoyama et al., 2008), and gingival stem cells (GING SCs; Mitrano et al., 2010). Like bone marrow–derived mesenchymal stem cells (BM-MSCs), dental-derived stem cells exhibit self-renewal capacity, possess high proliferation rates, have multilineage differentiation potential into a wide spectrum of cell types from the three germ layers, or, at least in part, express their specific markers under the appropriate culture conditions. Despite being similar at a coarse level, the transcriptomic and proteomic profiles of oral stem cells reveal several molecular differences, including differential expression of surface marker, structural proteins, growth hormones, and metabolites, indicating prospective developmental divergence (Hosmani et al., 2020; Krivanek et al., 2020). All these characteristics suggest that dental stem cells might be the optimal choice for tissue self-repair and regeneration (Al Madhoun et al., 2021).

Dental pulp stem cells

DPSCs, the most studied dental stem cells, are ectoderm-derived stem cells originating from migrating neural crest cells. DPSCs were initially isolated and characterized by Gronthos et al. (2000). The culturing method and accurate characterization are pivotal steps for the isolation of high-quality DPSCs. Following extraction of the teeth (especially and most appropriately a third molar), further procedures include mechanical extraction of the soft pulp connective tissue, maceration, enzymatic digestion of extracellular matrix (ECM) proteins, and cell growth in plastic tissue/cell culture plates. DPSCs remained viable up to five days after tooth storage at 4 °C in phosphate buffered saline (PBS), but viability was dramatically reduced after 24 hours of storage, indicating that teeth should be immediately processed to ensure the highest cell recovery (Perry et al., 2008). Ferro et al. (2014) recommended the use of fresh pasteurized milk for teeth transport due to its antimicrobial properties. Other procedures involve teeth or dental pulp storage with cryoprotectant agents (CPA; Rodas-Junco and Villicaña, 2017). For DPSC isolation, the most widely used methods are enzymatic digestion (ED) of tissues or outgrowth (OG) from tissue explants. ED enables isolation of single-cell suspensions from primary tissues by digestion with enzymes such as collagenase type I and II, dispase, trypsin, and accutase. On the other hand, the OG method is simpler and faster and consists of placing pulp fragments (1–2 mm^3 pieces) directly into the culture plate, so that cells outgrow from the pulp tissue explants (Rodas-Junco and Villicaña, 2017). Improving the optimal cell attachment in the plastic dish for primary culture involves precoating the plastic surfaces with ECM proteins, or using peptide-modified surfaces, synthetic polymeric cations, or culture-treated surfaces. The most common culture media used for DPSCs include alpha-minimal essential medium (α-MEM), Dulbecco's modified Eagle medium (DMEM), DMEM/Ham's F12 nutrient medium (DMEM/F12), DMEM low glucose (DMEM-LG), and DMEM Knock Out (DMEM-KO) media (Rodas-Junco and Villicaña, 2017). Standard cell culture media are commonly supplemented with fetal bovine serum (FBS; also called fetal calf serum, FCS), which provides many components required for

cell growth, metabolism, and proliferation. Basic fibroblast growth factor (bFGF, also known as FGF-2) and epidermal growth factor (EGF) have been used routinely for MSC culture because they have a pronounced mitogenic effect and retain differentiation potential toward several lineages (Rodas-Junco and Villicaña, 2017). A schematic representation of critical steps followed from tooth selection to DPSC cryopreservation and application is provided as Figure 24.5.

DPSCs are composed of progenitor cells that are marked by diverse characteristics, such as clonal heterogeneity, multilineage differentiation, self-renewal capacity, and phenotypic complexity. DPSC populations are functionally heterogeneous, as evidenced through their surface antigen profile or expression patterns of a variety of markers that are associated with progenitors of different lineages. DPSCs show surface expression of STRO-1, CD13, CD29, CD44, CD73, CD90, CD105, CD146, and CD166 – a profile that is reminiscent of BM-MSCs. Additionally, DPSCs express various pluripotency markers, such as Oct-3/4, Nanog, and Sox-2 – that is, the stemness-related markers observed in ESCs – which explains, at least in part, their self-renewal potential (Faruqu et al., 2020). As neuronal crest–derived cells, DPSCs express several neural stem cell markers, including nestin, neuronal nuclei antigen, vimentin, synaptophysin, musashi-1, Galactosyl-ceramidase, S100 calcium binding protein B, neurofilament heavy (NFH) chain, class III β-tubulin, and neurofilaments (Al Madhoun et al., 2021).

DPSCs could be a valuable source for cell therapy and advancing current regenerative medicine strategies. DPSCs have the potential to differentiate into endodermal (respiratory and gastrointestinal tracts, liver, pancreas, thyroid, prostate, and bladder lineages), mesodermal (adipogenic, osteogenic, and chondrogenic lineages), and ectodermal (skin and neural lineages; Yamada et al., 2019). In addition, DPSCs were shown to differentiate into myocytes, cardiomyocytes, hepatocyte-like cells, melanocytes, and active neurons (Patil et al., 2014). DPSCs also have remarkable potential as alternative sources to multipotent MSCs and, due mainly to their immunomodulatory properties (mediating G0/G1 cell cycle arrest of the chemically activated T cells), DPSCs constitute a highly valuable source for cell therapy of a variety of inflammatory diseases and other disorders. With regard to basic or preclinical studies in experimental animal models, human DPSC-based therapies have been successfully used in several disease conditions, including diabetes, neuropathy, hepatic diseases, oculopathies, spinal cord, peripheral nerve injury, cerebral ischemia, muscular dystrophy, myocardial infarction, Parkinson's disease, lung injury, and stroke (Anitua et al., 2018; Al Madhoun et al., 2021).

Periodontal ligament stem cells

The periodontal ligament (PDL), the connective tissue that connects the root cementum and the alveolar bone, is derived from embryonic cranial neural crest cells (CNCCs). The periodontium includes bone and cementum cells and a mix of fibroblasts, mesenchymal, and undifferentiated cells, all of which are seated on a hydrated fibrillar extracellular substance rich in collagen. PDLSCs contain 95% MSCs and 5% neural crest stem cells (Ng et al., 2015). These cells have the ability to grow clonally and express MSC markers (vimentin, STRO-1, CD90, scleraxis, and CD44), markers of ESCs (c-Myc, SSEA4, Klf4, Oct4, Nanog, and Sox2), and neural crest cells markers (Sox10, nestin, Snail, Slug, Sox10 p75, and Tuj1; Coura et al., 2008; Song et

al., 2012). These markers are considered as hallmarks of multipotency that highlight the differentiation capacity of PDLCs into various cell types, such as chondrogenic, cardiomyogenic, osteogenic, and neurogenic lineages.

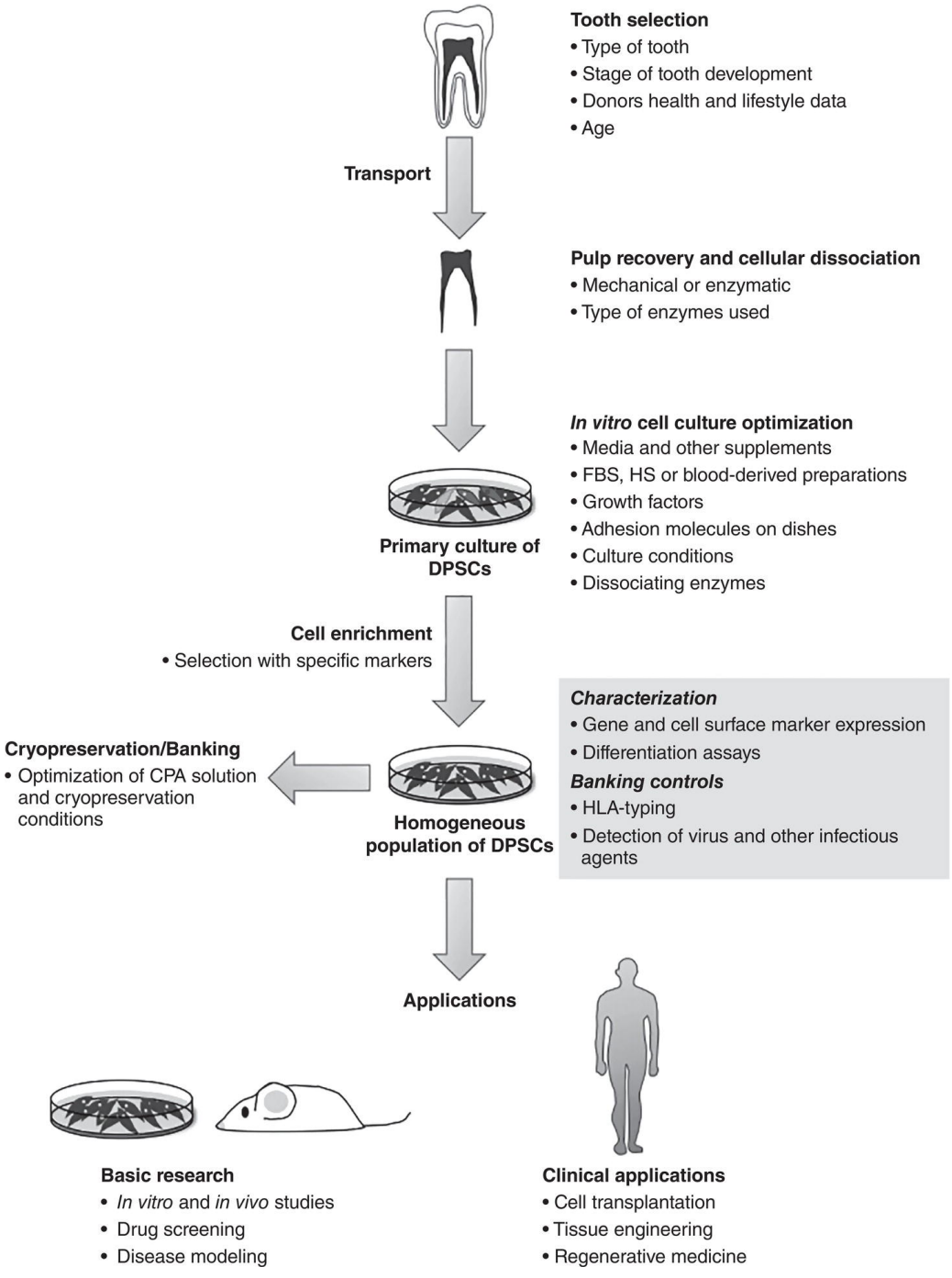
Tooth selection
• Type of tooth
• Stage of tooth development
• Donors health and lifestyle data
• Age
Transport
Pulp recovery and cellular dissociation
• Mechanical or enzymatic
• Type of enzymes used
In vitro cell culture optimization
• Media and other supplements
• FBS, HS or blood-derived preparations
• Growth factors
• Adhesion molecules on dishes
• Culture conditions
• Dissociating enzymes
Primary culture of DPSCs
Cell enrichment
• Selection with specific markers
Characterization
• Gene and cell surface marker expression
• Differentiation assays
Banking controls
• HLA-typing
• Detection of virus and other infectious agents
Cryopreservation/Banking
• Optimization of CPA solution and cryopreservation conditions
Homogeneous population of DPSCs
Applications
Basic research
• In vitro and in vivo studies
• Drug screening
• Disease modeling
Clinical applications
• Cell transplantation
• Tissue engineering
• Regenerative medicine

Figure 24.5 Schematic representation of critical steps followed from tooth selection to dental pulp stem cell (DPSC) cryopreservation and applications. Each step summarizes critical factors that should be considered for optimization in order to improve DPSC culture and stability during manufacturing. For tooth selection, several factors related to donor characteristics must be considered to establish specific criteria according to research interests. As we can see, many key factors fall into cell culture formulation, suggesting that this issue is one of the most important to establish general or tailored protocols and obtain DPSCs with specific properties, as well as the long-term maintenance of cultures. Homogeneous populations of DPSCs may be cryopreserved or directly applied to basic or clinical research, with either previous or simultaneous molecular and biochemical characterization. CPA, cryoprotective agents; FBS, fetal bovine system; HLA, human leukocyte antigen; HS, hematopoietic stem cells.

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PDLSC isolation was described for the first time by Seo et al. (2004). PDLSCs can be easily harvested from periodontal tissue during the noninvasive procedure. The first and second premolar teeth are suitable for the purpose of PDLSC isolation. Teeth are transferred in the cell culture medium supplemented with 1% antibiotic at 4 °C. In all seeding techniques, complete DMEM (supplemented with L-glutamine, 1% antibiotic, 10% FBS) is used in standard culture conditions (37 °C with 5% CO_2). The cells are isolated with two different methods through enzymatic digestion with type 1 collagenase or trypsin/EDTA and mechanical disaggregation and explant culture. Since PDLSCs have the same embryological origin of the neural crest and are less lineage divergent than neural cells, they are considered promising for neuroregenerative applications. Additionally, PDLSCs have an immunomodulatory ability that is comparable to BM-MSCs (Zhu and Liang, 2015). Briefly, PDLSCs can differentiate into cementoblasts, osteoblasts, and fibroblasts, the main cell types responsible for guaranteeing tissue homeostasis of the cementum, alveolar bone, and PDL, respectively, which highlights their application in regenerative periodontology. PDLSCs can also differentiate into neurons, cardiomyocytes, endothelial cells, pancreatic islet cells, and corneal keratocytes, which further expands their application in regenerative medicine. Eventually, PDLSCs have immunomodulatory properties that can be performed by direct cell-to-cell contact or by the synthesis of specific metabolites that alter the phenotype of different immune cells. Despite some promising clinical results and biological insights, several gaps need to be filled before adopting a protocol for their clinical use in patients with periodontitis or other inflammatory conditions (Trubiani et al., 2019; Queiroz et al., 2021).

Gingival mesenchymal stem cells

The human gingiva is a unique masticatory keratinized mucosal tissue and an essential component of the periodontal apparatus, the connective tissue of which develops from both the neural crest and the mesenchyme. The initial steps toward isolation and characterization of gingival MSCs (GMSCs) were made by Zhang et al. (2009). Accumulating studies have demonstrated the promising potential of GMSCs as a readily accessible and expandable source of MSCs that can be easily obtained through minimally invasive surgical techniques (Górski, 2016; Fawzy El-Sayed and Dörfer, 2016). Initially, it was found that human gingival tissues harbor clustered immunostaining signals for stem cell–related genes such as Oct-4, SSEA-4, and STRO-1

in the lamina propria/connective tissue layers, suggesting the existence of a subpopulation of adult stem cells in human gingival tissues. Subsequently, a unique population of progenitor cells was isolated from normal human gingival tissues, which are characterized by their fibroblast-like spindle morphology, the colony-forming unit–fibroblast (CFU-F), the expression of a panel of MSC-related cell surface markers such as CD73, CD90, CD105, SSEA-4, and STRO-1 but negative for hematopoietic cell markers like CD34 and CD45, and multipotent differentiation into osteocytes, adipocytes, and neural types of cells. The properties of these progenitor cells derived from human gingival tissues fulfill the minimal criteria of the International Society for Cell & Gene Therapy (ISCT) to define mesenchymal stromal/stem cells, thus designated gingiva-derived mesenchymal stem/stromal cells (Kim et al., 2021). In terms of their multipotency, GMSCs not only possess mesodermal trilineage differentiation potentials (osteocytes, adipocytes, and chondrocytes), but also the potential to transdifferentiate into ectodermal and endodermal cell lineages, such as neural cells, keratinocytes, endothelial cells, and odontogenic cells, under defined induction conditions. Easy accessibility, less morbidity of harvesting, the highly proliferative activity and genomic stability, and a neural crest origin as well as the potent immunomodulatory and regenerative potentials make GMSCs an attractive source of adult stem cells for tissue engineering and regenerative therapy (Kim et al., 2021).

Three-dimensional scaffolds

The purpose of fabricating scaffolds is to produce tissue-like materials such that they can eventually perform like the native tissues. The idea of scaffold fabrication is based on creating materials with optimum pore size, structure, and porosity for various applications. Generally, scaffolds are created first and cells are subsequently cultured on these scaffolds. Porous 3D scaffolds can be fabricated from various conventional and rapid prototyping techniques, depending on the type of materials used or type of pore structures needed. Open porous and interconnected networks are essential for cell nutrition, proliferation, and migration for tissue vascularization and formation of new tissues. Materials with high porosity enable effective release of biofactors such as proteins, genes, or cells, and provide good substrates for nutrient exchange. However, the mechanical property that is important in maintaining the structural stability of the biomaterial is often compromised as the result of increased porosity. These scaffolds serve to provide suitable microenvironments to support cell growth and function.

Various conventional techniques such as salt leaching, gas forming, phase separation, and freeze drying (Figure 24.6), as well as rapid prototyping techniques using computer-aided design (CAD) modeling, are utilized for fabrication of scaffolds (Figure 24.7). Fabrication using conventional methods does not enable precise control of internal scaffold architecture or fabrication of complex architectures. Moreover, scaffolds fabricated using these traditional processing techniques have compressive moduli at a maximum of 0.4 MPa, which is much lower than hard tissue (10–1500 MPa) or most soft tissues (0.4–350 MPa). Such fabrication also uses toxic solvents, which may result in cell death if they are not completely removed. Rapid prototyping fabrication techniques enable the fabrication of scaffolds with improved mechanical properties, with moduli ranging from soft to hard tissues, with better design repeatability, part consistency, and control of scaffold architecture at both micro and

macro levels. The main restriction is the limited number of biomaterials that can be processed by rapid prototyping compared to conventional techniques. Other approaches that mimic the way in which tissues are formed in the body, and their nanofibrous structure, can be found in modular assembly methods and electrospinning methods (Loh and Choong, 2013). A summary of scaffolds used for various tissue regeneration experiments is provided in Table 24.1.

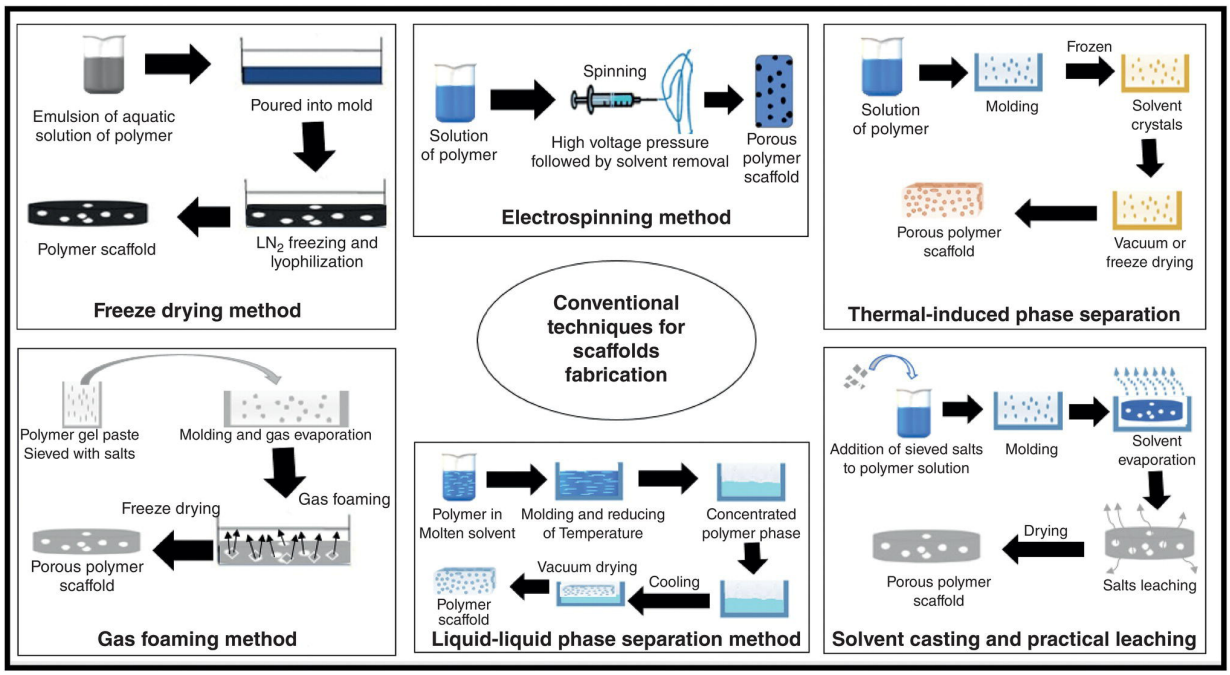

Figure 24.6 Schematic drawing of the biopolymer-forming process of conventional techniques for scaffold fabrication.

Source: Khalil et al. (2020) / MDPI / CC BY-4.0.

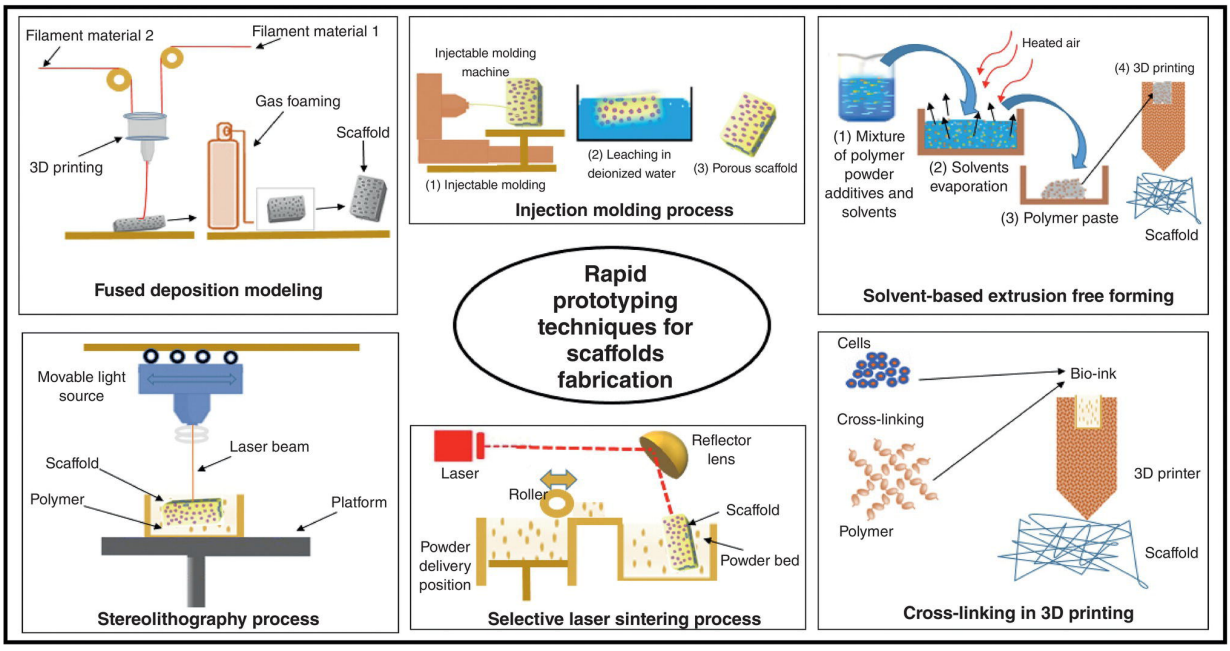

Figure 24.7 Schematic drawing of biopolymer-forming rapid prototyping techniques for scaffolds.

Source: Khalil et al. (2020) / MDPI / CC BY-4.0.

Table 24.1 Summary of the biomaterial class, scaffold, porosity range, and target tissue.

Source: Adapted from Mallick and Cox (2013).

Material class	Scaffold composition	Fabrication type	Pore size/porosity (μm/%)	Target tissue
Ceramic	HAP	Sintering	90–600	Bone
		SFF and image based	366, 444/38, 44	Bone
		Porous sintering	200–800/60–80	Bone
		Sintering (solid, porous particles, and porous coral replication)	50, 230/66, 70	Bone
	TCP cement	Salt leaching	0.2, 8.7/31, 62	Bone
	Calcium metaphosphate	Porous sintering	200	Bone
	Natural coral	Porous sintering	150–220/36	Bone
	HAP-TCP	Porous cylinder sintering	100–150/36	Bone
	Calcium phosphate	Compaction	–	Drug delivery

Material class	Scaffold composition	Fabrication type	Pore size/porosity (μm/%)	Target tissue
Glass and ceramic particles	Porous glassy carbon	Porous pellet sintering	100–200/40	Bone
	$Na_2O–CaO–SiO_2–P_2O5$	Reaction sintering under isostatic pressure	100–200	Bone
	Bioglass 45S5	Melt derived	–	Bone
		Foaming and porous sintering	100–600	Bone
	SiO_2-based sol-gel foams	Foaming	<10–500	Bone
	Silica-calcium phosphate	Phase transformation	10–300/43–51	Bone
	Hyaluronic acid	Phase inversion, particulate leaching	100–600/80–90	Bone
	Mesoporous bioactive glass	Polyurethane sponge technique Immersion in phosphate-buffered saline solution	0.002–0.05	Drug delivery
Natural polymers	Collagen	Freeze drying	11–134	Bone
	Collagen/hyaluronate	Cross-linking	45.7, 35.4	Bone
	Silk fibroin	Freeze drying, salt-leaching, gas foaming	15–100/84–99	–
		Salt leaching	202/84–98	Bone

Material class	Scaffold composition	Fabrication type	Pore size/porosity (μm/%)	Target tissue
Chemically synthesized polymers	PLA	Phase separation, emulsion-solvent diffusion, and porogen leaching	50–800	Bone

Material class	Scaffold composition	Fabrication type	Pore size/porosity (μm/%)	Target tissue
	PLA/PGA	Melt processing	800	Bone
	PLDLA	Solution coating, porogen decomposition	58–80	Bone
	PLGA	Sintered microsphere method	83–300/35	Bone
		Consolidation by pressure drop	100/60–66	Teeth implants
		Sintering	187/31	Bone
		Gas foaming	200	Bone
		Electrospinning	2–465/92	–
	PLGA/PEG	Porogen dissolving	300–500/85	Articular cartilage
	PLGA/PVA	Melt molding particulate leaching method	200–300/90	Bone
	Poly (multifunctional lactic acid-based oligomer)	Salt leaching	45–150, 300–600/80	Bone
	PPF	Gas forming with effervescent reaction	50–1000/51	Bone
		Porogen leaching and photo cross-linking	300–800/57–80	Bone
		Gas forming with effervescent reaction	100–500	Bone
	PET	Melt blowing	93–97	Bone
	Polymeric foams	High internal emulsion phase	40, 100/70–97	Bone
	Poly(desaminotyrosl-tyrosine ethyl ester carbonate)	Solid freeform	486/80–87.5	Bone

Material class	Scaffold composition	Fabrication type	Pore size/porosity (μm/%)	Target tissue
	PLLA/collagen/chitosan	Solvent castings Salt leaching	125–500	Bone

Composites

Material class	Scaffold composition	Fabrication type	Pore size/porosity (μm/%)	Target tissue
	PLGA/bioactive microsphere glass	Microsphere heating mold	350–500	Bone
	PPF/PLGA-PEG microparticles	Salt leaching	–	Bone
	PLA/calcium metaphosphate	Porous sintering	100–400	Bone
	PLLA/nHAP/collagen/chitin fibres	Ultrasonication, lyophilized	200	Bone
	PLGA/HAP	Gas forming Particulate leaching	100–250	Bone
	L-PLGA/TCP D, L-PLGA/L-PLA	TheriForm 3D printing	40–150/55, 90	Articular cartilage
	PGA fiber/fibrin	Freeze drying	300	Skin
	PLGA mesh/collagen sponge gel	Knitted mesh	–	Urinary bladder
	PLLA braid/collagen coating	Freeze drying	50–100	Ligament
	PCL fiber/pHEMA hydrogel	Polymerization, acetone etched	100–400/34–41	Neural tissue engineering
	PLGA/chitin	Electrospinning	–	Skin
	PGA mesh/bioglass 45S5	Bioglass particle in distilled water immerses PGA mesh	–	Soft tissue
	PLGA/bioglass tubular foam	Dispersion Freeze drying	10–50, 100	Intestine, trachea, blood vessel
	PLA/nHAP/collagen	Phase separation	–	Periodontal tissues
	HAP/PCL	Polymeric reticulate method	150–200/87	Drug delivery
	HAP/chitosan-gelatin	Freeze drying	300–500/91	Bone
	HAP/beta-TCP/chitosan	Porogen leaching Freeze drying	300–600	Bone
	Collagen/HAP	Freeze drying	30–100/85	Bone

Material class	Scaffold composition	Fabrication type	Pore size/porosity (μm/%)	Target tissue
	CO3Ap/collagen	Freeze drying	50–300/49, 73, 79	Bone
	Titanium alloy (Ti-6Al-4V)/CaP sol-gel	Porous sintering	50–200/35	Bone
		Sintering (porous)	250/86	Bone
	Titanium/nHAP	Soaking	–	Bone
	Ti-TiBx, Ni-Ti	Self-propagating high-temperature synthesis (porous)	15–55	Bone
	PPF/beta-TCP	Salt leaching	150–300/69, 74	Bone
	PLLA/bioglass	Phase separation	<10, >100	Bone
	Silica-calium phosphate	Sintering	10–300/43–51	Bone
	PLGA/collagen/apatite	Salt leaching	355–425/87	Bone
	Beta-TCP/calcium phosphate invert glass/chitosan	Thermally induced phase separation, immersion in phosphate-buffered saline solution	–	Drug delivery
	Bioactive glass/beta-cyclodextrin	Sol-gel	–	Drug delivery

Material class	Scaffold composition	Fabrication type	Pore size/porosity (μm/%)	Target tissue
Metals	Ni-Ti	Self-propagating high-temperature synthesis	229–641/47–66	Bone
	Titanium fiber meshes	Sintering	250/86	Bone
	Titanium	Plasma spraying	200–400/50–60	Bone
		Porous sintering	50–200/35	Dental
		Diffusion	350/45	Bone
		Laser texture (Ti-6Al-4V)	100, 300	Bone
		Electrochemical oxidation	1–8/13–24	Bone
		Shot blasting	<10/44, 48	Bone
		Acid etching	400	Bone
		Deposition through polystyrene latex beads	0.5, 16, 50	Bone

3D, three-dimensional; CaP, calcium phosphate; CO3Ap, carbonate apatite; HAP, hydroxy apatite; L-PLA, L-poly(lactic acid); L-PLGA, L- poly D,L-lactic-co-glycolic acid; nHAP, nano-hydroxy apatite; Ni-Ti, nickel–titanium; PCL, poly(ε-caprolactone); PEG, polyethylene glycol; PET, polyethylene terephthalate; PGA, polyglycolic acid; pHEMA, poly(2-hydroxyethylmethacrylate); PLA, poly(lactic acid); PLDLA, poly-L-co-D,L-lactic acid; PLGA, poly(D,L-lactide-co-glycolide); PLLA, poly-l-lactic acid; PPF, poly(propylene fumarate; PVA, polyvinyl alcohol; SFF, solid free form; TCP, tissue culture polystyrene; TCP D; Ti-6Al-4V, titanium, 6 aluminium, 4 vanadium; Ti-TiB, titanium-titanium boride.

Biomaterials

Biomaterials are frequently, but not always, needed for tissue engineering and tissue regeneration. For example, stem cells are infused for the repair of cardiac infarcts and can be delivered into cardiac muscle defects, typically without biomaterials as scaffolds. In contrast, a scaffold is frequently required for the regeneration of most dental, oral, and craniofacial structures, because they are 3D structures of functional and esthetic importance. A variety of scaffolds have been developed as extracellular matrix analogs, capable of supporting cells. At a minimum, biomaterial scaffolds should be biocompatible, nontoxic, and promote tissue regeneration (Box 24.1). Biodegradable materials are frequently desirable, given their predesigned purpose to undergo controlled degradation while tissue genesis takes place (Scheller et al., 2009).

Biomaterials can be of native origin, synthetic, or hybrids. The natural polymers, such as collagen, have the advantage of biocompatibility, whereas synthetic polymers allow precise control of physicochemical properties such as mechanical properties, degradation rate, porosity, and microstructures (Sharma and Elisseeff, 2004). Some of the popular synthetic biomaterials include co-polymers of polylactic-glycolic acid collagen, polyphosphazenes, polyurethanes, polycaprolactone, polyethylene glycol (PEG), poly(propylene fumarate), starch-based materials, alginate, silk, bioactive glasses and glass ceramics, calcium-phosphate ceramics, calcium-phosphate and collagen blends, and synthetic polymer/apatite composites (Scheller et al., 2009).

Box 24.1 Design requirements of biomaterials.

- Biocompatible.
- Promote attachment and proliferation of cells and production of extracellular matrix.
- Ability to integrate signaling factors to direct and enhance tissue growth.
- Support vascular integration for oxygen and biomolecule transport.
- Mechanical integrity to support load at the implant site.
- Controlled rate of degradation into nontoxic products that are easily metabolized or excreted.
- Easy and cost-effective processing into three-dimensional shapes of sufficient size to fill clinically relevant defects.

Poly(D,L-lactide-*co*-glycolide) (PLGA) is a synthetic material that can be fabricated into various kinds of structures to better mimic the extracellular matrix environment (Figure 24.8). They are widely used as scaffolding materials for several biomedical applications in humans as part of tissue engineering (Athanasiou et al., 1996; Agrawal and Ray, 2001; Fu et al., 2008). When seeded in PLGA nanofibers, hMSCs proliferate and maintain differentiation characteristics toward osteoblasts and chondrocytes (Xin et al., 2007; Figure 24.9). Another widely used nanofiber is poly(ε-caprolactone) (PCL), which has been used for the differentiation of hMSCs into adipogenic, osteogenic, and chondrogenic cells (Li et al., 2005).

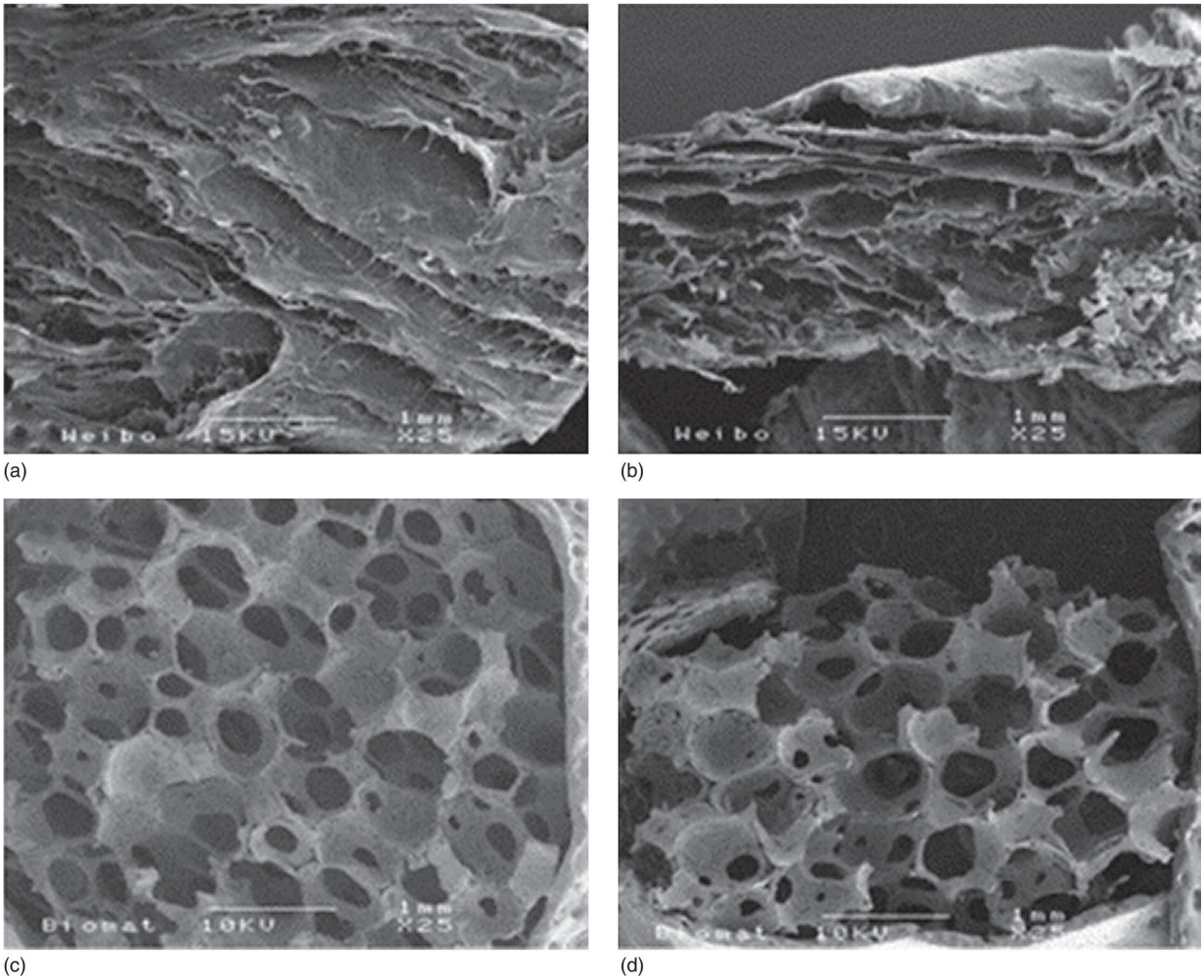

Figure 24.8 Various forms of poly-lactic-co-glycolic acid (PLGA)–based matrices and scaffolds for dental, oral, and craniofacial tissue engineering (Moioli et al., 2007). (a) Porous PLGA sponge fabricated using salt-leaching techniques. (b) PLGA microspheres encapsulating growth factors showing smooth spherical surface and wide range of diameters. (c) PLGA nanofibers fabricated using electrospining techniques. (d) PLGA microspheres in chitosan-based gels for advanced controlled delivery and cell interaction. (a–c) Scanning electron microscopy. (d) Phase contrast image.

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Tissue engineering of tooth and periodontal tissues has frequently used multiple polymer biomaterials, which include collagen, polyglycolic acid (PGA), peptides, gelatin-chondroitin-hyaluronan tri-copolymer, silk, and polycaprolactone (Scheller et al., 2009; Kim et al., 2010a; Kim et al., 2010b). A summary of the biomaterial class, scaffold, porosity range, and target tissue is provided in Table 24.1.

Signaling molecules

The cells employed in a tissue engineering approach must receive proper instructive cues to effect the desired tissue formation. In *in vivo* conditions, cells naturally reside in an extracellular matrix rich in biologically active factors to support tissue function

and homeostasis. The extracellular matrix transmits environmental stimuli, such as mechanical forces, to the resident cells, which can in turn direct cell behavior. Other features of the native tissue environment, such as oxygen tension and osmotic pressure, will influence the function of cells within the tissue. In tissue engineering, biomaterial scaffolds mimic key features of the extracellular matrix of the tissue or organ of interest and provide mechanical support to the cells and developing tissue. The biomaterials employed in tissue engineering scaffolds inherently lack biologically active domains to direct cell behavior. Accordingly, a variety of approaches have emerged to incorporate biologically active cues into scaffolds to inform tissue repair, as the cells that are delivered for tissue regeneration frequently need guidance signals to perform the desired functional roles (Kasper, 2017). Signaling molecules control multiple and complex cellular processes, including cell migration, growth, differentiation, and matrix synthesis. One of the key issues in the delivery of signaling molecules is their premature diffusion; they get denatured after *in vivo* injection and thereby fail to induce the intended effects at the site of delivery. Furthermore, premature diffusion of delivered signaling molecules may cause side effects in other unintended tissues and organs (Moioli et al., 2007). Controlled release is an effective approach that prolongs the bioactivity of signaling molecules by encapsulation of signaling molecules in polymer material shells. Only on gradual degradation of the polymer material shell is the encapsulated signaling cue released a small amount at a time.

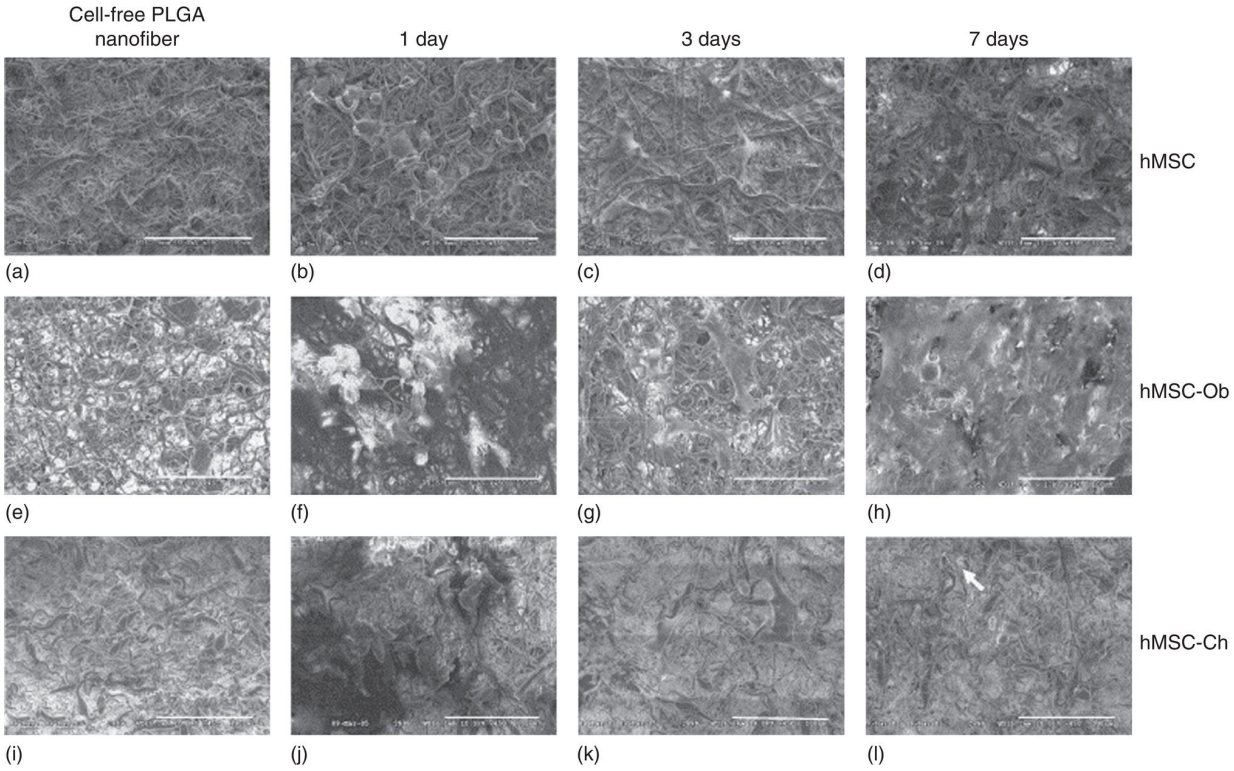

Figure 24.9 Electrospun poly-lactic-co-glycolic acid (PLGA) nanofibers and the seeding of human mesenchymal stem cells (hMSCs), as well as hMSC-derived osteoblasts (hMSC-Ob) and hMSC-derived chondrocytes (hMSC-Ch) (Xin et al., 2007). (a, e, i) Prior to cell seeding, three randomly selected PLGA nanofiber scaffolds showed similar characteristics. On seeding of hMSCs (b–d), various extracellular matrices were apparently synthesized among PLGA nanofibers over time. By 7 days following hMSC seeding, the seeded cells apparently have attached to the nanofiber surface and penetrated into the pores of the PLGA nanofiber scaffolds (d), in comparison with 1 and 3 days after cell seeding (b and c, respectively). The morphology of hMSC-Ob seeded in PLGA nanofibers also varied between 1, 3, and 7 days following cell seeding (f, g, and h, respectively). By 7 days following cell seeding, hMSC-Ob apparently synthesized a substantial amount of extracellular matrices (h), in comparison with 1 and 3 days after cell seeding (f and g, respectively). hMSC-Ob apparently attached to nanofiber substrates. hMSC-Ch revealed characteristic features after seeding in PLGA nanofibers (j–l). Most PLGA nanofibers were still visible at 7 days following the seeding of hMSC-Ch (l), in comparison to the characteristics of hMSC-Ob seeded in PLGA nanofiber scaffolds after 7 days (h). A number of seeded hMSC-Ch apparently were located in lacunae-like structures, see arrow (l). Scale bar 100 μm.

Source: Xin et al. (2007) / with permission from Elsevier.

Growth factors and other proteins have been a primary target for incorporation into tissue engineering scaffolds, given the natural roles they play in the development and maintenance of tissues. For example, growth factors can be chemically tethered to a scaffold surface or they can be incorporated into a scaffold and released in a controlled fashion. However, the biological activity of growth factors generally depends on maintenance of a complex 3D structure, and these structures can rapidly denature on

release from a scaffold. Moreover, proteins can be quickly cleared from the extracellular space following release. In order to overcome challenges associated with the susceptibility of proteins to degradation on release from a scaffold, some tissue engineering approaches take advantage of select peptide sequences derived from or inspired by growth factors and ECM molecules to induce a biological effect. Tissue engineering scaffolds functionalized with specific peptide sequences can direct the attachment, migration, and phenotype of cells. In some cases, scaffolds modified with peptide sequences can induce differentiation of stem and progenitor cells down a desired lineage. The application of peptides in tissue engineering strategies presents numerous advantages relative to proteins with respect to lowering susceptibility to degradation and reducing potential immunogenicity. Nucleic acid delivery presents another alternative to protein delivery to inform tissue formation in tissue engineering applications. Specifically, nucleic acids encoding proteins of interest can be developed and released from tissue engineering scaffolds. Although nucleic acids are susceptible to degradation, they generally present greater stability with respect to the proteins that they encode. A variety of approaches aim to use scaffolds to deliver DNA, for example containing a gene or genes of interest along with appropriate promoters to cells to facilitate expression of the desired factors. In this way, the recipient cells can serve as local sources of sustained production of the desired factor(s) to promote tissue formation and overcome key issues associated with the direct delivery of the factor itself.

While various viral strategies have been explored to deliver genes encoding factors in tissue engineering with high efficiency over the years, considerable ethical and regulatory challenges presently continue to impede translation of the approaches to the clinic. Alternative nonviral gene delivery strategies continue to be a focus of investigation for some tissue engineering approaches (Kasper, 2017).

Impact of regenerative medicine in dentistry and orthodontics

Reconstruction of oral and craniofacial defects frequently involves multiple and complex issues, and is highly demanded for the sake of improving both function and esthetics. Current approaches for facial reconstruction suffer from several intrinsic deficiencies. For example, autologous tissue grafts necessitate donor site morbidity; prostheses may not fully integrate with host tissues; allogeneic and other grafts are associated with immune incompatibility and potential pathogen transmission. Clinicians and scientists have aspired to restore facial defects with the patient's own cells, in approaches that minimize current deficiencies, such as donor site morbidity, immuno-rejection, pathogen transmission, and suboptimal repair. A number of studies have demonstrated the proof of principle of using stem cells in the reconstruction of dental, oral, and craniofacial defects (Mao et al., 2006). Tissue engineering is constituted by multiple disciplines that utilize biomaterials, mechanical stresses, bioactive factors, and/or stem cells for tissue regeneration (Figure 24.2).

Dental pulp-dentin complex

Considerable research in materials science and clinical techniques have advanced the options available to restore the function and morphology of damaged or missing tooth

structures. Major interest is directed toward regeneration of the pulp-dentin complex. A variety of regenerative approaches involving scaffold materials, cells, and biologically active factors have been explored toward pulp regeneration, with many approaches involving the encapsulation of stem cell populations in a hydrogel material to promote tissue regeneration. The biomaterial scaffold for pulp-dentin complex regeneration approaches utilizes naturally derived polymers, such as polysaccharides and proteins, including those from the ECM of natural dentinal tissues, that are obtained from natural sources and form hydrogels and incorporate up to 99% water content. Among polysaccharides, alginate, chitosan, and cellulose are the most commonly used for pulp-dentin complex regeneration. ECM-derived proteins and peptides, which can be easily manipulated for constructing various types of polymeric and composite scaffolds such as hyaluronic acid, collagen, and gelatin, are used for fabrication of scaffolds, which allows the controlled release of the incorporated growth factors. However, scaffolds made of ECM molecules are difficult to process and sterilize and have considerable batch variations. Proteins such as fibrin and silk as well as peptide-based molecules specifically designed to self-assemble in nanofibers are sometimes utilized as scaffolds, as are conventional scaffolds such as ceramics and composites (Moussa and Aparicio, 2019). Although pulp regeneration has been reported in a variety of animal models, an assortment of challenges remains on the pathway to clinical translation, including suitable vascularization and innervation of the pulp tissue and rapid abatement of the inflammatory environment associated with the original pulpal pathology (Hunag, 2009; Colombo et al., 2014).

Cell transplantation, including its role in the regeneration of dental, oral, and craniofacial tissues, is a valid and meritorious scientific concept and approach. However, there are hurdles in the translation of cell delivery–based tooth regeneration into therapeutics. Autologous embryonic tooth germ cells are inaccessible for human applications (Modino and Sharpe, 2005; Nakao et al., 2007; Ikeda et al., 2009). Xenogenic embryonic tooth germ cells (from nonhuman species) may elicit immuno-rejection and tooth dysmorphogenesis. Autologous postnatal tooth germ cells (e.g. third molars) or autologous dental pulp stem cells are of limited availability. Regardless of cell source, cell delivery for tooth regeneration, like cell-based therapies for other tissues, encounters translational barriers (Maeda et al., 2008). Excessive cost of commercialization and difficulties in regulatory approval have precluded, to date, any significant clinical translation of tooth regeneration.

Cell delivery has been the predominant approach in orofacial regeneration. Disassociated cells of porcine or rat tooth buds in biomaterials yielded putative dentin and enamel organ (Young et al., 2002; Duailibi et al., 2004). Tooth bud cells and bone marrow osteoprogenitor cells in collagen, PLGA, or silk-protein scaffolds induced putative tooth-like tissues, alveolar bone, and PDL (Young et al., 2005; Duailibi et al., 2008; Kuo et al., 2008). Embryonic oral epithelium and adult mesenchyme together upregulate odontogenesis genes on mutual induction, and yielded dental structures on transplantation into adult renal capsules or jaw bone (Ohazama et al., 2004). Similarly, implantation of E14.5 rat molar rudiments into adult mouse maxilla has been shown to produce tooth-like structures with surrounding bone (Modino and Sharpe, 2005; Mantesso and Sharpe, 2009). Multipotent cells of the tooth apical papilla in tricalcium phosphate in swine incisor extraction sockets were shown to generate soft and mineralized tissues resembling the PDL (Sonoyama et al., 2006). E14.5 oral epithelium

and dental mesenchyme were reconstituted in collagen gels and cultured *ex vivo* (Nakao et al., 2007), and when implanted into the maxillary molar extraction sockets in 5-week-old mice, tooth morphogenesis took place and was followed by eruption into occlusion (Ikeda et al., 2009). Several studies have begun to tackle the obligatory task of scaling up toward human tooth size (Xu et al., 2008; Abukawa et al., 2009).

Alveolar bone and periodontal ligament

Protein-based therapies are being developed or are now available for the regeneration of multiple dental, oral, and craniofacial tissues, including the periodontal bone. Enamel matrix derivatives (EMDs) are a mix of amelogenins and metallo-endoproteases and serine proteases. EMDs have been shown to improve the healing of human periodontal infrabony defects (Tonetti et al., 2002; Esposito et al., 2009). The first clinical trial on the EMD Emdogain's role in periodontal regeneration was carried out in 1997. Additional studies have further shown the clinical efficacy of Emdogain in the regeneration of periodontium structures. It is primarily used in repairing infrabony defects, frequently with a grafting material (Palmer and Cortellini, 2008; Lyngstadaas et al., 2009). Platelet-derived growth factor (PDGF) promotes alveolar bone repair in periodontal defects as a chemoattractant and proliferative factor for mesenchymal cells (Hollinger et al., 2008). PDGF promotes osteogenesis and angiogenesis at the site of periodontal bone repair (Hollinger et al., 2008). GEM21s is a commercial product that contains PDGF-BB for the treatment of periodontal infrabony and furcation defects (Pellegrini et al., 2009).

Bone morphogenetic proteins (BMPs) induce ectopic bone formation, especially BMP-2 and BMP-7 (Krebsbach et al., 2000; Nakashima and Reddi, 2003). When fibroblasts were transduced to release greater amounts of BMP-2 and BMP-7, a significant increase was noted in the amount of bone in critical-sized calvarial defects (Krebsbach et al., 2000; Shin et al., 2010), and both additionally also promote cementogenesis (Moioli et al., 2007). There is also a commercially available INFUSE bone graft, which consists of BMP-2 and a collagen sponge, for the following conditions: tibial fractures, spinal fusions, sinus augmentation, and alveolar ridge defects due to tooth extractions (Bessa et al., 2008).

Basic fibroblast growth factor (bFGF or FGF-2) promotes the formation of bone, cementum, and the PDL (Nakahara et al., 2003; Sato et al., 2004). FGF-2 delivered topically with gelatinous carriers in furcation defects in dogs induces increase in new bone formation rate, trabecular bone formation, as well as cementum (Murakami et al., 2003). Multiple scaffolds have been exploited to enhance periodontal regeneration, including cell occlusive barrier membranes, collagen membranes, bioglasses, beta-tricalcium phosphates (Figure 24.10), PLGA, and EMDs, with varying success in the results (Moioli et al., 2007).

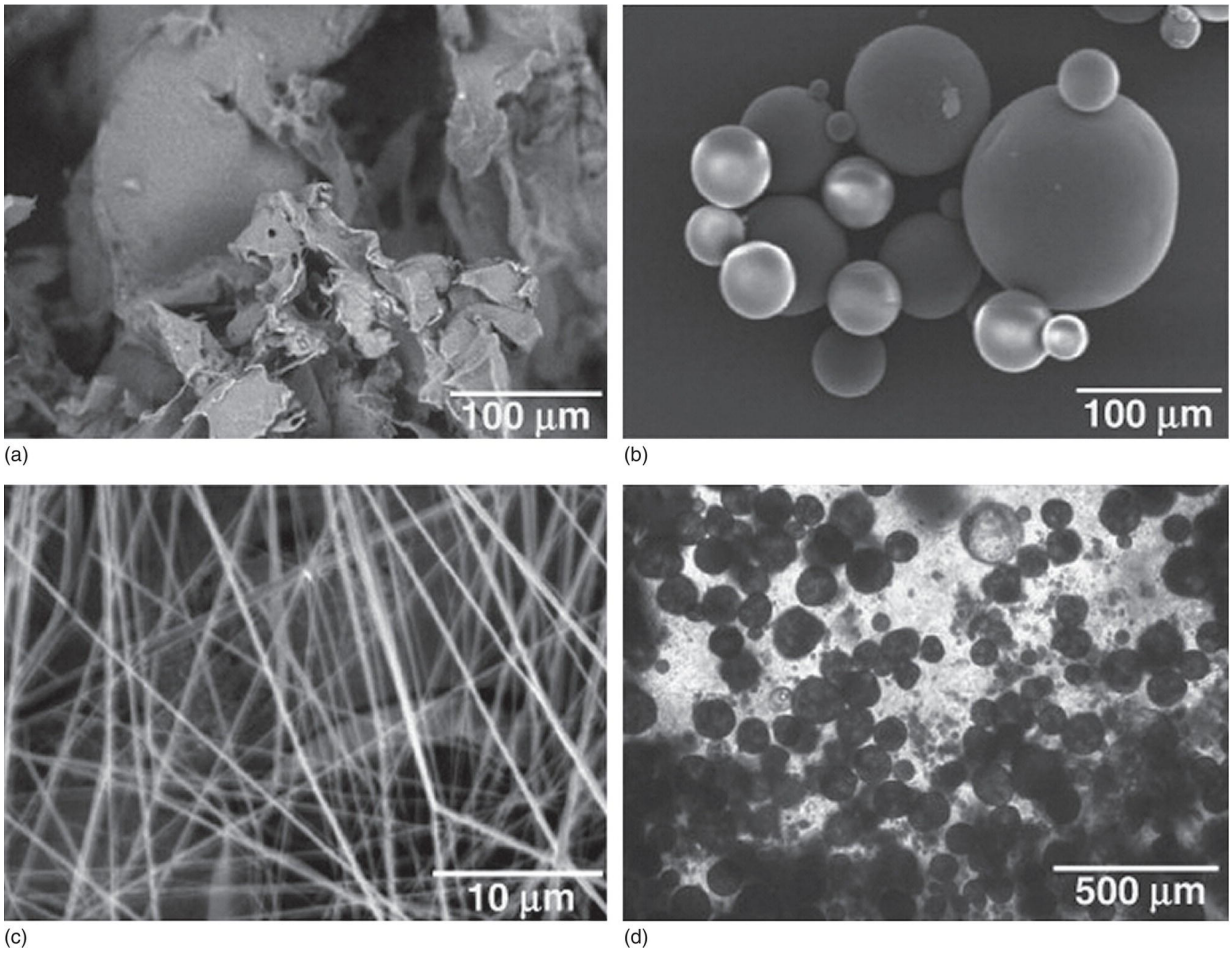

Figure 24.10 Scanning electron micrographs of different scaffolds (magnification ×25). (a) Collagen scaffold surface structure; (b) collagen scaffold cross-section; (c) hydroxyapatite/tricalcium phosphate (HA/TCP) ceramic surface structure; (d) HA/TCP ceramic cross-section.

Source: Zhang et al. (2006) / with permission from Elsevier.

Whole tooth regeneration

While dental implants provide a functional replacement for missing teeth, they lack the vital cementum and PDL structures of natural teeth, which are essential in dampening mechanical forces and facilitating orthodontic tooth movement (Kasper, 2017; Yelick and Sharpe, 2019). An anatomically correct tooth was regenerated with a PDL and integrated into native alveolar bone orthotopically *in vivo* in a rat model (Kim et al., 2010b). As an initial attempt to regenerate teeth, an anatomically shaped and dimensioned scaffold from biomaterials was first fabricated, using a previously reported approach (Figure 24.11; Lee et al., 2009; Stosich et al., 2009). Scaffolds with the shape of the human mandibular first molar (Figure 24.11a) were fabricated. The composite consisted of PCL and hydroxyapatite with interconnecting microchannels (Figure 24.11b; Kim et al., 2010b).

Kim et al. (2010b) infused a blended cocktail of stromal-derived factor-1 (SDF-1) and BMP-7 into the scaffold's microchannels. SDF-1 was selected for its effects on binding to CXCR4 receptors of multiple cell lineages, including mesenchymal stem/progenitor cells (Belema-Bedada et al., 2008; Kitaori et al., 2009). BMP-7 was selected for its effects on dental pulp cells, fibroblasts, and osteoblasts in elaborating mineralization (Rutherford, 2001; Vaccaro et al., 2008). A rat mandibular incisor was regenerated with PDL and newly formed alveolar bone. The rat mandibular central incisor was extracted, followed by implantation of the anatomically shaped mandibular incisor scaffold (data available in Kim et al., 2010b) into the extraction socket. Combined SDF-1 and BMP-7 delivery homed significantly more cells and elaborated more blood vessels into the microchannels of the human molar scaffolds than without growth factor delivery ($p < 0.05$). Scaffolds in the shape of the rat mandibular incisor integrated with surrounding tissue clearly showed multiple tissue phenotypes, including native alveolar bone, newly formed bone, and a fibrous tissue interface reminiscent of the PDL (Figure 24.12) that integrated with the host alveolar bone.

These findings, which are described in detail in Kim et al. (2010b), represent the first report of regeneration of anatomically shaped tooth-like structures *in vivo*, and by cell homing without cell delivery. The potency of cell homing is substantiated not only by cell recruitment into the scaffold's microchannels, but also by regeneration of a putative PDL and newly formed alveolar bone (Kim et al., 2010b). The observed putative PDL and newly formed alveolar bone suggest that SDF-1 and/or BMP-7 have the ability to recruit multiple cell lineages. Here, SDF-1 likely has homed mesenchymal and endothelial stem/progenitor cells in native alveolar bone into porous tooth scaffolds in rat jaw bone, and connective tissue progenitor cells in dorsal subcutaneous tissue into human molar scaffold (Alhadlaq and Mao, 2004; Steinhardt et al., 2008; Crisan et al., 2009). Enamel is not formed due to the fact that ameloblasts, which normally form the enamel matrix or their progenitors, do not exist in the adult tissue. It is the one true challenge left to explore. BMP-7 plays important roles in osteoblast differentiation (Itoh et al., 2001). Here, BMP-7 likely is responsible for newly formed, mineralized alveolar bone in the rat extraction socket, and ectopic mineralization in a human tooth scaffold implanted in the dorsum. Cell homing is an under-recognized approach in tissue regeneration (Mao, 2009) and offers an alternative to cell delivery–based tooth regeneration. Omission of cell isolation and *ex vivo* cell manipulation may accelerate regulatory, commercialization, and clinical processes. The costs related to tooth regeneration by cell homing are not anticipated to be nearly as excessive as for cell delivery. One of the pivotal issues in tooth regeneration is to devise economically viable approaches that are not cost prohibitive, and can translate into therapies for patients who cannot afford expensive treatments or are contraindicated for dental implants. Cell homing–based tooth regeneration may provide a tangible pathway toward clinical translation (Mao, 2009).

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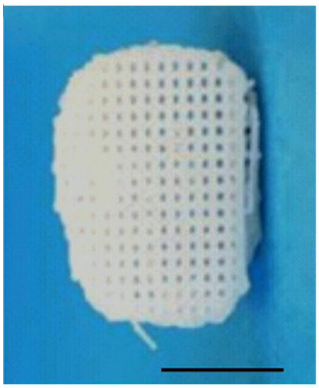
(b)



(c)

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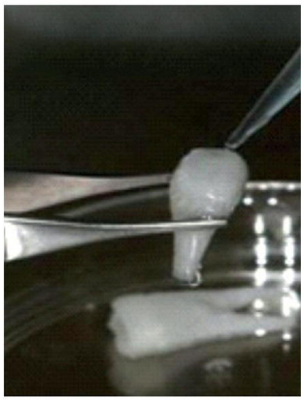

(f)

Figure 24.11 Design and fabrication of anatomically shaped human and rat tooth scaffolds by three-dimensional (3D) bioprinting. Anatomical shapes of the rat mandibular central incisor (a) and human mandibular first molar (b) were used for 3D reconstruction and bioprinting of a hybrid scaffold of poly-ε- caprolactone and hydroxyapatite, with 200 μm microstrands and interconnecting microchannels (diam. 200 μm), which serve as conduits for cell homing and angiogenesis (c, d). A blended cocktail of stromal-derived factor-1 (100 ng/mL) and bone morphogenetic protein-7 (100 ng/mL) was delivered in 2 mg/mL neutralized type I collagen solution and infused in scaffold microchannels for rat incisor scaffold (e) and human molar scaffold (f), followed by gelation.

Source: Kim et al. (2010b) / with permission from Sage Publications.

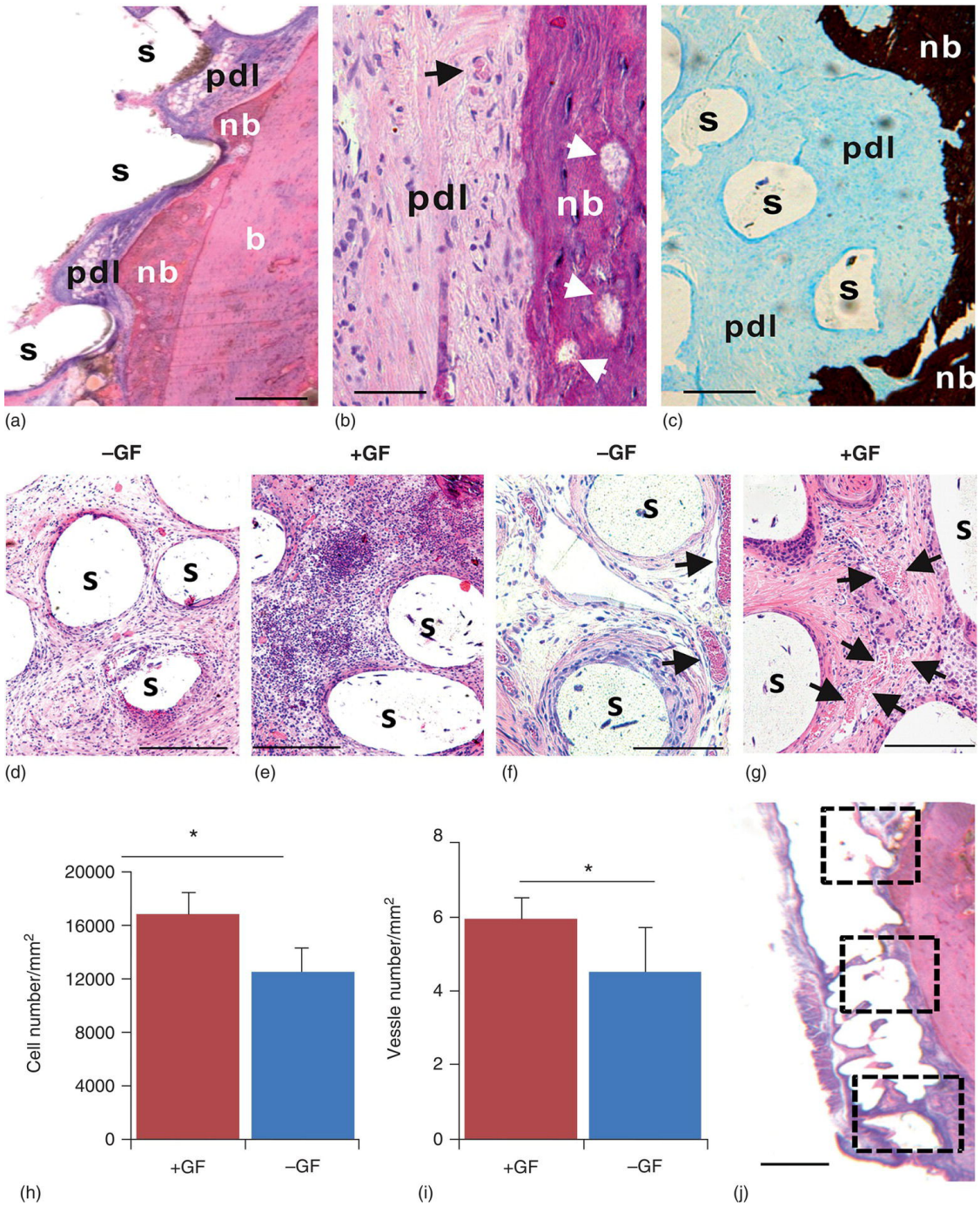
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Figure 24.12 Orthotopic tooth regeneration. (a) The rat mandibular incisor scaffold (s) integrated with surrounding tissue, showing tissue ingrowth into scaffold microchannels and multiple tissue phenotypes, including the native alveolar bone (b), newly formed bone (nb), and a fibrous tissue interface reminiscent of the periodontal ligament (pdl). The newly formed bone showed ingrowth into microchannel openings and inter-staggered with scaffold microstrands (s). (b) Newly formed bone has bone trabeculae-like structures (arrows) and embedded osteocyte-like cells, immediately adjacent to a putative periodontal ligament consisting of fibroblast-like cells and collagen buddle-like structures. (c) Newly formed bone is well mineralized (von Kossa preparation), in contrast to the adjacent unmineralized, putative periodontal ligament. (d) Cells populated the scaffold's microchannels even without growth factor (GF) delivery. (e) Remarkably, stromal-derived factor-1 (SDF-1) and bone morphogenetic protein-7 (BMP-7) delivery yielded substantial cell homing in microchannels. (f) Combined SDF-1 and BMP-7 delivery homed significantly more cells into microchannels than without growth factor delivery ($p < 0.01$; $n = 11$). (g) Angiogenesis took place in scaffolds' microchannels without growth factor delivery, but (h) was more substantial with growth factor delivery. (i) Combined SDF-1 and BMP-7 delivery elaborated significantly more blood vessels than without growth factor delivery ($p < 0.05$; $n = 11$). (j) The numbers of recruited cells and blood vessels were quantified from three different locations along the entire root length of the rat mandibular incisor scaffold: the superior region of the alveolar ridge and the inferior region of the root apex, with a midpoint in between. Scale 100 μm.

Source: Kim et al. (2010b) / with permission from Sage Publications.

While tissue engineering strategies have demonstrated great potential toward regenerating teeth, numerous challenges remain, including control of the size, color, and anatomy of the engineered tooth and integration of the engineered tooth with vasculature and a functional periodontium. Nevertheless, as tissue engineering technologies for generation of viable teeth continue to advance, they present increasing potential to provide not only an alternative to traditional dental implants, but viable teeth that might be moved into the proper position through orthodontic treatment (Monteiro and Yelick, 2017). Clearly, tissue-engineered teeth offer exciting potential to address malformed or missing dentition associated with a variety of conditions, such as ectodermal dysplasia and oligodontia. Indeed, looking forward to clinical translation of the approach, orthodontists should be involved to ensure that proper space is present for implantation or eruption of a tissue-engineered tooth (Kasper, 2017).

Craniofacial bone

Large-scale tissue engineering research in the craniofacial region or elsewhere began to take place in the early 1990s. Thus far, substantial advances have been made in tissue engineering due to advances from several seemingly unrelated disciplines, such as cell and molecular biology, polymer chemistry, molecular genetics, materials science, robotics, and mechanical engineering, converged into the self-assembling field of tissue engineering (Nerem, 1991; Langer and Vacanti, 1993; Mao et al., 2006). While numerous clinical successes have been realized in tissue engineering approaches to address small bony defects, the repair of larger bony defects remains a significant challenge. A primary hurdle in bone regeneration in large defects can be found in

developing sufficient vascularization to support the viability of cells throughout the tissue construct. Some approaches seek to develop vasculature within a tissue engineered construct that may inosculate with host vasculature over the course of days, while other approaches apply 3D printing technologies to create constructs containing microvessel networks that can be directly connected to vasculature at a recipient site (Sooppan et al. 2016). These approaches present the potential to facilitate vascularization of large tissue engineered constructs created outside of the body for bone regeneration (Kasper et al., 2017). Recently, 3D printing has garnered significant attention and presents opportunities to use craniofacial bone tissue engineering as a technology that offers a personalized approach to bony reconstruction (Shen et al., 2020).

Temporomandibular joints, oral mucosa, and salivary glands

Tissue engineering approaches have been proposed for the generation of various anatomical components of the TMJ, which may ultimately facilitate treatment of some disorders and anomalies of the joint in an indication-specific fashion (Salash et al., 2016; Acri et al., 2019). In addition, numerous tissue engineering approaches for the repair or replacement of oral mucosa and gingiva have been explored, which could provide exciting new options for periodontal graft surgeries and the treatment of gingival recession (Iwata et al., 2015). The salivary gland has also been a target for regeneration to overcome challenges associated with loss of function associated with Sjögren syndrome or radiation therapy. Despite the complexity of the salivary gland, emerging approaches demonstrate an ability to replicate key anatomical structures and functions of the glands in preclinical studies. Tissue engineered salivary gland replacements could potentially address conditions such as rampant caries and dysphagia associated with the loss of salivary gland function (Ozdemir et al., 2016).

Orthodontics and dentofacial orthopedics as clinical motivation for tissue engineering

A newly regenerated PDL will surely have an impact on orthodontics. Experimental approaches are also being explored toward the regeneration of cementum, dentin, dental pulp, and even the entire tooth (Mao et al., 2006; Mao, 2008). What would be the impact of these regenerated tooth structures or entire teeth on orthodontic treatment as we know it today? If it takes 1.5–2.5 years for orthodontic treatment, would there be motivation for the placement of dental implants in esthetically pleasing positions, or one day to have whole teeth regenerated in esthetically pleasing positions? Would bioengineered cementum and/or dentin be a solution for root resorption? Even the decision of tooth extraction versus nonextraction may be influenced by recent interest from the general public to have dental stem cells from their extracted teeth “banked” or cryopreserved (Mao, 2008). Would a patient be more likely be receptive to tooth extraction, since extracted teeth are sources of their stem cells? For cleft lip or cleft palate and craniofacial or temporomandibular anomalies, what is the impact of bioengineered bone and soft tissue grafting, which shows promise for becoming standard practice in surgical approaches related to orthodontics (Alhadlaq and Mao, 2003; Moioli et al., 2008; Stosich et al., 2009)? Separate approaches are being

explored for tissue engineering of skin and soft tissues such as adipose and muscle fibers (Egles et al., 2010; Mao et al., 2010; Stosich et al., 2007).

Bone grafts are typically autografts, allografts, xenografts, and alloplastics. Autografts are bone grafting materials taken from the same individual, whereas allografts are taken from a different individual of the same species. Xenografts are taken from a different species, whereas alloplastics are synthetically made bone grafting materials. Osteo-conductive grafts indicate that they only have the capacity to guide new bone growth. Osteo-inductive grafts, on the other hand, promote differentiation of progenitor cells to form bone. Teeth have been shown to move into areas where bone has been augmented with beta-tricalcium-phosphate, hydroxyapatite, bovine bone graft material, PGLA/gelatin sponges with BMP-2, and bioglass (Eichhorn et al., 2009; Reichert et al., 2009). These regenerative graft materials look promising, but high-quality clinical trials are still lacking (Alkaabi et al, 2022). Allografts in combination with different materials, such as bioglass or EMDs, have also been shown to be successful in augmenting alveolar defects before moving teeth into that area. Hydroxyapatite alone as a filling material is another successful approach. Furthermore, in one case report, teeth were moved into bone grafts formed from a synthetic alloplast with a bioglass (Yilmaz et al., 2000), as well as into bovine bone grafts (Reichert et al., 2009). A collagen bovine bone mineral (bio-Oss) has also been used for augmenting periodontal defects, with subsequent successful orthodontic tooth movement (Cardaropoli et al., 2006).

Barrier membranes have been used to block ingrowth of gingival epithelium into the PDL. After control of periodontitis, the area around the cemento-enamel junction is treated with expanded polytetrafluoroethylene (e-PTFE) membrane, a synthetic polymer better known by its brand name Gore-Tex® (W.L. Gore & Associates, Newark, DE, USA), followed by orthodontic tooth movement (Reichert et al., 2009). There are at least two case reports of successful orthodontic tooth movement into tissue-engineered bone in alveolar cleft defects, treated with a synthetic alloplast or hydroxyapatite. Here, tissue engineering principles have successfully shown that they are applicable in the craniofacial area with the potential for normal function, and have the capability to work synergistically in conjunction with orthodontic treatment.

Conclusion

Orthodontics and regenerative medicine are two separate disciplines of learning, but nonetheless have a great deal in common. Tissue engineering as part of the regenerative medicine discipline represents an opportunity that orthodontics should capture, incorporate, and individualize. Tissues of interest to orthodontics are those that are being regenerated by stem cells, scaffolds, and bioactive cues in experimental studies. Currently, several bioactive cues have been developed into products for periodontal regeneration, and novel technologies that regenerate bone modules, PDL, cementum, cartilage, and soft tissue will inevitably have an impact on orthodontics in the near future.

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References

Abukawa, H., Zhang, W., Young, C.S. et al. (2009). Reconstructing mandibular defects using autologous tissue engineered tooth and bone constructs. *Journal of Oral and Maxillofacial Surgery* 67: 335–347.

Acri, T.M., Shin, K., Seol, D. et al. (2019). Tissue engineering for the temporomandibular joint. *Advanced Healthcare Materials* 8(2): e1801236. doi: 10.1002/adhm.201801236.

Agrawal, C.M., and Ray, R.B. (2001). Biodegradable polymeric scaffolds for musculoskeletal tissue engineering. *Journal of Biomedical Materials Research* 55: 141–150.

Alhadlaq, A., and Mao, J.J. (2003). Tissue-engineered neogenesis of human-shaped mandibular condyle from rat mesenchymal stem cells. *Journal of Dental Research* 82: 951–956.

Alhadlaq, A., and Mao, J.J. (2004). Mesenchymal stem cells: Isolation and therapeutics. *Stem Cells and Development* 13: 436–448.

Alhadlaq, A., Tang, M., and Mao, J.J. (2005). Engineered adipose tissue from human mesenchymal stem cells maintains predefined shape and dimension: Implications in soft tissue augmentation and reconstruction. *Tissue Engineering* 11: 556–566.

Alkaabi, S.A., Alsabri, G.A., NatsirKalla, D.S. et al. (2022). A systematic review on regenerative alveolar graft materials in clinical trials: Risk of bias and meta-analysis. *Journal of Plastic, Reconstructive & Aesthetic Surgery* 75(1): 356–365. doi: 10.1016/j.bjps.2021.08.026.

Al Madhoun, A., Sindhu, S., Haddad, D. et al. (2021). Dental pulp stem cells derived from adult human third molar tooth: A brief review. *Frontiers in Cell and Developmental Biology* 9: 717624. doi: 10.3389/fcell.2021.717624.

Anitua, E., Troya, M., and Zalduendo, M. (2018). Progress in the use of dental pulp stem cells in regenerative medicine. *Cytotherapy* 20(4): 479–498. doi: 10.1016/j.jcyt.2017.12.011.

Athanasiou, K.A., Niederauer, G.G., and Agrawal, C.M. (1996). Sterilization, toxicity, biocompatibility and clinical applications of polylactic acid/polyglycolic acid copolymers. *Biomaterials* 17: 93–102.

Belema-Bedada, F., Uchida, S., Martire, A. et al. (2008). Efficient homing of multipotent adult mesenchymal stem cells depends on FROUNT-mediated clustering of CCR2. *Cell Stem Cell* 2: 566–575.

Bessa, P.C., Casal, M., and Reis, R.L. (2008). Bone morphogenetic proteins in tissue engineering: The road from laboratory to clinic, part II (BMP delivery). *Journal of Tissue Engineering and Regenerative Medicine* 2: 81–96.

Bhattacherjee, V., Mukhopadhyay, P., Singh, S. et al. (2007). Neural crest and mesoderm lineage-dependent gene expression in orofacial development. *Differentiation* 75: 463–477.

Caddeo, S., Boffito, M., and Sartori, S. (2017). Tissue engineering approaches in the design of healthy and pathological *in vitro* tissue models. *Frontiers in Bioengineering and Biotechnology* 5: 40. doi: 10.3389/fbioe.2017.00040.

Cardaropoli, D., Re, S., Manuzzi, W. et al. (2006). Bio-Oss collagen and orthodontic movement for the treatment of infrabony defects in the esthetic zone. *International Journal of Periodontics and Restorative Dentistry* 26: 553–559.

Chai, Y., Jiang, X., Ito, Y. et al. (2000). Fate of the mammalian cranial neural crest during tooth and mandibular morphogenesis. *Development* 127: 1671–1679.

Colombo, J.S., Moore, A.N., Hartgerink, J.D. et al. (2014). Scaffolds to control inflammation and facilitate dental pulp regeneration. *Journal of Endodontics* 40(4 Suppl):S6–S12. doi: 10.1016/j.joen.2014.01.019.

Coura, G.S., Garcez, R.C., de Aguiar, C.B. et al. (2008). Human periodontal ligament: A niche of neural crest stem cells. *Journal of Periodontal Research* 43(5): 531–536. doi: 10.1111/j.1600-0765.2007.01065.x.

Crisan, M., Chen, C.W., Corselli, M. et al. (2009). Perivascular multipotent progenitor cells in human organs. *Annals of the New York Academy of Sciences* 1176: 118–123.

Duailibi, M.T., Duailibi, S.E., Young, C.S. et al. (2004). Bioengineered teeth from cultured rat tooth bud cells. *Journal of Dental Research* 83: 523–528.

Duailibi, S.E., Duailibi, M.T., Zhang, W. et al. (2008). Bioengineered dental tissues grown in the rat jaw. *Journal of Dental Research* 87: 745–750.

Egles, C., Garlick, J.A., and Shamis, Y. (2010). Three-dimensional human tissue models of wounded skin. *Methods in Molecular Biology* 585: 345–359.

Eichhorn, W., Blessmann, M., Pohlenz, P. et al. (2009). Primary osteoplasty using calvarian bone in patients with cleft lip, alveolus and palate. *Journal of Cranio-Maxillofacial Surgery* 37: 429–433.

Esposito, M., Grusovin, M.G., Papanikolaou, N. et al. (2009). Enamel matrix derivative (Emdogain(R)) for periodontal tissue regeneration in intrabony defects. *Cochrane Database of Systematic Reviews* 4: CD003875. doi: 10.1002/14651858.CD003875.pub3.

Faruqu, F.N., Zhou, S., Sami, N. et al. (2020). Three-dimensional culture of dental pulp pluripotent-like stem cells (DPPSCs) enhances *Nanog* expression and provides a serum-free condition for exosome isolation. *FASEB BioAdvances 2*(7): 419–433. doi: 10.1096/fba.2020-00025.

Fawzy El-Sayed, K.M., and Dörfer, C.E. (2016). Gingival mesenchymal stem/progenitor cells: A unique tissue engineering gem. *Stem Cells International* 2016: 7154327. doi: 10.1155/2016/7154327.

Ferro, F., Spelat, R., and Baheney, C.S. (2014). Dental pulp stem cell (DPSC) isolation, characterization, and differentiation. *Methods in Molecular Biology* 1210: 91–115. doi: 10.1007/978-1-4939-1435-7_8.

Fleischmannova, J., Matalova, E., Sharpe, P.T. et al. (2010). Formation of the tooth-bone interface. *Journal of Dental Research* 89: 108–115.

Friedenstein, A.J., Deriglasova, U.F., Kulagina, N.N. et al. (1974). Precursors for fibroblasts in different populations of hematopoietic cells as detected by the in vitro colony assay method. *Experimental Hematology* 2: 83–92.

Fu, Y.C., Nie, H., Ho, M. et al. (2008). Optimized bone regeneration based on sustained release from three-dimensional fibrous PLGA/HAp composite scaffolds loaded with BMP-2. *Biotechnology and Bioengineering* 99: 996–1006.

Górski, B. (2016). Gingiva as a new and the most accessible source of mesenchymal stem cells from the oral cavity to be used in regenerative therapies. *Postepy Higieny i Medycyny Doswiadczalnej* 70: 858–871. doi: 10.5604/17322693.1214383.

Graham, A., and Smith, A. (2001). Patterning the pharyngeal arches. *Bioessays* 23: 54–61.

Gronthos, S., Mankani, M., Brahim, J. et al. (2000). Postnatal human dental pulp stem cells (DPSCs) in vitro and in vivo. *Proceedings of the National Academy of Sciences of the United States of America* 97(25): 13625–13630. doi: 10.1073/pnas.240309797.

Hollinger, J.O., Hart, C.E., Hirsch, S.N. et al. (2008). Recombinant human platelet-derived growth factor: Biology and clinical applications. *Journal of Bone and Joint Surgery American* 90: 48–54.

Honda, M.J., Shinohara, Y., Hata, K.I. et al. (2007). Subcultured odontogenic epithelial cells in combination with dental mesenchymal cells produce enamel-dentin-like complex structures. *Cell Transplantation* 16: 833–847.

Hosmani, J., Assiri, K., Almubarak, H.M. et al. (2020). Proteomic profiling of various human dental stem cells – a systematic review. *World Journal of Stem Cells* 12(10): 1214–1236. doi: 10.4252/wjsc.v12.i10.1214.

Huang, G.T. (2009). Pulp and dentin tissue engineering and regeneration: Current progress. *Regenerative Medicine* 4(5): 697–707. doi: 10.2217/rme.09.45.

Ikeda, E., Morita, R., Nakao, K. et al. (2009). Fully functional bioengineered tooth replacement as an organ replacement therapy. *Proceedings of the National Academy of Sciences of the United States of America* 106: 13475–13480.

Itoh, F., Asao, H., Sugamura, K. et al. (2001). Promoting bone morphogenetic protein signaling through negative regulation of inhibitory Smads. *EMBO Journal* 20: 4132–4142.

Iwata, T., Washio, K., Yoshida, T. et al. (2015). Cell sheet engineering and its application for periodontal regeneration. *Journal of Tissue Engineering and Regenerative Medicine* 9(4): 343–356. doi: 10.1002/term.1785.

Jiang, Y., Jahagirdar, B.N., Reinhardt, R.L. et al. (2002). Pluripotency of mesenchymal stem cells derived from adult marrow. *Nature* 418: 41–49.

Kasper, F.K. (2017). Tissue engineering for orthodontists: The transforming science simplified. *Seminars in Orthodontics* 23(4): 355–365.

Kasper, F.K., Melville, J., Shum, J. et al. (2017). Tissue engineered prevascularized bone and soft tissue flaps. *Oral and Maxillofacial Surgery Clinics of North America* 29(1): 63–73. doi: 10.1016/j.coms.2016.08.005.

Kawaguchi, H., Hirachi, A., Hasegawa, N. et al. (2004). Enhancement of periodontal tissue regeneration by transplantation of bone marrow mesenchymal stem cells. *Journal of Periodontology* 75: 1281–1287.

Khalil, H., Jummaat, F., Yahya, E.B. et al. (2020). A review on micro- to nanocellulose biopolymer scaffold forming for tissue engineering applications. *Polymers* 12(9): 2043. doi: 10.3390/polym12092043.

Kim, D., Lee, A.E., Xu, Q. et al. (2021). Gingiva-derived mesenchymal stem cells: potential application in tissue engineering and regenerative medicine – a comprehensive review. *Frontiers in Immunology* 12: 667221. doi: 10.3389/fimmu.2021.667221.

Kim, J.Y., Xin, X., Moioli, E.K. et al. (2010a). Regeneration of dental-pulp-like tissue by chemotaxis-induced cell homing. *Tissue Engineering Part A* 16: 3023–3031.

Kim, K., Lee, C.H., Kim, B.K. et al. (2010b). Anatomically shaped tooth and periodontal regeneration by cell homing. *Journal of Dental Research* 89: 842–847.

Kitaori, T., Ito, H., Schwarz, E.M. et al. (2009). Stromal cell-derived factor 1/CXCR4 signaling is critical for the recruitment of mesenchymal stem cells to the fracture site during skeletal repair in a mouse model. *Arthritis and Rheumatism* 60: 813–823.

Krebsbach, P.H., Gu, K., Franceschi, R.T. et al. (2000). Gene therapy-directed osteogenesis: BMP-7-transduced human fibroblasts form bone in vivo. *Human Gene Therapy* 11: 1201–1210.

Krivanek, J., Soldatov, R.A., Kastriti, M.E. et al. (2020). Dental cell type atlas reveals stem and differentiated cell types in mouse and human teeth. *Nature Communications* 11(1): 4816. doi: 10.1038/s41467-020-18512-7.

Kuo, T.F., Huang, A.T., Chang, H.H. et al. (2008). Regeneration of dentin-pulp complex with cementum and periodontal ligament formation using dental bud cells in gelatin-chondroitin-hyaluronan tri-copolymer scaffold in swine. *Journal of Biomedical Materials Research Part A* 86: 1062–1068.

Kyba, M. (2005). Genesis of hematopoietic stem cells in vitro and in vivo: New insights into developmental maturation. *International Journal of Hematology* 81: 275–280.

Langer, R., and Vacanti, J.P. (1993). Tissue engineering. *Science* 260: 920–926. doi: 10.1126/science.8493529.

Le Douarin, N.M., Calloni, G.W., and Dupin, E. (2008). The stem cells of the neural crest. *Cell Cycle* 7: 1013–1019.

Lee, C.H., Cook, J.L., Mendelson, A. et al. (2010a). Regeneration of the articular surface of the rabbit synovial joint by cell homing: A proof of concept study. *Lancet* 376: 440–448.

Lee, C.H., Marion, N.W., Hollister, S. et al. (2009). Tissue formation and vascularization of anatomically shaped human tibial condyle in vivo. *Tissue Engineering Part A* 15: 3923–3930.

Lee, C.H., Shah, B., Moioli, K. et al. (2010b). CTGF directs fibroblast differentiation from human mesenchymal stem/stromal cells and defines connective tissue healing in a rodent injury model. *Journal of Clinical Investigation* 120: 3340–3349.

Li, W.J., Tuli, R., Huang, X. et al. (2005). Multilineage differentiation of human mesenchymal stem cells in a three-dimensional nanofibrous scaffold. *Biomaterials* 26: 5158–5166.

Loh, Q.L., and Choong, C. (2013). Three-dimensional scaffolds for tissue engineering applications: Role of porosity and pore size. *Tissue Engineering. Part B Reviews* 19(6): 485–502. doi: 10.1089/ten.TEB.2012.0437.

Lyngstadaas, S.P., Wohlfahrt, J.C., Brookes, S.J. et al. (2009). Enamel matrix proteins; old molecules for new applications. *Orthodontics and Craniofacial Research* 12: 243–253.

Maeda, S., Ono, Y., Nakamura, K. et al. (2008). Molar uprighting with extrusion for implant site bone regeneration and improvement of the periodontal environment. *International Journal of Periodontics and Restorative Dentistry* 28: 375–381.

Mallick, K.K., and Cox, S.C. (2013). Biomaterial scaffolds for tissue engineering. *Frontiers in Bioscience* 5(1): 341–360. doi: 10.2741/e620.

Mantesso, A., and Sharpe, P. (2009). Dental stem cells for tooth regeneration and repair. *Expert Opinion on Biological Therapy* 9: 1143–1154.

Mao, J.J. (2008). Stem cells and the future of dental care. *New York State Dental Journal* 74: 20–24.

Mao, J.J. (2009). Stem cells and dentistry. *Journal of Dental Hygiene* 83: 173–174.

Mao, J.J., Giannobile, W.V., Helms, J.A. et al. (2006). Craniofacial tissue engineering by stem cells. *Journal of Dental Research* 85: 966–979.

Mao, J.J., Stosich, M.S., Moioli, E.K. et al. (2010). Facial reconstruction by biosurgery: Cell transplantation versus cell homing. *Tissue Engineering*. *Part B Reviews* 16: 257–262.

Maria, O.M., Khosravi, R., Mezey, E. et al. (2007). Cells from bone marrow that evolve into oral tissues and their clinical applications. *Oral Diseases* 13: 11–16.

Marion, N.W., and Mao, J.J. (2006). Mesenchymal stem cells and tissue engineering. *Methods in Enzymology* 420: 339–361.

Mezey, E., Key, S., Vogelsang, G. et al. (2003). Transplanted bone marrow generates new neurons in human brains. *Proceedings of the National Academy of Sciences of the United States of America* 100: 1364–1369.

Mitrano, T.I., Grob, M.S., Carrión, F. et al. (2010). Culture and characterization of mesenchymal stem cells from human gingival tissue. *Journal of Periodontology* 81(6): 917–925. doi: 10.1902/jop.2010.090566.

Miura, M., Gronthos, S., Zhao, M. et al. (2003). SHED: Stem cells from human exfoliated deciduous teeth. *Proceedings of the National Academy of Sciences of the United States of America* 100: 5807–5812. doi: 10.1073/pnas.0937635100.

Modino, S.A., and Sharpe, P.T. (2005). Tissue engineering of teeth using adult stem cells. *Archives of Oral Biology* 50: 255–258.

Moioli, E.K., Clark, P.A., Sumner, D.R. et al. (2008). Autologous stem cell regeneration in craniosynostosis. *Bone* 42: 332–340.

Moioli, E.K., Clark, P.A., Xin, X. et al. (2007). Matrices and scaffolds for drug delivery in dental, oral and craniofacial tissue engineering. *Advanced Drug Delivery Reviews* 59: 308–324.

Monteiro, N., and Yelick, P.C. (2017). Advances and perspectives in tooth tissue engineering. *Journal of Tissue Engineering and Regenerative Medicine* 11(9): 2443–2461. doi: 10.1002/term.2134.

Morsczeck, C., Götz, W., Schierholz, J. et al. (2005). Isolation of precursor cells (PCs) from human dental follicle of wisdom teeth. *Matrix Biology* 24(2): 155–165. doi: 10.1016/j.matbio.2004.12.004.

Moussa, D.G., and Aparicio, C. (2019). Present and future of tissue engineering scaffolds for dentin-pulp complex regeneration. *Journal of Tissue Engineering and Regenerative Medicine* 13(1): 58–75. doi: 10.1002/term.2769.

Murakami, S., Takayama, S., Kitamura, M. et al. (2003). Recombinant human basic fibroblast growth factor (bFGF) stimulates periodontal regeneration in class II furcation defects created in beagle dogs. *Journal of Periodontal Research* 38: 97–103.

Nakagawa, M., Koyanagi, M., Tanabe, K. et al. (2008). Generation of induced pluripotent stem cells without Myc from mouse and human fibroblasts. *Nature Biotechnology* 26(1): 101–106. doi: 10.1038/nbt1374.

Nakahara, T., Nakamura, T., Kobayashi, E. et al. (2003). Novel approach to regeneration of periodontal tissues based on in situ tissue engineering: Effects of controlled release of basic fibroblast growth factor from a sandwich membrane. *Tissue Engineering* 9: 153–162.

Nakao, K., Morita, R., Saji, Y. et al. (2007). The development of a bioengineered organ germ method. *Nature Methods* 4: 227–230.

Nakashima, M., and Reddi, A.H. (2003). The application of bone morphogenetic proteins to dental tissue engineering. *Nature Biotechnology* 21: 1025–1032.

National Institutes of Health (2009). Stem cell basics. https://stemcells.nih.gov/info/basics/stc-basics.

National Research Council (US) and Institute of Medicine (US) Committee on the Biological and Biomedical Applications of Stem Cell Research (2002). Embryonic stem cells. In: *Stem Cells and the Future of Regenerative Medicine*. Washington, DC: National Academies Press, ch. 3. https://www.ncbi.nlm.nih.gov/books/NBK223690.

Nerem, R.M. (1991). Cellular engineering. *Annals of Biomedical Engineering* 19: 529–545.

Ng, T.K., Huang, L., Cao, D. et al. (2015). Cigarette smoking hinders human periodontal ligament-derived stem cell proliferation, migration and differentiation potentials. *Scientific Reports* 5: 7828. doi: 10.1038/srep07828.

Noden, D.M., and Trainor, P.A. (2005). Relations and interactions between cranial mesoderm and neural crest populations. *Journal of Anatomy* 207: 575–601.

Ohazama, A., Modino, S.A., Miletich, I. et al. (2004). Stem-cell-based tissue engineering of murine teeth. *Journal of Dental Research* 83: 518–522.

Olsen, B.R., Reginato, A.M., and Wang, W. (2000). Bone development. *Annual Review of Cell and Developmental Biology* 16: 191–220.

Ozdemir, T., Fowler, E.W., Hao, Y. et al. (2016). Biomaterials-based strategies for salivary gland tissue regeneration. *Biomaterials Science* 4(4): 592–604. doi: 10.1039/c5bm00358j.

Palmer, R.M., and Cortellini, P. (2008). Periodontal tissue engineering and regeneration: Consensus Report of the Sixth European Workshop on Periodontology. *Journal of Clinical Periodontology* 35: 83–86.

Patil, R., Kumar, B.M., Lee, W.J. et al. (2014). Multilineage potential and proteomic profiling of human dental stem cells derived from a single donor. *Experimental Cell Research* 320(1): 92–107. doi: 10.1016/j.yexcr.2013.10.005.

Pellegrini, G., Seol, Y.J., Gruber, R. et al. (2009). Pre-clinical models for oral and periodontal reconstructive therapies. *Journal of Dental Research* 88: 1065–1076.

Perry, B.C., Zhou, D., Wu, X. et al. (2008). Collection, cryopreservation, and characterization of human dental pulp-derived mesenchymal stem cells for banking and clinical use. *Tissue Engineering. Part C Methods* 14(2): 149–156. doi: 10.1089/ten.tec.2008.0031.

Queiroz, A., Albuquerque-Souza, E., Gasparoni, L.M. et al. (2021). Therapeutic potential of periodontal ligament stem cells. *World Journal of Stem Cells* 13(6): 605–618. doi: 10.4252/wjsc.v13.i6.605.

Rahaman, M.N., and Mao, J.J. (2005). Stem cell-based composite tissue constructs for regenerative medicine. *Biotechnology and Bioengineering* 91: 261–284.

Reichert, C., Deschner, J., Kasaj, A. et al. (2009). Guided tissue regeneration and orthodontics. A review of the literature. *Journal of Orofacial Orthopedics* 70: 6–19.

Rodas-Junco, B.A., and Villicaña, C. (2017). Dental pulp stem cells: Current advances in isolation, expansion and preservation. *Tissue Engineering and Regenerative Medicine* 14(4): 333–347. doi: 10.1007/s13770-017-0036-3.

Rutherford, B. (2001). BMP-7 gene transfer to inflamed feret dental pulps. *European Journal of Oral Sciences* 109: 422–424.

Saito, M., Nishida, E., Sasaki, T. et al. (2009). The KK-Periome database for transcripts of periodontal ligament development. *Journal of Experimental Zoology Part B, Molecular and Developmental Evolution* 31: 495–502.

Salash, J.R., Hossameldin, R.H., Almarza, A.J. et al. (2016). Potential indications for tissue engineering in temporomandibular joint surgery. *Journal of Oral and Maxillofacial Surgery* 74(4): 705–711. doi: 10.1016/j.joms.2015.11.008.

Sato, Y., Kikuchi, M., Ohata, N. et al. (2004). Enhanced cementum formation in experimentally induced cementum defects of the root surface with the application of recombinant basic fibroblast growth factor in collagen gel in vivo. *Journal of Clinical Periodontology* 75: 243–248.

Scheller, E.L., Krebsbach, P.H., and Kohn, D.H. (2009). Tissue engineering: State of the art in oral rehabilitation. *Journal of Oral Rehabilitation* 36: 368–389.

Seo, B.M., Miura, M., Gronthos, S. et al. (2004). Investigation of multipotent postnatal stem cells from human periodontal ligament. *Lancet* 364: 149–155.

Seo, B.M., Miura, M., Gronthos, S. et al. (2004). Investigation of multipotent postnatal stem cells from human periodontal ligament. *Lancet* 364(9429): 149–155. doi: 10.1016/S0140-6736(04)16627-0.

Sharma, B., and Elisseeff, J.H. (2004). Engineering structurally organized cartilage and bone tissues. *Annals of Biomedical Engineering* 32: 148–159.

Shen, C., Witek, L., Flores, R.L. et al. (2020). Three-dimensional printing for craniofacial bone tissue engineering. *Tissue Engineering. Part A* 26(23–24): 1303–

1311. doi: 10.1089/ten.TEA.2020.0186.

Shin, J.H., Kim, K.H., Kim, S.H. et al. (2010). Ex vivo bone morphogenetic protein-2 gene delivery using gingival fibroblasts promotes bone regeneration in rats. *Journal of Clinical Periodontology* 37: 305–311.

Song, J.S., Kim, S.O., Kim, S.H. et al. (2012). In vitro and in vivo characteristics of stem cells derived from the periodontal ligament of human deciduous and permanent teeth. *Tissue Engineering. Part A* 18(19–20): 2040–2051. doi: 10.1089/ten.TEA.2011.0318.

Sonoyama, W., Coppe, C., Gronthos, S. et al. (2005). Skeletal stem cells in regenerative medicine. *Current Topics in Developmental Biology* 67: 305–323.

Sonoyama, W., Liu, Y., Fang, D. et al. (2006). Mesenchymal stem cell-mediated functional tooth regeneration in swine. *PLoS One* 1: e79.

Sonoyama, W., Liu, Y., Yamaza, T. et al. (2008). Characterization of the apical papilla and its residing stem cells from human immature permanent teeth: A pilot study. *Journal of Endodontics* 34: 166–171. doi: 10.1016/j.joen.2007.11.02.

Sooppan, R., Paulsen, S.J., Han, J. et al. (2016). In vivo anastomosis and perfusion of a three-dimensionally-printed construct containing microchannel networks. *Tissue Engineering. Part C Methods 22*(1): 1–7. doi: 10.1089/ten.TEC.2015.0239.

Steinhardt, Y., Aslan, H., Regev, E. et al. (2008). Maxillofacial-derived stem cells regenerate critical mandibular bone defect. *Tissue Engineering Part A* 14: 1763–1773.

Stosich, M.S., and Mao, J.J. (2007). Adipose tissue engineering from human adult stem cells: Clinical implications in plastic and reconstructive surgery. *Plastic and Reconstructive Surgery* 119: 71–83.

Stosich, M.S., Moioli, E.K., Wu, J.K. et al. (2009). Bioengineering strategies to generate vascularized soft tissue grafts with sustained shape. *Methods* 47: 116–121.

Thomson, J.A., Itskovitz-Eldor, J., Shapiro, S.S. et al. (1998). Embryonic stem cell lines derived from human blastocysts. *Science* 282(5391): 1145–1147. doi: 10.1126/science.282.5391.1145.

Tonelli, F.M.P., Oliveira Paiva, N. de C., de Medeiros, R.V.B. et al. (2017) Tissue engineering: The use of stem cells in regenerative medicine. In: V. Thomaz-Soccol, A. Pandey, and R.R. Resende (eds.), *Current Developments in Biotechnology and Bioengineering*. St. Louis, MO: Elsevier, pp. 315–324.

Tonetti, M.S., Lang, N.P., Cortellini, P. et al. (2002). Enamel matrix proteins in the regenerative therapy of deep intrabony defects. *Journal of Clinical Periodontology* 29: 317–325.

Trubiani, O., Pizzicannella, J., Caputi, S. et al. (2019). Periodontal ligament stem cells: Current knowledge and future perspectives. *Stem Cells and Development* 28(15): 995–1003. doi: 10.1089/scd.2019.0025.

Tucker, A., and Sharpe, P. (2004). The cutting-edge of mammalian development; how the embryo makes teeth. *Nature Reviews Genetics* 5: 499–508.

Vaccaro, A.R., Lawrence, J.P., Patel, T. et al. (2008). The safety and efficacy of OP-1 (rhBMP-7) as a replacement for iliac crest autograft in posterolateral lumbar arthrodesis: A long-term (>4 years) pivotal study. *Spine* 33: 2850–2862.

Vaglia, J.L., and Hall, B.K. (1999). Regulation of neural crest cell populations: Occurrence, distribution and underlying mechanisms. *International Journal of Developmental Biology* 43: 95–110.

Verfaillie, C.M. (2002). Adult stem cells: Assessing the case for pluripotency. *Trends in Cell Biology* 12: 502–508.

Watt, F.M., and Hogan, B.L. (2000). Out of Eden: Stem cells and their niches. *Science* 287: 1427–1430.

Xin, X., Hussain, M., and Mao, J.J. (2007). Continuing differentiation of human mesenchymal stem cells and induced chondrogenic and osteogenic lineages in electrospun PLGA nanofiber scaffold. *Biomaterials* 28: 316–325.

Xu, W.P., Zhang, W., Asrican, R. et al. (2008). Accurately shaped tooth bud cell-derived mineralized tissue formation on silk scaffolds. *Tissue Engineering Part A* 14: 549–557.

Yamada, Y., Nakamura-Yamada, S., Kusano, K. et al. (2019). Clinical potential and current progress of dental pulp stem cells for various systemic diseases in regenerative medicine: A concise review. *International Journal of Molecular Sciences* 20(5): 1132. doi: 10.3390/ijms20051132.

Yao, S., Pan, F., Prpic, V. et al. (2008). Differentiation of stem cells in the dental follicle. *Journal of Dental Research* 87: 767–771.

Ye, L., Swingen, C., and Zhang, J. (2013). Induced pluripotent stem cells and their potential for basic and clinical sciences. *Current Cardiology Reviews* 9(1): 63–72. doi: 10.2174/157340313805076278.

Yelick, P.C., and Sharpe, P.T. (2019). Tooth bioengineering and regenerative dentistry. *Journal of Dental Research* 98(11): 1173–1182. doi: 10.1177/0022034519861903.

Yilmaz, S., Kiliç, A.R., Keles, A. et al. (2000). Reconstruction of an alveolar cleft for orthodontic tooth movement. *American Journal of Orthodontics and Dentofacial Orthopedics* 117: 156–163.

Young, C.S., Abukawa, H., Asrican, R. et al. (2005). Tissue-engineered hybrid tooth and bone. *Tissue Engineering* 11: 1599–1610.

Young, C.S., Terada, S., Vacanti, J.P. et al. (2002). Tissue engineering of complex tooth structures on biodegradable polymer scaffolds. *Journal of Dental Research* 81: 695–700.

Zakrzewski, W., Dobrzyński, M., Szymonowicz, M. et al. (2019). Stem cells: Past, present, and future. *Stem Cell Research & Therapy* 10(1): 68. doi: 10.1186/s13287-

019-1165-5.

Zhang, Q., Shi, S., Liu, Y. et al. (2009). Mesenchymal stem cells derived from human gingiva are capable of immunomodulatory functions and ameliorate inflammation-related tissue destruction in experimental colitis. *Journal of Immunology* 183(12): 7787–7798. doi: 10.4049/jimmunol.0902318.

Zhang, W., Walboomers, X.F., van Kuppevelt, T.H. et al. (2006). The performance of human dental pulp stem cells on different three-dimensional scaffold materials. *Biomaterials* 27: 5658–5668.

Zhu, W., and Liang, M. (2015). Periodontal ligament stem cells: Current status, concerns, and future prospects. *Stem Cells International* 2015: 972313. doi: 10.1155/2015/972313.

25
Artificial Intelligence and Orthodontic Practice: The Future Unveiled

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Summary

Recent years have witnessed tremendous advances in healthcare, with artificial intelligence making forays into the way we diagnose, treatment plan, and deliver truly precision or personalized medicine. In this chapter we provide a high-level overview of artificial intelligence and its applications in orthodontics, introduce the concept of blockchain technology and its potential impact and applications in healthcare, and highlight the ethical considerations around using these technologies. Big data and artificial intelligence methods are poised to change the narrative on our medical model. Disruptive technologies are unlikely to replace healthcare providers. Instead, they stand to serve as valuable companion aids to harness technology and improve the care we deliver to our patients.

Artificial intelligence (AI) is a branch of computer science that describes the research and development of simulated human intelligent behavior in machines. A modern definition of AI is a "System's ability to correctly interpret external data, to learn from

such data, and to use those learnings to achieve specific goals and tasks through flexible adaptation" (Kaplan and Haenlein, 2019). Thanks to recent advances in computing power and the availability of big data, AI has evolved and become part of our daily life. Machine learning (ML) is a subset of AI that refers to the computer's ability to learn without being explicitly programmed. In ML, different models generally fall into three different categories:

- *Supervised learning*: the machine is taught by the example of the desired inputs and outputs. The "machine" uses this input to determine correlations and logic that can be used to predict the answer.
- *Unsupervised learning*: the machine studies data to identify patterns.
- *Reinforcement learning*: the machine is provided with a set of allowed actions, rules, and potential end states.

Deep learning (DL) is the most recent subset of ML, with networks capable of learning unsupervised from unstructured data. DL is inspired by the functionality of our brain cells/neurons. It allows computational models composed of multiple processing layers to learn data representations with multiple levels of abstraction (Figure 25.1; Lecun et al., 2015).

AI has made many inroads in the last few years in the field of orthodontics. The advent of fast processing computers, availability of data from a large number of sources, and emphasis on a data-driven approach to precision and personalized orthodontics have all been significant contributors to this trend. A search of the PubMed database using the term "Artificial Intelligence and Orthodontics" yielded 292 articles as of May 2022. Of these 292 articles, 209 had been published since 2019. This bears testimony to the advances in the use of AI technology in orthodontics. In this chapter we provide an overview of various AI-based applications in orthodontics (Figure 25.2), introduce the concept of "blockchain" and its potential applications in healthcare, and briefly discuss the ethical implications of using AI technology.

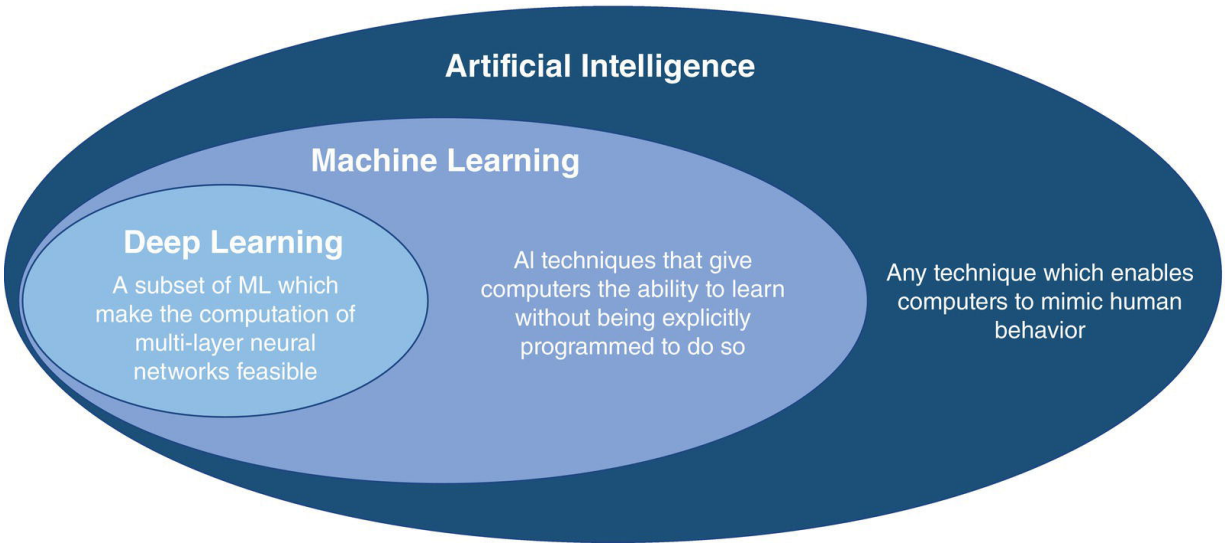

Figure 25.1 Evolution of artificial intelligence (AI). ML, machine learning.

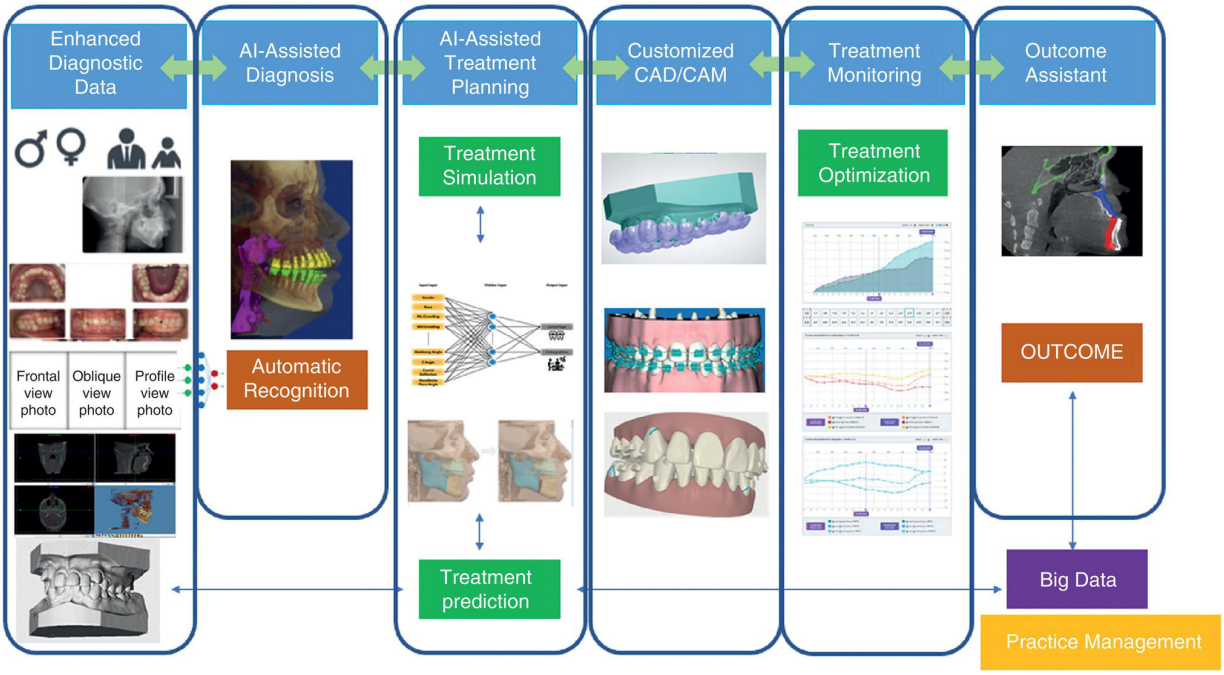

Figure 25.2 Holistic vision for artificial intelligence (AI)-driven orthodontics practice. CAD/CAM, computer-aided design/computer-aided manufacturing.

Applications of artificial intelligence technology in orthodontics

Artificial intelligence–assisted diagnosis

Automated cephalometric landmarks localization

AI-based cephalometric analysis is one of the most common applications of AI in orthodontics. The seminal work on automated cephalometric landmark detection was done in 1984 to detect one landmark (Cohen et al., 1984), followed by numerous methods using computer vision and AI techniques (Leonardi et al., 2008). Usually, supervised ML methods are used for automated identification of cephalometric landmarks (Park et al., 2019). The primary goal is to eliminate or minimize human errors and to reduce time to identify landmarks (Durão et al., 2015). An ML approach using random forest regression voting automatically located 19 landmarks in 24 seconds. The overall average point-to-point error was 2.2 ± 0.03 mm (Lindner et al., 2016). Recently, the more advanced ML method of deep learning has been introduced. DL consists of an input layer, multiple hidden layers, and an output layer (Lecun et al., 2015). For automated cephalometry, the radiographs serve as input data and the numerical grayscale values of each pixel serve as individual inputs for neurons of the input layer. The output layer is defined as pairs of X and Y coordinates for each cephalometric landmark (Kunz et al., 2020). Kunz et al. in 2020 showed that a customized convolutional neural network (CNN) DL algorithm could localize anatomical landmarks with precision comparable to that of experienced human examiners, but in a fraction of a second. However, this customized DL algorithm can detect a limited set of landmarks (Arik et al., 2017; Kunz et al., 2020; Nishimoto et al., 2019). To detect more anatomical landmarks, an advanced YOLO (you only look once) model, called YOLO v. 3, showed faster detection and higher accuracy in 1028 cephalograms with less than 0.9 mm in the mean absolute error (MAE) of coordinates when compared to the human (Park et al., 2019). Currently, automatic cephalometric analysis using AI is available in the form of web-based services. Some of these are open source and several others are commercial (Figure 25.3).

Classification of skeletal maturation stages

Dentofacial orthopedic and orthodontic treatment planning is primarily influenced by the pubertal growth spurt and skeletal maturation. Traditionally, hand–wrist radiographic analysis is considered the gold standard in determining individuals' growth rate and peak stage of growth. But cervical vertebrae maturation (CVM) staging has become a more favorable alternative method. Lateral cephalometric radiographs are part of the routine orthodontic records set and by avoiding exposing a hand–wrist radiograph we can avoid unnecessarily increased ionizing radiation exposure (McNamara and Franchi, 2018). However, CVM staging is usually assessed visually, which needs an experienced orthodontist. Furthermore, it is not integrated with digital cephalometric software. AI could assist in developing a computer-based system to determine CVM maturation stages. A semi-automated method was recently introduced to reduce human error (Amasya et al., 2020). In this method, the orthodontist digitizes 26 landmarks on the cervical vertebrae for manual extraction of the image feature. Then, an ML clinical decision support system uses the numerical values of the features to determine the CVM stage (Amasya et al., 2020).

Recently, DL has been extensively used in the medical field for image pattern recognition and classification. At the University of Illinois Chicago (UIC), a research group developed a fully automated high-performance system to detect and classify CVM stages. Its system consisted of an aggregate channel features (ACF) object detector that automatically identifies cervical vertebrae in the lateral cephalometric radiograph as the region of interest (ROI). The outputs are fed to a DL custom-designed CNN with directional filter (CNNDF). The initial layer of the CNN consists of directional filters to emphasize the edges of vertebral bodies in the ROI images. Then the convolution layers extract the information from the images using a two-dimensional (2D) convolution operation, and the outputs are the images classified according to the CVM maturation stages. The UIC system can classify CVM stages into six classes (CS1–CS6) and the modified five-stage classification methods (CVMS I–CVMS V) (Figure 25.4; Atici et al., 2022).

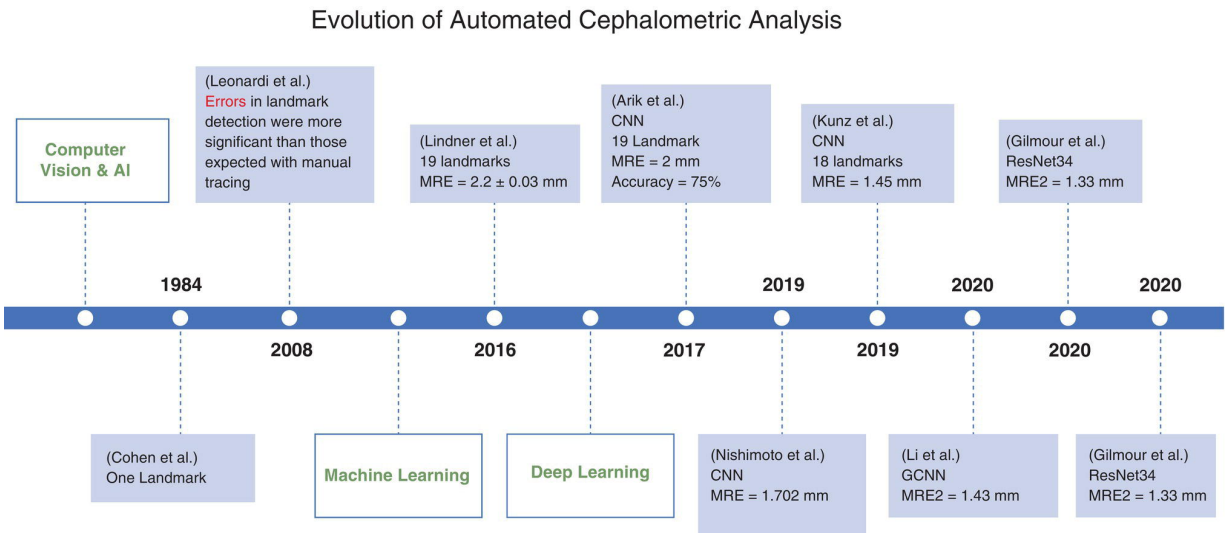

Figure 25.3 Evolution of automated cephalometric analysis. AI, artificial intelligence; CNN, convolutional neural network; GCNN, graph convolutional neural network; MRE, mean radial error.

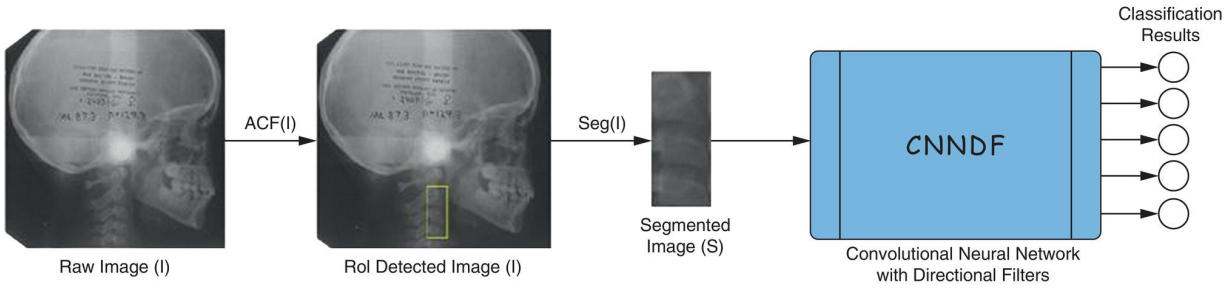

Figure 25.4 The University of Illinois Chicago fully automated determination of the cervical vertebrae maturation stages pipeline. ACF, aggregate channel features; RoI, region of interest.

Cone beam computed tomography

Cone-beam computed tomography (CBCT) can reconstruct a three-dimensional (3D) image of the patient's head, which is very useful in many orthodontic applications. CBCT is commonly used in 3D diagnosis, virtual treatment planning, and for localization of impacted and supernumerary teeth. Other applications include assessment of bone thickness, of root resorption, and examination of the temporomandibular joint (Scarfe et al., 2017). The first step in the 3D analysis is the localization of anatomical landmarks, which is a tedious and time-consuming task. Shahidi et al. (2014) proposed an ML algorithm to automatically locate 14 anatomical landmarks on

CBCT images. However, the mean deviation (3.40 mm) for all of the automatically identified landmarks was higher than the mean deviation (1.41 mm) for those that were manually detected. Montúfar et al. (2018a, 2018b) proposed two automatic landmark localization systems based on active shape models and a hybrid approach using active shape models followed by a 3D knowledge-based searching algorithm. However, the mean deviation (2.51 mm) for all of the automatically identified landmarks in the hybrid system was lower than that of the system that only used active shape models (3.64 mm). Developing an automated ML-based 3D cephalometry analysis framework is challenging because the 3D volume data has greater computational complexity (Lee et al., 2019) than the 2D version of cephalometry. The existing AI systems are not accurate enough for clinical use, but could be used for preliminary localization of orthodontic landmarks followed by manual correction before further orthodontic analyses.

Another application of AI in CBCT is the automated segmentation of anatomical structures. Chen et al. (2020) proposed a method for automatic segmentation of individual teeth in dental CBCT images. They used a V-Net, which is a fully convolutional neural network, to generate a tooth probability map and a tooth surface map. This is input into a marker-controlled watershed transform for tooth segmentation. They showed that a patch size of 64 is optimal for their segmentation method. They had a small dataset comprising only 25 dental CBCT scans due to the time requirement of making voxel-level masks (Chen et al., 2020). Ezhov et al. (2019) presented the results of using a DL model V-Net for segmenting CBCT into 32 teeth plus background. The method consists of two sequential models: the coarse model that outputs 33 classes and the fine model that outputs 2 classes if the data are of a given tooth type or not. They also presented the coarse–fine segmentation pipeline, which uses two types of datasets, coarse and fine. The coarse dataset is created with linearly interpreted bounding boxes of CBCT axial slices. The fine dataset is a per-voxel mask created manually. The method uses average symmetric surface distance (ASD) as one of the metrics to evaluate the model. ASD is the average distance from all points on the boundary of the machine-predicted mask to the ground truth mask and vice versa. Their model achieved 0.17 mm ASD. They

also assessed the overall tooth localization performance by measuring binary voxel-wise intersection over union (IoU) between the ground truth volumetric mask and the model prediction. They achieved 0.94 IoU (Ezhov et al., 2019).

Dental panoramic radiographs

The orthodontist uses dental panoramic radiographs as a popular initial tool for diagnosis. It allows for assessing both the presence and position of tooth buds, supernumerary teeth, impacted teeth, missing tooth buds, and temporomandibular joints. Analysis of these images is done by visual inspection (Wirtz et al., 2018). A robust and accurate AI model for automated analysis of these images could be a helpful screening tool. Automated analysis of panoramic radiographs requires building AI models capable of detecting, labeling, segmenting, and classifying the teeth and surrounding structures. Abdi et al. (2015) developed an algorithm for auto-segmenting the mandible in dental panoramic radiographs. The algorithm was tested on a set of 95 panoramic x-rays, with the results evaluated against the manual segmentations of three expert dentists. It achieved an average performance of >93% in dice similarity, specificity, and sensitivity. Wirtz et al. (2018) reported a novel method for automatic teeth segmentation of dental panoramic radiographs using a coupled shape model in combination with a neural network, but the wisdom teeth were not included in the model. Vinayahalingam et al. (2019) developed and validated an automated approach to detect and segment the third molars and mandibular nerve by DL using panoramic radiographs. Krois et al. (2019) applied deep CNNs to detect periodontal bone loss (PBL) on panoramic dental radiographs. CNNs trained on a limited number of radiographic image segments showed similar discrimination ability to dentists for assessing PBL on panoramic radiographs.

Digital three-dimensional dental models

An essential diagnostic step is analysis of the orthodontic models. This analysis includes arch length analysis and relations of the anterior and posterior width of the dental arches, as well as sagittal occlusion of the canine, Angle's classification of molar occlusion, and anterior vertical and horizontal overlap. Digital 3D dental models

have replaced traditional plaster models as they provide an accurate, valid, and clinically useful alternative, and for the diagnostic set-up too. Furthermore, digital 3D dental models are fundamental for computer-aided-design (CAD) dental systems, customized orthodontic appliances, and virtual surgical planning (Elnagar et al., 2017). Tooth segmentation and labeling are the most critical components of digital model analysis and CAD orthodontics; however, manual segmentation of the 3D digital models is a time-consuming and tedious task (Elnagar et al., 2020). Automated segmentation of digital models would save time, reduce human error, and streamline the digital workflow in contemporary orthodontics practice.

Xu et al. (2019) proposed a data-driven method for 3D dental mesh segmentation by using a deep CNN model. It receives a 3D dental model as input and outputs the label list of each triangle face. They suggested a label-free mesh simplification method for preserving teeth boundary information and significantly improving the efficiency of the networks. The authors claim that their model achieves 99.06% accuracy for the upper dental model and 98.79% for the lower dental model.

Another DL AI method called MeshSegNet has been proposed to automatically label individual teeth on raw dental surfaces acquired by 3D intraoral scanners. MeshSegNet achieves segmentation results of 0.938, 0.946, and 0.934 for Dice similarity coefficient, sensitivity, and positive predictive value, respectively (Lian et al., 2020). To solve the lack of accurate scan data in narrow interdental spaces, Kim et al. (2020) used generative neural networks (GANs), consisting of a generator and a critic, for 3D digital model segmentation. The generator generates synthetic images, and the critic has to discriminate whether each is a real or a synthetic image. This leads to a feedback loop where the synthetic images and the critic improve. For the tooth segmentation task, they obtain results that prove an average improvement of 0.04 mm (Kim et al., 2020).

Decision-making systems and orthodontic treatment planning

An AI-based decision support system uses all relevant patient data to reach promising diagnostic and treatment paths. AI decision support systems could be applied in many orthodontic clinical scenarios, starting from the decision about the patient's need for orthodontic treatment. Thanathornwong in 2018 developed software based on the Bayesian network (BN) model to assess the need for orthodontic treatment; The Bayesian decision support module consisted of relevant variables taken from treatment need indexes, including overbite, anterior open bite, diastema, anterior crossbite, anterior displacement, and anterior–posterior molar relationship. The system could be an auxiliary for the general dentist to assess whether the patient would need orthodontic treatment (Thanathornwong, 2018). A recent study developed a DL CNN model to detect and localize orthodontic malocclusions from intraoral clinical images. In determining whether the patient needs orthodontic treatment, the model was able to detect crowding, spacing, increased overjet, crossbite, open bite, and deep bite (Talaat et al., 2021).

An AI decision-making system can also assist in treatment planning decisions, of which we give some examples here. Arch length analysis in the mixed dentition is an essential step for treatment planning. It requires prediction of the sizes of unerupted canines and premolars to determine whether the available space is sufficient for the permanent teeth to erupt in good alignment. A hybrid genetic algorithm and artificial neural network (GA-ANN) was developed to improve prediction accuracy. The hybrid GA–ANN selected the mandibular first molars and incisors and the maxillary central incisors as the reference teeth for predicting the sum of the mesiodistal widths of the canines and premolars (Moghimi et al., 2012).

Another example of the application of an AI-based decision-making system is in extraction cases. Extraction is a critical irreversible decision. ANN-based AI models can be used to decide on the need for orthodontic extraction; a recent model achieved 92% accuracy in predicting the need for extraction (Jung and Kim, 2016). A more

recent study used ANNs to predict orthodontic treatment plans, including the determination of extraction/nonextraction, extraction patterns, and anchorage patterns. The neural network can provide useful guidance for orthodontic treatment planning, especially for less experienced orthodontists (Li et al., 2019).

Another decision relates to the need for orthognathic surgery. Knoops et al. (2019) used 3D face scans to develop an ML framework to diagnose whether patients need orthognathic surgery or not. The model can help in clinical decision making and improve the clinical understanding of face shape. However, this model is based only on 3D facial scans, and information about the underlying skeletal structures was not considered.

The decision to treat adult patients with Class III malocclusion is complicated by limited options: orthodontic camouflage or orthognathic surgery. The decision-making process is often guided by the clinician's expertise in managing similar malocclusions and influenced by a myriad of phenotypic and psychosocial factors unique to each patient. A research group at UIC developed an ML decision support system for treatment planning of adult patients with Class III malocclusion. The model can predict if the patient can be treated successfully by orthodontics only or if orthognathic surgery is required. To develop the ML model, records of adult Class III patients who received treatment were analyzed and 40 demographic, radiographic, and clinical parameters were collected for each case. Data mining steps were applied to the parameters to identify differences between the two groups (Group1: Orthodontic camouflage; Group2: Orthognathic surgery). The cases were also divided into testing and validation datasets. Eight different ML models were tested. These models included support vector machine (SVM), random forest, k-nearest neighbor (kNN), logistic regression, multi-layer perceptron (MLP), CNN, extreme gradient boosting (XGBoost), and pruned XGBoost plus selected features. The performance metrics of the various models were calculated and compared. Different ML models produced the desired binary output with an accuracy ranging from 78% for the kNN algorithm to 93% for the pruned XGBoost model. The authors concluded that their ML model is highly predictive and more accurate than all existing statistical models (Taraji, 2022).

Similarly, treatment of children with Class III malocclusion is challenging. The orthodontist needs to predict whether orthodontic/orthopedic therapy would be successful or not. A model derived from fuzzy clustering repartition and network analysis of craniofacial features can be used to predict treatment outcomes of rapid maxillary expansion and facial mask therapy (Auconi et al., 2015). Subjects who could be successfully treated with orthodontic/orthopedic appliances would receive treatment during childhood or adolescence, while the treatment plan for individuals who would eventually need orthognathic surgery could be modified accordingly.

There are also some reports of using AI models to select the ideal force system during orthodontic treatment. The proposed AI model could assist in determining the geometry of orthodontic springs needed to close extraction spaces and the forces required to align teeth (Lim et al., 2010; Omran et al., 2018). Another reported AI model can assist in determining the type of headgear to use (low-, medium-, or high-pull headgear; Okan Akçam and Takada, 2002).

Evaluation of treatment outcomes

An AI model capable of predicting treatment success would be a tremendous resource for the orthodontist. It could provide useful information to orthodontic patients before the start of treatment. For example, the most common motivation for seeking orthodontic treatment is the improvement of facial esthetics. Hence, predicting the impact of treatment on facial appearance is crucial. With the help of an ANN, the accuracy and reliability of postsurgical profile video image predictions can be improved to a clinically appropriate level (Lu et al., 2009). Furthermore, AI has been used to score facial attractiveness in patients who have undergone orthognathic surgery (Patcas et al., 2019). These examples illustrate the promise seen with the initial results of AI-based automated systems. However, most of the authors reported that these systems need further improvement and refinement to be suitable for clinical use (Zarei et al., 2006; Lu et al., 2009; Moghimi et al., 2012).

Artificial intelligence–driven remote monitoring

Artificial intelligence–driven remote monitoring (AIDRM) is an innovative new technology that allows patients to take photos of their mouths that an AI algorithm then evaluates. Real-time alerts can be sent to the patient and doctor regarding the specific conditions the AI detects. Developing AIDRM requires collecting large amounts of data from the patient's photos to train an AI model to identify specific conditions. Dental Monitoring™ (DM; Dental Monitoring SAS, Austin, TX, USA) is one of the most popular AIDRM applications in orthodontics. DM is a remote monitoring system consisting of three interconnected platforms: a smartphone application for patients, a patented tooth movement and oral health tracking algorithm, and a web-based Doctor Dashboard for the orthodontist to view treatment progress. DM uses a proprietary AI image analysis algorithm to track the patient's tooth movement and oral hygiene during orthodontic treatment, among other features (Kravitz et al., 2016). It uses initial 3D stereolithographic (STL) files uploaded at baseline to monitor changes over time. While analyzing patients' regularly scheduled 2D photographic scans taken by their smartphone camera, the AI algorithm can evaluate tooth movement, monitor oral hygiene, and detect appliance breakage. The DM software then sends specific notifications to the patient and the doctor to take the appropriate next steps based on the problem detected by the AI algorithm. Patients usually are instructed to take weekly or biweekly scans during active treatment, so potential emergencies like broken brackets, de-ligation of wires, embedding of a palatal appliance into the gingival tissue, or an unseated aligner can be addressed sooner rather than later and may can help orthodontists schedule their chair time more efficiently (https://dental-monitoring.com). Also, remote DM scans could be used for retention checks. Although DM may have multiple applications in daily orthodontic practice, few studies have evaluated the accuracy of DM applications. Future studies are needed to assess the clinical effectiveness of implementing DM in orthodontic treatment (Figures 25.5 and 25.6; Morris et al., 2019; Elnagar et al., 2020).

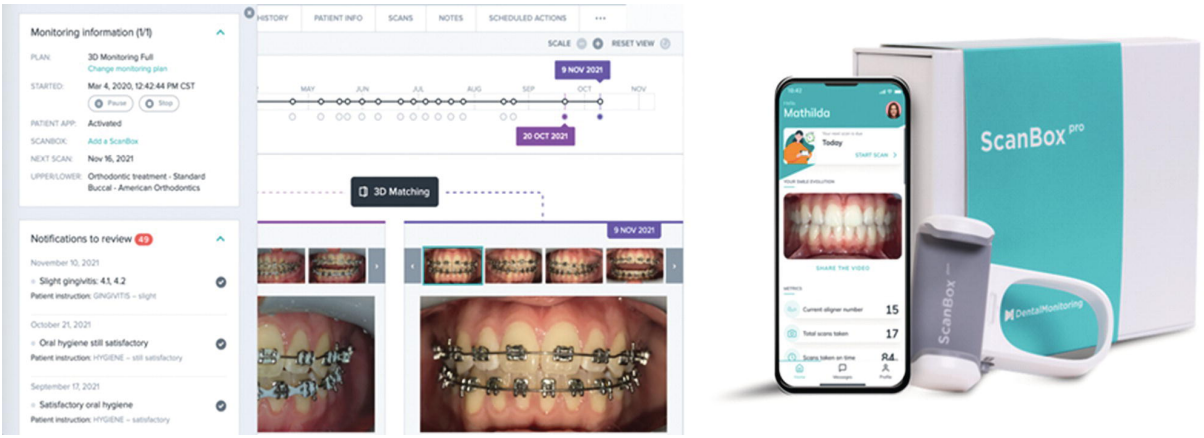

Figure 25.5 The Dental Monitoring Doctor Dashboard, smartphone application, and ScanBox.

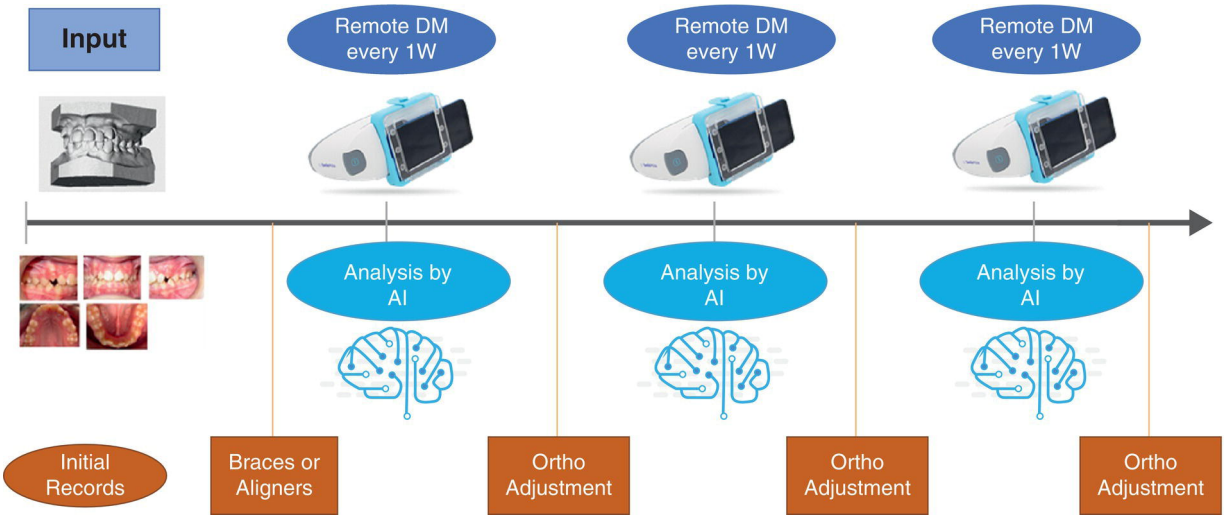

Figure 25.6 A workflow for implementing artificial intelligence–driven remote monitoring (AIDRM) during orthodontics treatment to monitor the patient between in-office visits. DM, dental monitoring.

Blockchain technology in healthcare

Blockchain technology holds significant promise in healthcare. In addition to the technological advances that signify this era, the implications of decentralization and access to data have the potential to revolutionize data-centric personalized care. As a distributed public ledger, a blockchain records transactions in an immutable manner. A “hash” or unique digital fingerprint is contained within

each block. Multiple blocks, connected in chronological order, form a blockchain. Hence, the blockchain is a sequential series of blocks containing a list of complete and correct transaction records (Tagde et al., 2021). The very first block is called the genesis block, while a block that precedes any given block is recognized as its block header (Ahmad et al., 2019). The data on the blockchain network are immutable, any changes in one block resulting in simultaneous changes in all the subsequent blocks. The data in the chain are protected by cryptographic algorithms, ensuring data security. Another utilitarian addition to the blockchain is a smart contract. While this is an entity that is independent of the blockchain, smart contracts operate as computer protocols that run on blockchains autonomously when predetermined conditions are met (Yoon 2019). Smart contracts provide consensus for the operation of the ledger. The parties provide agreement under the contract to validate transactions on a block and add it to the chain.

As a system for recording information, a blockchain makes it difficult to change, cheat, or hack the system. Favorable characteristics of the technology, such as known data provenance, enhanced security, an immutable audit trail, and a decentralized system of management have created interest in blockchains in the healthcare sector. It is anticipated that this technology will enhance medical record management, streamline insurance claim processes, and advance clinical and biomedical research (Kuo et al., 2017). Ease of access to and transfer of information between stakeholders in healthcare could lead to a collaborative treatment planning process. This has applications in areas including diagnostics, treatment planning, and financial and interdisciplinary care. The technological era of the blockchain has spurned changes that have implications for dentistry with impacts on clinical care, research, education, and social considerations. Disruptive technologies such as artificial intelligence, 3D printing, the Internet of Medical Things, and augmented reality are set to emerge as major forces in this era of automation and digital analytics.

Medical data are routinely and continuously collected, and are increasingly being stored electronically. While this trend has been in existence for more than a decade (Jha et al., 2008), greater adoption of electronic health records and the decreased cost of such

technological adoption have significantly increased the rate of digitization of data in recent years. The increase in data volume, diversity, and quality is providing opportunities for other technologies such as AI that provide the tools for the review of data and offer meaningful opportunities for clinical translation. Reflective of this increase in attention to blockchain in healthcare has been a dramatic increase in PubMed-indexed articles on the subject. These published articles illustrate a wide variety of applications, including management of healthcare data, interoperability, management of clinical trials, remote patient monitoring, precision medicine, and research. Increased integration of health data, dental data, genomic data, and data from wearable devices provides opportunities for data-centered care in dentistry. A breakdown of publications on PubMed in 2018 shows that about 32% of the publications were related to healthcare data (Mackey et al., 2019). A distributed ledger system of encrypted information allows for the patient, as a user, to have full access and control over the data and how it is shared. This makes a scenario possible wherein the user, through a dashboard on a mobile application, can control who has permission to access their blockchain. One's ability to audit blockchain data also enables the user to view individual user access logs on the chain, and subsequently revoke permissions as necessary. Blockchain application verification processes to preserve electronic health records will need to identify creative ways to integrate conventional and electronic health records (Tagde et al., 2021). "MedRec" is a prototype electronic health record system that provides a secure cloud-based data recording system. It integrates honesty, security, and fast data exchange in its model, and operates on a decentralized basis. Hence, patients would have complete, quick, and easy access to their healthcare records, which would be immutable (Wang and Song, 2018).

The next generation of healthcare data technology, built on decentralization, openness, and greater user utility, could potentially be disruptive to existing paradigms of care. Decision making in healthcare has traditionally been an independent process between providers. A shared decision-making paradigm has been considered as an optimum way of healthcare decision making. Collaborative decision making is when two or more providers contribute their

diverse expertise and skills to the decision-making mechanism (Christensen and Larson, 1993). The facilitation of collaborative decision making involves sharing sensitive electronic health records (EHRs) among the stakeholders, including physicians, insurance companies, pharmacies, researchers, and the patients under care. Currently, such stored data and the means of sharing the information are vulnerable to insecurity and data breaches. Privacy-aware blockchain could be a substantial option when designing new paradigms to overcome these security issues (Yang et al., 2019). Studies have included patient engagement in healthcare as a significant factor in the improvement of the medical decision-making process (Barello and Graffigna, 2015). The future of patient care that incorporates decentralized data storage and collaborative decision making with the patient, as a user, at the center of this model has the potential to significantly enhance healthcare outcomes. In a system based on advanced healthcare blockchain technology, smart contracts can be structured to handle patient data and simplify complex medical treatments (Campanella et al., 2016).

This technology is not without its challenges. Variations between healthcare providers and hospitals in definitions of data points, demographic differences, and varying clinical/ laboratory practices may cause data bias when it is being utilized, and especially when AI-based systems are used (Krittanawong et al., 2017). While blockchain as a technology is being widely adopted, the speed and scalability requirements for its adoption as a primary healthcare data storage system would be significant. Hence, the adoption of a decentralized healthcare data storage network will require extensive investments in the technology in terms of hardware, software, and staff resources. With such a hyperefficient means of data maintenance that incorporates the potential for significant automation, there also exists the possibility of the loss of millions of jobs in the data maintenance sector. Further, many of the current blockchain consensus mechanisms are resource intensive in hardware and power requirements, thus raising concerns related to environmental sustainability.

While blockchain can offer many pragmatic solutions in healthcare applications, many ethical concerns remain around its adoption. Although many studies exist evaluating ethical considerations in

blockchains, most of these address legal considerations often related to cryptocurrencies. This reinforces the need for deeper understanding of philosophical ethics, especially when evaluating healthcare applications. Hyrynsalmi et al. (2021) summarized their findings with the following observations: (i) while many articles discuss blockchain and health, there is a dearth of articles that address ethical considerations in the field; (ii) there is lack of analytical information on the ethical consequences of blockchain in healthcare; and (iii) with the adoption of blockchain in various areas, there is a need for ethical analysis of the blockchain-based solutions being proposed. These authors went on to state that there is a need for concrete tools, frameworks, and methods to analyze the ethical aspects of blockchain solutions (Hyrynsalmi et al., 2021). While the adoption of blockchain technology has far-reaching positive implications for healthcare, it is important for the technological and ethical concerns to be addressed as adoption of the technology becomes more prevalent. With an ever-greater number of disruptive technologies at our disposal, the future holds promise for our ability to improve the health of our patients and to upgrade our practice.

Ethical considerations in artificial intelligence

While AI research and application in orthodontics have been growing exponentially, policies and regulations to ensure the safety and protection of patient rights are lagging behind. In the realm of healthcare, the same fundamental medical ethics that exist in the doctor–patient relationship apply to the AI–patient relationship. The framework of ethics adopted by both the American Medical Association and the American Dental Association in their respective professional codes of ethics derives from the classic textbook *Principles of Biomedical Ethics*, first published in 1979 by philosophers Tom Beauchamp and James Childress, contemporaneous with the Belmont Report (National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1978). These two seminal works in modern medical ethics were prompted by the 1972 revelation of the Tuskegee Syphilis Study, conducted by the US Public Health Service and the Centers for Disease Control and Prevention over 40 years (Centers for

Disease Control and Prevention, 2021). As AI grows in its presence in orthodontic research and practice, orthodontists and dentists at large have a duty to reflect on and apply the same core principles of biomedical ethics that emerged from the painful history of the Tuskegee study as a guideline for our actions in patient care, research, and teaching and training future professionals.

The four core moral principles proposed by Beauchamp and Childress (2013) have served as pillars of medical ethics for decades, and were in turn descended from common morality, a "set of universal norms shared by all persons committed to morality." The four clusters of moral principles are "*respect for autonomy* (a norm of respecting and supporting autonomous decisions), *non-maleficence* (a norm of avoiding the causation of harm), *beneficence* (a group of norms pertaining to relieving, lessening, or preventing harm and providing benefits and balancing benefits against risks and costs), and *justice* (a cluster of norms for fairly distributing benefits, risks, and costs)" (Beauchamp and Childress, 2013: 3). Within the principle of autonomy are embedded substantive rules such as truth-telling, confidentiality, privacy, and informed consent. Some of these concepts are often discussed in the medical ethics literature as separate entities. For example, truth-telling exists separately in the American Dental Association Principles of Ethics and Code of Professional Conduct as the fifth principle of *veracity* or truthfulness, a "duty to communicate truthfully" (American Dental Association, 2023).

The fundamental ethical principles of autonomy, nonmaleficence, beneficence, justice, and veracity should be given due consideration as we begin to adopt disruptive technologies such as ML and blockchain in the healthcare landscape. While deep or self-sufficient AI wherein a machine can mimic human intelligence may only be a theoretical reality at present, as AI becomes more human-minded and fully functioning issues of trust (protection of private data, confidentiality, legality of the system), respect for autonomy, and preservation of human dignity and safety must be addressed, and a set of agreed guidelines placed well ahead of the development and application of advanced technology. In effect, deep AI functions not as mere tools but as agents mimicking human healthcare professionals, in which case supervision equivalent to licensing

examinations and certification may be appropriate as the AI technology matures further (Kluge, 2020).

References

Abdi, A.H., Kasaei, S., and Mehdizadeh, M. (2015). Automatic segmentation of mandible in panoramic x-ray. *Journal of Medical Imaging*. 2(4): 044003. doi: 10.1117/1.jmi.2.4.044003.

Ahmad, S.S., Khan, S., and Kamal, M.A. (2019). What is blockchain technology and its significance in the current healthcare system? *A brief insight. Current Pharmaceutical Design* 25(12): 1402–1408.

Amasya, H., Yildirim, D., Aydogan, T. et al. (2020). Cervical vertebral maturation assessment on lateral cephalometric radiographs using artificial intelligence: Comparison of machine learning classifier models. *Dentomaxillofacial Radiology* 49(5): 20190441. doi: 10.1259/dmfr.20190441.

American Dental Association (2023). Principles of Ethics and Code of Professional Conduct. https://www.ada.org/-/media/project/ada-organization/ada/ada-org/files/about/ada_code_of_ethics.pdf?rev=86aeaa6fb0d0467f8a380a3de35e8301&hash=89BAA88FB9305B8F134414E337CAE55A.

Arik, S.Ö., Ibragimov, B., and Xing, L. (2017). Fully automated quantitative cephalometry using convolutional neural networks. *Journal of Medical Imaging* 4(1): 014501. doi: 10.1117/1.jmi.4.1.014501.

Atici, S.F., Rashid Ansari, R., Allareddy, V. et al. (2022). Fully automated determination of the cervical vertebrae maturation stages using deep learning with directional filters. *PLoS One* 17(7): e0269198.

Auconi, P., Scazzocchio, M., Cozza, P. et al. (2015). Prediction of Class III treatment outcomes through orthodontic data mining.

European Journal of Orthodontics 37(3): 257–267. doi: 10.1093/ejo/cju038.

Barello, S., and Graffigna, G. (2015). Patient engagement in healthcare: Pathways for effective medical decision making. *Neuropsychological Trends* 17: 53-65.

Beauchamp, T.L., and Childress, J.F. (2013). *Principles of Biomedical Ethics*, 7th ed. Oxford: Oxford University Press.

Campanella, P., Lovato, E., Marone, C. et al. (2016). The impact of electronic health records on healthcare quality: A systematic review and meta-analysis. *European Journal of Public Health* 26(1): 60–64.

Centers for Disease Control and Prevention (2021). The U.S. Public Health Service Syphilis Study at Tuskegee. https://www.cdc.gov/tuskegee/index.html.

Chen, Y., Du., H., Yun, Z. et al. (2020) Automatic segmentation of individual tooth in dental CBCT images from tooth surface map by a multi-task FCN. *IEEE Access* 8: 97296–97309. doi: 10.1109/ACCESS.2020.2991799.

Christensen, C., and Larson, J.R., Jr. (1993). Collaborative medical decision making. *Medical Decision Making* 13(4): 339–346.

Cohen, A.M., Ip, H.H., and Linney, A.D. (1984) A preliminary study of computer recognition and identification of skeletal landmarks as a new method of cephalometric analysis. *British Journal of Orthodontics* 11(3): 143–154. doi: 10.1179/bjo.11.3.143.

Durão, A.P.R., Morosolli, A., Pittayapat, P. et al. (2015). Cephalometric landmark variability among orthodontists and dentomaxillofacial radiologists: A comparative study. *Imaging Science in Dentistry* 45(4): 213–220. doi: 10.5624/isd.2015.45.4.213.

Elnagar, M.H., Aronovich, S., and Kusnoto, B. (2020). Digital workflow for combined orthodontics and orthognathic surgery. *Oral and Maxillofacial Surgery Clinics of North America* 32(1): 1–14. doi: 10.1016/j.coms.2019.08.004.

Elnagar, M.H., Elshourbagy, E., Ghobashy, S. et al. (2017). Dentoalveolar and arch dimension changes in patients treated with miniplate-anchored maxillary protraction. *American Journal of Orthodontics and Dentofacial Orthopedics* 151(6): 1092–1106. doi: 10.1016/j.ajodo.2016.10.038.

Ezhov, M., Zakirov, A., and Gusarev, M. (2019). Coarse-to-fine volumetric segmentation of teeth in cone-beam CT. *Proceedings – International Symposium on Biomedical Imaging* 2019:A 52–56. doi: 10.1109/ISBI.2019.8759310.

Gilmour, L., and Ray, N. (2020). Locating cephalometric x-ray landmarks with foveated pyramid attention. In: *Proceedings of the Third Conference on Medical Imaging with Deep Learning*, Montreal, QC, Canada, 6–8 July 2020, pp. 262–276.

Hyrynsalmi, S., Hyrynsalmi, S.M., and Kimppa, K.K. (2021). The state of the art of the blockchain ethics in healthcare: A systematic literature review. *Finnish Journal of eHealth and eWelfare* 13(3): 193–206.

Jha, A.K., Doolan, D., Grandt, D. et al. (2008). The use of health information technology in seven nations. *International Journal of Medical Informatics* 77(12): 848–854.

Jung, S.K., and Kim, T.W. (2016). New approach for the diagnosis of extractions with neural network machine learning. *American Journal of Orthodontics and Dentofacial Orthopedics* 149(1): 127–133. doi: 10.1016/j.ajodo.2015.07.030.

Kaplan, A., and Haenlein, M. (2019). "Siri, Siri, in my hand: Who's the fairest in the land?" On the interpretations, illustrations, and implications of artificial intelligence. *Business Horizons* 62(1): 15–25. doi: 10.1016/J.BUSHOR.2018.08.004.

Kim, T., Cho, Y., Kim, D. et al. (2020). Tooth segmentation of 3D scan data using generative adversarial networks. *Applied Sciences* 10(2): 490. doi: 10.3390/APP10020490.

Kluge, E.W. (2020. Artificial intelligence in healthcare: Ethical considerations. *Healthcare Management Forum* 33(1): 47–49.

doi: 10.1177/0840470419850438.

Knoops, P.G.M., Papaioannou, A., Borghi, A. et al. (2019). A machine learning framework for automated diagnosis and computer-assisted planning in plastic and reconstructive surgery. *Scientific Reports* 9(1): 1–12. doi: 10.1038/s41598-019-49506-1.

Kravitz, N.D., Burris, B., Butler, D. et al. (2016). Teledentistry, do-it-yourself orthodontics, and remote treatment monitoring. *Journal of Clinical Orthodontics* 50(12): 718–726.

Krittanawong, C., Zhang, H., Wang, Z. et al. (2017). Artificial intelligence in precision cardiovascular medicine. *Journal of the American College of Cardiology* 69(21): 2657–2664.

Krois, J., Ekert, T., Meinhold, L. et al. (2019). Deep learning for the radiographic detection of periodontal bone loss. *Scientific Reports* 9(1): 1–6. doi: 10.1038/s41598-019-44839-3.

Kuo, T.T., Kim, H.E., and Ohno-Machado, L. (2017). Blockchain distributed ledger technologies for biomedical and health care applications. *Journal of the American Medical Informatics Association* 24(6): 1211–1220.

Kunz, F., Stellzig-Eisenhauer, A., Zeman, F. et al. (2020). Artificial intelligence in orthodontics: Evaluation of a fully automated cephalometric analysis using a customized convolutional neural network. *Journal of Orofacial Orthopedics* 81(1): 52–68. doi: 10.1007/s00056-019-00203-8.

Lecun, Y., Bengio, Y., and Hinton, G. (2015). Deep learning. *Nature* 521: 436–444. doi: 10.1038/nature14539.

Lee, S.M., Kim, H.P., Jeon, K. et al. (2019). Automatic 3D cephalometric annotation system using shadowed 2D image-based machine learning. *Physics in Medicine and Biology* 64(5): 055002. doi: 10.1088/1361-6560/ab00c9.

Leonardi, R., Giordano, D., Maiorana, F. et al. (2008). Automatic cephalometric analysis: A systematic review. *Angle Orthodontist* 78(1): 145–151. doi: 10.2319/120506-491.1.

Li, P., Kong, D., Tang, T. et al. (2019). Orthodontic treatment planning based on artificial neural networks. *Scientific Reports* 9(1): 1–9. doi: 10.1038/s41598-018-38439-w.

Lian, C., Wang, L., Wu, T.-H. et al. (2020). Deep multi-scale mesh feature learning for automated labeling of raw dental surfaces from 3D intraoral scanners. *IEEE Transactions on Medical Imaging* 39(7): 2440–2450. doi: 10.1109/TMI.2020.2971730.

Lim, D., Ong. Y.S., Setiawan, R. et al. (2010). Classifier-assisted constrained evolutionary optimization for automated geometry selection of orthodontic retraction spring. *IEEE Congress on Evolutionary Computation* 2010: 1–8. doi: 10.1109/CEC.2010.5586460.

Lindner, C., Wang, C.-W., Huang, C.-T. et al. (2016). Fully automatic system for accurate localisation and analysis of cephalometric landmarks in lateral cephalograms. *Scientific Reports* 6(September): 1–10. doi: 10.1038/srep33581.

Lu, C.H., Ko, E.W.C., and Liu, L. (2009). Improving the video imaging prediction of postsurgical facial profiles with an artificial neural network. *Journal of Dental Sciences* 4(3): 118–129. doi: 10.1016/S1991-7902(09)60017-9.

Mackey, T.K., Kuo, T.T., Gummadi, B. (2019). "Fit-for-purpose?" Challenges and opportunities for applications of blockchain technology in the future of healthcare. *BMC Medicine* 17(1): 68.

McNamara, J.A., and Franchi, L. (2018). The cervical vertebral maturation method: A user's guide. *Angle Orthodontist* 88(2): 133. doi: 10.2319/111517-787.1.

Moghimi, S., Talebi, M., and Parisay, I. (2012). Design and implementation of a hybrid genetic algorithm and artificial neural network system for predicting the sizes of unerupted canines and premolars. *European Journal of Orthodontics* 34(4): 480–486. doi: 10.1093/ejo/cjr042.

Montúfar, J., Romero, M., and Scougall-Vilchis, R.J. (2018a). Automatic 3-dimensional cephalometric landmarking based on

active shape models in related projections. *American Journal of Orthodontics and Dentofacial Orthopedics* 153(3): 449–458. doi: 10.1016/j.ajodo.2017.06.028.

Montúfar, J., Romero, M., and Scougall-Vilchis, R.J. (2018b). Hybrid approach for automatic cephalometric landmark annotation on cone-beam computed tomography volumes. *American Journal of Orthodontics and Dentofacial Orthopedics* 154(1): 140–150. doi: 10.1016/j.ajodo.2017.08.028.

Morris, R.S., Hoye, L.N., Elnagar, M.H. et al. (2019). Accuracy of dental monitoring 3D digital dental models using photograph and video mode. *American Journal of Orthodontics and Dentofacial Orthopedics* 156(3): 420–428. doi: 10.1016/j.ajodo.2019.02.014.

National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (1978). *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*. Bethesda, MD: NCPHSBBR.

Nishimoto, S., Sotsuka, Y., Kawai, K. et al. (2019). Personal computer-based cephalometric landmark detection with deep learning, using cephalograms on the internet. *Journal of Craniofacial Surgery* 30(1): 91–95. doi: 10.1097/SCS.0000000000004901.

Okan Akçam, M., and Takada, K. (2002). Fuzzy modelling for selecting headgear types. *European Journal of Orthodontics* 24(1): 99–106. doi: 10.1093/ejo/24.1.99.

Omran, L.N., Ezzat, K.A., and Hassanien, A.E. (2018). Decision support system for determination of forces applied in orthodontic based on fuzzy logic. In: *International Conference on Advanced Machine Learning Technologies and Applications*. Berlin: Springer, pp. 158–168. doi: 10.1007/978-3-319-74690-6_16.

Park, J.H., Hwang, H.-W., Moon, J.-H. et al. (2019). Automated identification of cephalometric landmarks: Part 1—Comparisons between the latest deep-learning methods YOLOV3 and SSD. *Angle Orthodontist* 89(6): 903–909. doi: 10.2319/022019-127.1.

Patcas, R., Bernini, D.A.J., Volokitin, A. et al. (2019). Applying artificial intelligence to assess the impact of orthognathic treatment on facial attractiveness and estimated age. *International Journal of Oral and Maxillofacial Surgery* 48(1): 77–83. doi: 10.1016/j.ijom.2018.07.010.

Scarfe, W.C., Azevedo, B., Toghyani, S. et al. (2017). Cone beam computed tomographic imaging in orthodontics. *Australian Dental Journal* 62: 33–50. doi: 10.1111/adj.12479.

Shahidi, S., Bahrampour, E., Soltanimehr, E. et al. (2014). The accuracy of a designed software for automated localization of craniofacial landmarks on CBCT images. *BMC Medical Imaging* 14(1): 32. doi: 10.1186/1471-2342-14-32.

Tagde, P., Tagde, S., Bhattacharya, T. et al. (2021). Blockchain and artificial intelligence technology in e-Health. *Environmental Science and Pollution Research International* 28(38): 52810–52831.

Talaat, S., Kaboudan, A., Talaat, W. et al. (2021). The validity of an artificial intelligence application for assessment of orthodontic treatment need from clinical images. *Seminars in Orthodontics* 27(2): 164–171. doi: 10.1053/j.sodo.2021.05.012.

Taraji, S. (2022). *Novel machine learning algorithms for prediction and treatment decision in adult patients with Class III*. Thesis, University of Illinois Chicago. https://indigo.uic.edu/articles/thesis/Novel_Machine_Learning_Algorithms_for_Prediction_and_Treatment_Decision_in_Patients_with_Class_III/20254257 .

Thanathornwong, B. (2018). Bayesian-based decision support system for assessing the needs for orthodontic treatment. *Healthcare Informatics Research* 24(1): 22–28. doi: 10.4258/hir.2018.24.1.22.

Vinayahalingam, S., Xi, T., Bergé, S. et al. (2019). Automated detection of third molars and mandibular nerve by deep learning. *Scientific Reports* 9(1): 1–7. doi: 10.1038/s41598-019-45487-3.

Wang, H., and Song, Y. (2018). Secure cloud-based EHR system using attribute-based cryptosystem and blockchain. *Journal of Medical Systems* 42(8): 152.

Wirtz, A., Mirashi, S.G., and Wesarg, S. (2018). Automatic teeth segmentation in panoramic X-ray images using a coupled shape model in combination with a neural network. In: A. Frangi, J. Schnabel, C, Davatzikos et al. (eds.), *Medical Image Computing and Computer Assisted Intervention – MICCAI 2018*. Lecture Notes in Computer Science vol. 11073. Cham: Springer, pp. 712–719. doi: 10.1007/978-3-030-00937-3_81.

Xu, X., Liu, C., and Zheng, Y. (2019). 3D tooth segmentation and labeling using deep convolutional neural networks. *IEEE Transactions on Visualization and Computer Graphics* 25(7): 2336–2348. doi: 10.1109/TVCG.2018.2839685.

Yang, J., Onik, M.M.H., Lee, N.-Y. et al. (2019). Proof-of-familiarity: A privacy-preserved blockchain scheme for collaborative medical decision-making. *Applied Sciences* 9(7): 1370.

Yoon, H.J. (2019). Blockchain technology and healthcare. *Healthcare Informatics Research* 25(2): 59–60.

Zarei, A., El-Sharkawi, M., Hairfield, M. et al. (2006). An intelligent system for prediction of orthodontic treatment outcome. In: *The 2006 IEEE International Joint Conference on Neural Networks Proceedings*. Vancouver: Institute of Electrical and Electronics Engineers, pp. 2702–2706. doi: 10.1109/ijcnn.2006.247173.

26
The Seven Pillars of Professionalism

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Summary

The concept of professionalism continued to thrive as medical schools were founded over time. Professionalism is essential because our patients are placed in a position of vulnerability. Our patients readily place their trust in us, despite our initially brief contact with them as a stranger. Within a short period, they give us their physical selves, their emotional trust, and often a significant financial commitment despite their minimal initial exposure to us. This chapter answers the most pertinent questions that are relevant today: If professionalism evolved as an exemplar in healthcare, does the concept of professionalism prevail today? If it does, is it held in the same high esteem as it used to be, or is it doomed to deteriorate? And what is the pertinence of professionalism in the delivery of orthodontic care and in orthodontic education? The chapter details the seven Pillars of Professionalism, which might provide a practical framework for maintaining ethical conduct in parallel to our success, amid a world of temptations, distractions, and occasionally insurmountable pressures.

"There is nothing permanent except change."

—Heraclitus, Greek philosopher (d. 475 BCE)

Maybe sometimes that doesn't have to be the case.

The Seven Wonders of the World

To the Greeks, the number seven was a lucky number. As ancient Greeks traveled through Persia, Egypt, and Babylonia (now modern-day Iran and Iraq), they were in awe of the magnificent structures that were constructed solely by brilliant ingenuity and mere muscle power. Depiction of these creations by photography and other methods was nonexistent until centuries later, and therefore their experiences were recorded by drawings and written accounts. The second-century Greek writer Antipater of Sidon is credited with cataloging the most exquisite structural accomplishments in the vicinity of ancient Greece. Although accounts of these achievements excluded those of Africa, Europe, Asia, and the Americas, these remarkable creations were labeled the *Seven Wonders of the World* (National Geographic, n.d.).

Each of these magnificent creations was more exquisite than the next. The Seven Wonders were as follows:

- Reigning as the tallest manmade creation for over 4000 years is the *Great Pyramid of Giza,* erected on the Nile River in approximately 2500 BCE. It stands over 450 ft tall (138 m). Laborers needed over 20 years to assemble the 2.3 million blocks of stone that comprise it. The pyramid was erected to glorify the burial site of the great pharaoh Khufu (Cheops).
- The *Hanging Gardens of Babylon* were assembled around 600 BCE by Nebuchadnezzar II, who was king of Babylonia between 605 and 562 BCE.
- The *Statue of Zeus* was a 40 ft, gold-plated statue of Zeus, the father of all gods in Greek mythology. Zeus holds a smaller statue, Nike, the goddess of victory, in one hand, and an eagle in the other.
- The *Temple of Artemis*, a magnificent temple built in what is now modern-day Turkey, was intended to commemorate Artemis, the Greek goddess of hunting. The structure was decorated with the most ornate artwork of the day.

- The *Mausoleum of Halicarnassus*, also in Turkey, was created to honor the wife (and coincidentally the sister) of a governor named Mausolus, and also houses beautiful works of art.
- The *Colossus of Rhodes* was a 110 ft statue that welcomed seafaring visitors to the island of Rhodes.
- Finally, the *Lighthouse of Alexandria* guarded Alexandria Harbor in Egypt. Standing over 350 ft tall, it has been considered the prototype of lighthouses that were built since its construction.

All Seven Wonders were examples of superb intellect and creativity, as testimony to humankind's dedication and ingenuity, created in an age devoid of mechanization.

At about the time these ancient wonders arose, so emerged the concept of *professionalism*. One of the early role models of professionalism was Hippocrates, who lived and practiced medicine between the third and fourth centuries BCE. He is considered the "Father of Medicine," and helped transform the medical profession from a philosophical discipline to one of observation and reasoning. Although little is known about the extent of his contribution to the famous Hippocratic Oath, that document still serves as a conduct guide for the profession. We know that Hippocrates believed that disease was not caused by superstition but by natural causes, and that his emphasis on the physician's ethics was emphatic. His writings entitled *On the Physician* stressed that the physician should be "well kept, honest, calm, understanding and serious" (https://en.wikipedia.org/wiki/Hippocrates). At about the same time that Hippocrates was practicing medicine, Alexander the Great established the Alexandria Medical School in Egypt in 311 BCE. This institution continued the medical tradition of Hippocrates as well as that of Aristotle, who is credited with being the founder of the study of anatomy (https://en.wikipedia.org/wiki/Hippocrates).

During the Middle Ages the only three professional disciplines were the church, law, and medicine. Although many physicians of the time had no formal education, the Italian medical school of Salerno was established in the twelfth century in an attempt to formalize medical education. Founded by a Christian, an Arab, and a Jew, this diverse

and innovative medical school accepted women for study and remained independent of clerical dominance (Bishop et al., 2002). This was a rare circumstance for that epoch.

The concept of professionalism

The concept of professionalism continued to thrive as medical schools were founded over time. Dentistry eventually elevated its status from that of a trade. Originally practiced by unskilled individuals as an adjunct to other business endeavors such as barbering or blacksmithing, dentistry rose to a level where it was considered to be a specialized branch of medicine (https://en.wikipedia.org/wiki/Seven_Pillars_of_Wisdom). In the early 1800s in the United States there were approximately 1200 dentists, of whom 300 were physicians who decided to concentrate on practicing dentistry. They had learned clinical procedures by completing dental apprenticeships.

The nationwide financial collapse of 1837 affected dentistry as severely as the rest of the country's economy. Unemployed workers paid tuition fees to some dentists who touted themselves as dental educators, and graduates of these "programs" entered the profession with suboptimal skills, negligible clinical experience, and deficient knowledge of the profession. Yet those whose interest was to protect the profession saw the ensuing loss of public trust in dentistry as an opportunity to reinforce the level of professionalism. They established the first dental journal in 1839, the *American Journal of Dental Science*. These men also established a formal program for teaching dentistry in 1840 that was housed in the Baltimore College of Dental Surgery. This institution later evolved to become the University of Maryland's School of Dentistry. These same devoted dentists also formed the American Organization of Dental Surgeons as the nation's first dental society. Those who remained affiliated with the organization were considered the elite of the profession. All three of these efforts to establish dental professionalism occurred in a mere three years and elevated the status of dentistry as a profession. Although these events took place in the United States, they exemplify the rise of professionalism on a worldwide scale.

Fast forward to the twenty-first century. If professionalism evolved as an exemplar in healthcare, does the concept of professionalism prevail today? If it does, is it held in the same high esteem as it used to be, or is it doomed to deteriorate? And what is the pertinence of professionalism in the delivery of orthodontic care and in orthodontic education?

Most simply, professionalism is essential because our patients are placed in a position of *vulnerability*. Our patients readily place their trust in us, despite our initially brief contact with them as a stranger. Within a short period, they give us their physical selves, their emotional trust, and often a significant financial commitment despite their minimal initial exposure to us. Contrast this to the vast time and effort invested in establishing trust in an acquaintance in a social context. The vulnerability of the patient mandates that the provider commit to a *fiduciary relationship*, in which the provider holds the patient's interests and well-being above his or her own in an enduring, persistent fashion.

The seven pillars of professionalism

In 1926, the British colonel T.E. Lawrence, the fabled Lawrence of Arabia, wrote an autobiographical book entitled *Seven Pillars of Wisdom*. In his book, Lawrence recounted the experience of his military command of Bedouin forces in battle against the Ottoman Turks spanning 1916 through 1918. The book's title was developed from the Book of Proverbs (Proverbs 9:1), which states that "Wisdom hath builded her house, she hath hewn other seven pillars" (Scarlett, 1991).

If there were a majestic Seven Wonders of the World and Seven Pillars of Wisdom, might there be *Seven Pillars of Professionalism* that we can keep at the ready throughout our careers (Scarlett, 1991)? As time constraints, educational loan demands, family and financial obligations, and our quest for new cases start to loom over us, can we maintain the level of consistent professionalism and ethical discipline that has taken centuries to evolve?

Admittedly, the pressures the young practitioner or academician faces are unprecedented in the history of the specialty. In a 2015

letter to its members, the American Association of Orthodontists listed the salient factors that have strong contemporary influence on the orthodontic profession. Many were minimal or nonexistent a decade or two ago. Issues such as the decrease in restorative needs that entice nonorthodontists to provide orthodontic care, an increased number of orthodontic graduates, an increase in deceptive advertising, and an increase in self-treatment are examples. In this chaotic arena, a prominent dental educator asked an everlasting question almost a century ago: can we "combine the new economy with the old morality?" (Nash, 2014). The question is a global one. That is, can we maintain our elite professional stature, despite the financial demands we face in managing a practice or addressing the challenges of ascending the ranks of academia?

The Seven Pillars of Professionalism are intended to provide a practical framework for maintaining ethical conduct in parallel to our success, amid a world of temptations, distractions, and occasionally insurmountable pressures (Figure 26.1).

The First Pillar: Knowledge, technical skill, and a sense of pride in what we do

An old orthodontist once told me that most often our patients don't know what we do in their mouths. They judge us instead by obvious criteria: our demeanor, our staff's accommodation of their needs, the decor of our office, or whether we run on time. We can change elastomeric ties for months on end and tell them they are progressing nicely – even if the archwires have long since ceased to be active. We can ignore the position of their second molars. If they are scheduled for scans for retainers after a lower canine has rotated since its bracket was displaced, we can ignore it when they ask whether treatment is truly complete. Our patients might think that canine guidance is a veterinary term, and certainly cannot judge the harmony of marginal ridge relationships. Yet *we* know when we've done the best we can, or whether we have compromised case quality. The patient does not. Authentic professionals will push themselves to the limit and always feel they can do more – even when no one is overseeing or judging their performance or their result.

We spend years finessing our clinical skills and honing our diagnostic acumen during our lengthy educational process. But once in practice or at the podium as academics, our most severe critics should be ourselves. The more critical we are of the care we provide, the closer to the goal of excellence will be the result.

It has been said that a good orthodontist is an unhappy orthodontist (Greco, 2011). Those who can admit that they can always do better are those who realize that perfection is impossible, but excellence is within reach. That is the mark of an artist – and it should be the aspiration of every member of our specialty.

> *He who works with his hands is a laborer.*
>
> *He who works with his hands and his head is a craftsman.*
>
> *He who works with his hands and his head and his heart is an artist.*
>
> *(St. Francis of Assisi, disputed as the authentic source)*

Figure 26.1 The Seven Pillars of Professionalism.

Source: Bryan Faust / Adobe Stock.

The Second Pillar: Social responsibility

Ms. Wallace provides a custodial service to your office building. She is embarrassed by her appearance, and her main objection is understandably her proclined, spaced maxillary incisors. Her profile displays lower lip entrapment. Her presentation is that of classic posterior bite collapse. Furthermore, she experienced severe head trauma earlier in life, which resulted in a brain injury that limits her ability to ascend to a more lucrative career. Despite her modest income, her pride prevents her from enrolling in public assistance to help her meet living expenses. She vows that she will work as long as she is able, "without taking any charity from the government." She had enrolled for general dental care in the university where you teach, but fell into arrears due to several unforeseen financial demands that have recently dominated her budget. You offer to provide orthodontic therapy for her at no fee so that she can receive partial dentures from the university, but she requires more preliminary dental treatment before you can begin. Yet the dental school will not allow completion of the operative dentistry she needs until she resolves the outstanding balance from previous care she received. Her dialog with you confirms that she does not have the money to settle the charges she has accumulated at the university.

Unbeknown to her, the next time you are teaching at the university you stop by the financial office. You are told that she will be reassigned to a student if she can pay her outstanding account. After just a minute's hesitation, you take out a check and pay her remaining balance from your personal funds.

A week later as you are leaving your office, you encounter Ms. Wallace in the elevator. You are surprised when she breaks into tears at the sight of you. These are tears of gratitude and appreciation. The dental school has contacted her and informed her that you were her benefactor. They encouraged her to make an appointment for treatment as soon as possible.

Your ride home that night was a fine one for sure.

We are indeed blessed to live in this era and, moreover, to have found a profession that is among the most fulfilling in the world. When we delight in both performing service to others and

simultaneously earn a comfortable living, we become fulfilled from multiple perspectives. Perhaps the best way to display our gratitude for our good fortune is to pay forward to other individuals, to other families, and to society.

It is estimated that 5% of all dental care is provided on a *pro bono* basis. This equals the combined dental expenditures of Medicaid, prison populations, uniformed, and Native American health services combined (Chambers, 2015). Our benevolence toward others, using the skills we have developed, is a significant way to express our thanks for all that we have.

Columnist/author David Brooks captures the feeling of gratitude that might embrace us as members of a privileged profession:

> *Gratitude is also a form of social glue. In the capitalist economy, debt is to be repaid to the lender. But a debt of gratitude is (also) repaid forward to another person who also doesn't deserve it. In this way, each gift ripples outward and yokes circles of people in bonds of affection. It reminds us that a society isn't just a contract based on mutual benefit, but an organic connection based on natural sympathy – connections that are nurtured not by self-interest, but by loyalty and service.*
>
> *(Brooks, 2015)*

The Third Pillar: Appreciation of our legacy

Orthodontics was the first official dental specialty and the third medical specialty, only preceded by ophthalmology and otolaryngology. Since the specialty's founding in 1900, a cadre of orthodontic clinicians and educators have worked in earnest to advance the level of patient care through experience and science. The authentic attempts to establish diagnostic and treatment regimens based on evidence-based information continue to this day. Exemplary individuals have emerged that stood as mentors to a long line of subsequent academicians and clinicians. We are forever indebted to our specialty's ancestors who served as luminaries and visionaries. They did so by elevating and maintaining our image within the dental and medical communities. Each of us carries

mental images of these icons who preceded us as we navigate through our careers at the chair or at the podium in the lecture hall.

By definition, professionals embrace a specialized field of knowledge achieved by a university-based or organized education. This status carries certain responsibilities to which professionals are held. For example, professionals have the responsibility to remain current in the advancements in their field. Professionals are educated and mentored by individuals who are members of the same profession, and who are able to serve as arbiters in times of conflict. The challenge of being professional holds the requirement that emphasis on service should always override the quest for profit. The obligation to uphold this value can result in a conflict between doing what is right for the patient and doing what is advantageous for oneself. Professionals are bound by a code of ethics that defines their positive behavior, and this code elevates the profession from both collegial and public perspectives. In return, society grants the profession the autonomy to govern itself without significant influence from external sources. Society also allows the profession the freedom to determine those who are accepted into its ranks, as well as to independently discipline its members if need be (Garfunkel and Cohen, 2018).

Those within our legacy have opened the door of opportunity for each of us by accepting us into their programs. The chance they provided allowed us to prove that we were worthy of their trust in us. We are each responsible for upholding that trust – not only by excelling clinically and academically, but also by maintaining the ethical responsibility that defines our legacy.

We so often hear our mentors' voices or adages in our minds as we treat patients or lecture to our residents: "Don't be afraid to see the backs of their heads" in the case of patients who are sure to bring us monthly misery, or "Activate that closing loop the width of a thin dime." A favorite is "The worst thing that can happen to a resident is for things to go right!" The thinking is that the learning process is enhanced by an unpredicted treatment response. The unexpected result encourages thought and creativity to produce a solution. Each of us can recall an array of axioms for guidance, but the universal intent of the mentor is/was to instill lifelong guidance for action. Our faculty were and will always be our role models. They emphasized

that the interests of the patient come first, without the priority of financial gain. They not only taught us how to retract upper incisors, but moreover how to set priorities and interact appropriately with patients and colleagues.

> *We do not remember Martin Luther or Abraham Lincoln in the true physical sense. What makes us akin to them lies in the bond we feel through the principles and ideals they taught and stood for.*
>
> *(George Hahn, Angle School Class of 1921)*

The Fourth Pillar: The Golden Rule

Susan returns to your office two months after debonding. She is barely aware that the incisal edges of the upper central incisors are now irregular in height. Your final records confirm that her smile arc and incisal edge relationship were perfect at debonding. Your first thought was that she did not wear her maxillary retainer, but she confirms that she has diligently worn it. Yet the teeth moved. A quick perusal of her initial records confirms a mild anterior open bite with the same irregular incisal relationship that she now displays. You offer to retreat her at no fee and she accepts, this time planning a fixed retainer to decrease the potential for future relapse. A tongue crib for bedtime wear is also suggested for further protection against relapse.

Do we treat others as we want to be treated, as if he/she were our daughter, son, or sibling? In the clinical arena, do we respect our patients' vulnerability with honesty? When patients place themselves in our hands, do we respect the trust they invest in us?

The Golden Rule is universal, regardless of creed:

- Judeo-Christianity: "Do unto others as you would have them do unto you."
- Islam: "Wish for your brother what you wish for yourself."
- Hinduism: "One should never do that to another which one regards as injurious to oneself."
- Buddhism: "Just as I am, so are they; just as they are, so am I."

A frequent violation of the Golden Rule is a professional's failure to reply promptly to correspondence from a patient, colleague, or any other individual. Once a patient is under our care, it is our strict obligation to return phone calls, texts, emails, or other forms of correspondence that pertain to the patient's welfare. One need only place oneself in the patient's position to sense the importance of – at the very least – a prompt and authentic intention to respond. In fact, this is a common courtesy owed to any human being.

As the allure of technological advances evolves, the concept of the "centrality of the patient" should always prevail, in which the patient's welfare always supersedes the clinician's convenience, ease, or the speed of treatment delivery (Garfunkel and Cohen, 2018; Johnson and Ridley, 2008). Most patients cannot be treated with a "one-shoe-fits-all" philosophy in which therapy is prescribed according to the revenue it generates or the simplicity of delivery. And discriminating patients perceive, respect, and value the authentic level of compassion we maintain in respect to their needs.

The Fifth Pillar: Personal integrity

James, who is 7 years old, is the docile grandson of the senior partner of your city's most prominent law firm. This affluent family owns almost the entire next block of real estate near your office. Despite the end-to-end transverse relationship of the right first permanent molars, the remainder of James's dentition and profile are developing within normal range. His parents tell you that they'll do whatever you recommend, regardless of cost, because he is their only child and they "can afford it." They also wish to exhaust their health shelter account as soon as possible.

You are momentarily tempted to place a maxillary expander to utilize the family's offer, but realize that the problem might resolve without intervention and could also be addressed during future comprehensive correction. So you place James on an appropriate surveillance schedule and continue to monitor his growth and development.

Integrity represents the core of professional ethics (Beauchamp and Childress, 2007). It is the litmus test of character, especially in the

face of temptation or adversity. Integrity is the root of confidentiality and the impetus for respect of patient vulnerability. Integrity encompasses the ability to admit one's errors, leading to prompt fulfillment of the ethical principle of reparation without qualification or accusation.

The commitment to care for another individual consists of five principal virtues: integrity, compassion, discernment, trustworthiness, and conscientiousness (Beauchamp and Childress, 2007). Integrity reigns supreme over them all. Assessing a high treatment fee or initiating unnecessary therapy, based predominantly on a patient's financial ability, is to disregard the virtue of integrity.

Orthodontic treatment is most often elective. Thus, the ubiquitous question of whether to treat or not to treat frequently arises. Issues such as "Do I start early treatment now, or rely on continued surveillance?" and "Will this temporomandibular disorder issue resolve spontaneously, or do I need to intervene immediately?" are examples. The following criteria are integral when seeking justification for the need to intervene (Gross, 2001):

- Will the problem get worse if treatment is not performed?
- Does the treatment have valid clinical value?
- Would a less involved procedure solve the problem?
- Does the risk/benefit ratio justify the invasiveness of the procedure?

Should there be insufficient evidence to answer any or all of these questions affirmatively, the patient must be informed. *Shared decision making* is the process of initiating collaborative treatment planning decisions between the patient and the doctor using available evidence. This interaction is essential in determining the need for further diagnostic procedures or whether treatment should be initiated. Shared decision making involves full disclosure of the risks and benefits of treatment, including the option of eliminating any treatment endeavor. It incorporates the patient's preferences. Shared decision making balances paternalism with full autonomy, and respects the *ethical imperative* – the individual's obligation to

act with respect for ethical and moral principles inclusive of the following (Beauchamp and Childress, 2007):

- *Autonomy* in the form of shared decision making, incorporating the patient's consent to treatment.
- *Beneficence* or providing significant benefit to the patient.
- *Nonmaleficence* or doing no harm, inclusive of demonstrating adequate competence in any procedures provided.
- Respect for *justice*, which is the appropriate distribution of costs and availability of treatment (Stiggelbout et al., 2012).
- *Veracity* (truth telling) is also upheld when the patient remains accurately apprised of the positive and negative effects of potential treatment.

Sir William Osler, one of the most famous physicians of all time and one of the co-founders of the Johns Hopkins School of Medicine, stated: “Medicine is a science of uncertainty and an art of probability” (brainyquote.com/quotes/william_osler_159326). Orthodontics is no more and no less. The patient should know that although there are no guarantees of the level of therapeutic outcome, our treatment plan should be a sincere and concerted effort to fulfill whatever objectives have been disclosed to the patient.

Comparison of the “culture of dentistry as a profession versus dentistry as proprietary” stresses that we cannot allow dentistry or orthodontics to become merely another way of making money, akin to any other mundane business endeavor (Nash, 1994). If that occurs, orthodontics becomes a commodity that depersonalizes and devalues both the practitioner and the patient. Price wars evolve and professional status becomes seriously challenged, as we revert to the level of a competitive bidding war for the patient’s engagement with our service. When success is measured solely by financial gain rather than the quality of the treatment result, we begin to conclude that patients do not discriminate between levels of quality. They accept whatever is cheaper, regardless of quality. Our image deteriorates to that of entrepreneurial merchandisers, and our legacy as professionals is severely challenged.

The Sixth Pillar: The meaning of life

Aidan is the youngest member of the McCormick family and has just commenced comprehensive therapy to resolve his severe overjet. He is well motivated to cooperate in any way he can, since he suffers from peer ridicule for his appearance. His father is a city employee whose work schedule, based on shift work, lends itself to shuttling Aidan to your office on a regular basis. The family values your expertise and your commitment to quality. Aidan soon becomes a model patient. Soon after you begin Aidan's treatment, his father is tragically killed in an automobile accident. Mrs. McCormick is not employed and the family is understandably devastated. You convey your condolences by attending the funeral. While there, it becomes obvious to you that there is little financial support available for them given the family's modest means. As you drive home from the funeral, you decide to forgive Aidan's entire treatment fee. The family is ecstatic, and a week later you receive a wonderful thank-you letter for your good deed, signed by Aidan, his two brothers, and his mother.

One of my most cherished professors once told me that our main mission as orthodontists – and our life's mission as humans for that matter – is to make others happy. There are few more direct roads to professional fulfillment than providing resolution of pain, succeeding in improvement of an individual's self-image, or receiving appreciation for a deed well done. Orthodontics provides ample opportunity to accomplish all of these and more, as well as the ability to earn a comfortable living. Yet our fulfillment in our delivery of care reaches far beyond bolstering our bank account.

As the saying goes, "Some cause happiness wherever they go, and others whenever they go" (https://www.goodreads.com/quotes/1347349-some-cause-happiness-wherever-they-go-others-whenever-they-go). Our role should be seen as bringing happiness to others, and our own generosity is one sure way to achieve that goal.

The Seventh Pillar: Humility

You are bending a lower closing loop at the next chair when you hear the yelp. Helen, your assistant, was placing a separator for the delivery of Kevin's lower lingual holding arch when the separator split and the plier gauged his sublingual and vestibular tissue. You immediately approach Kevin's chair and put him at ease. The tissues were traumatized by the procedure. Although it was not you who was involved in the misadventure, you know that you are ultimately responsible for the incident. You call Kevin's mother into the operatory, explain what happened, and promptly apologize. You encourage him to see the oral surgeon in the building and offer to reimburse the family for any fees related to the injury.

Humility takes many forms in clinical practice and in academia. Certainly the phrase "I don't know" in reply to an inquiry by a patient or a parent in the clinical setting, or to a resident in a seminar, is not an embarrassment or diminution of scholarly status. An instructor's offer to answer a complex question once he or she has had an opportunity to review the literature is a humble gesture. Identifying an appropriate professional referral for a patient whose treatment needs are beyond one's experience or expertise is both noble and humble.

Admitting errors along with an apology is another example. Misadventures or errors can have negative effects on the provider by invoking feelings of loss of confidence, ego violation, embarrassment, or fear of litigation (Greco, 2012). Apologies help to mitigate all of these perceptions. Apologies for a clinical error restore a patient's self-respect by diminishing patient humiliation, reaffirming trust, and confirming that he or she remains in safe hands. Injuries related to therapy are especially traumatic because the patient has invested trust in the provider. When a therapeutic error is made, the patient might infer that this trust has been violated (Vincent, 2003; Leape, 2005; Greco, 2012). And the academician who provides misinformation might fear inadequacy or a threat to his or her reputation. Clarification of an inaccurate statement made in a seminar or the classroom signifies that the lecturer values accuracy and is authentically interested in disseminating only factual information.

Apologies can provide veracity and are not considered to be an admission of guilt. Studies have shown that apologies do not increase a practitioner's vulnerability to a lawsuit. In an effort to encourage physicians' apologies, there are 34 states as well as the District of Columbia that disqualify an apology as admissible evidence in malpractice cases (Saitta and Hodge, 2011).

Do we have the humility to admit our appreciation that it is a vast honor to become a member of this highly constructive and fulfilling profession? Brooks defines *dispositional gratitude* as a personality characteristic of individuals who are naturally inclined to express gratitude for all they have. These people see life's gifts as more than they deserve (Brooks, 2015). They are people who are not only motivated by the universal urge for self-gain, but are also empowered by their sympathy and empathy for others. They are good citizens because they find motivation in service and in "paying forward." They accept the fact that they will continually be dependent on their relationship with other individuals to achieve a successful and fulfilling life of their own. That is humility and gratitude combined.

There is perhaps no other medical or dental specialty in which one can influence a patient's life as profoundly as ours. Our constructive service is achieved within a work atmosphere of happiness rather than one of misery, anxiety, and gloom. We are endowed with a *fiduciary responsibility* that places our patients' interests above our own. The most gracious – and most humble – among us are adept at accomplishing this.

Humility is also essential to intellectual growth. Humility breeds self-improvement. Humble people are never satisfied with what they know. They remain perpetual students and accept their role as lifetime learners.

> *The fool doth think he is wise, but the wise man knows himself to be a fool.*
>
> *(William Shakespeare, As You Like It, Act V, Scene 1)*

Our public image of professionalism

A final but very important note for practitioners of all levels of experience: Our public image of professionalism needs to be upheld

to prevent it deteriorating to that of merely skilled tradesfolk engaged in the mundane *business* of orthodontics. The value we place on humility is reflected in the way we portray ourselves to the public. One example of the projection of our image is in advertising. It is therefore essential to maintain our level of professionalism through humility – especially in advertising – to sustain our professional image.

Four levels of professional advertising have been clearly defined by Graskemper (2019):

- *Comparable advertising*. This is seen as unethical because it involves comparison between two similarly educated/credentialed individuals, and thus can result in misinterpretation by the public. It can create an inference of superiority, devoid of humility, and is thus misleading. A statement such as “Dr. X is the only Board-certified orthodontist in the city of Nicetown” is an example.
- *Competitive advertising*. This involves offering additional services, discounts, or other perks in an effort to attract/solicit/enlist patients. The acceptability of this form of advertising varies within jurisdictions, but it does little to elevate the public's perception of our level of professionalism. “Free diagnostic records at initial visit” and “Five-hundred-dollar discount for initial examination until the New Year” are examples. Again, this is advertising that is heavily slanted toward commercialism.

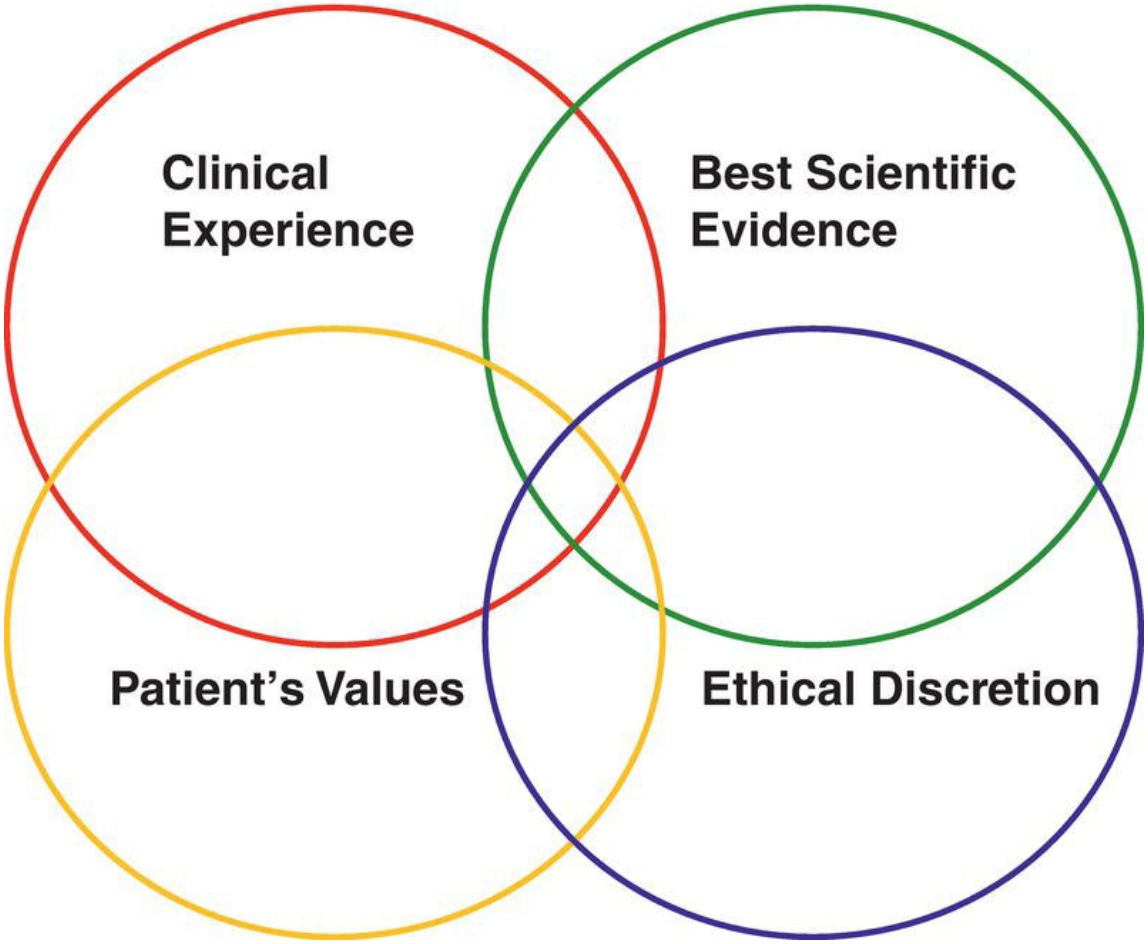

Figure 26.2 Optimal medico-dental care, including orthodontic therapy, involves the interplay of several key factors.

- *Informational advertising*. This informs the public of the provider's professional philosophy, credentials, and details about office policies such as location, hours, and so on. It is considered the most ethical form of advertising and complies with state and local ethical codes. It projects a factual, humble image.
- *Advertisements in "bad taste."* These advertisements might be classified as marginally ethical, but certainly convey a poor or inappropriate image of dentistry or the specialty. They fail to elevate the image of professionalism.

The hallmarks of authentic professional care are interwoven like the links of a chain (Figure 26.2). All four elements are essential to the specialist's respect for patient vulnerability and trust. The first link is

evidence-based practice, based on best scientific evidence. This link is intimately coupled with *clinical experience* as indispensable keys to diagnosis, treatment planning, and care delivery. An *appreciation of the patient's values* contributes to shared decision making via the patient's participation, with authentic respect for the patient's vulnerability. Equally important is appreciation of *ethical principles* and virtuous behavior, with integrity as the figurehead.

Now, what about those Seven Wonders of the World: Where are they now?

Unfortunately, six have been destroyed by plunder, weather, or earthquakes. Only the Great Pyramid of Giza has endured the test of time. Our supreme responsibility as a specialty is to ensure that the Pillars of Professionalism or values akin to them, unlike the Seven Wonders of the World, will endure the test of time for future generations of our specialty.

Heraclitus was not the last visionary to proclaim that change is inevitable. It certainly is. But if we believe that the pillars of ethics are essential to support the pillars of professionalism – if there is any role for stability in our values – let it emanate from the behavior we exhibit as we represent our specialty.

While change is inevitable, the challenge to expend the effort to preserve and nurture the glorious gift we have received is in our hands. If we do not accept that commitment, orthodontics will be doomed to mediocrity or, even worse, to obsolescence.

We must never let that happen.

References

Beauchamp, T., and Childress, J. (2007). Moral character. In: T.L. Beauchamp and J.K. Childress, *Principles of Biomedical Ethics*. New York: Oxford University Press, ch. 2.

Bishop, M.G., Gibbons, D., and Gelbier, S. (2002). Ethics; "in consideration of the love he bears." Apprenticeship in the nineteenth century, and the development of professional ethics in

dentistry. Part 1. The practical reality. *British Dental Journal* 193(5): 261–266. doi: 10.1038/sj.bdj.4801540.

Brooks, D. (2015). The structure of gratitude. *New York Times*, July 28. https://www.nytimes.com/2015/07/28/opinion/david-brooks-the-structure-of-gratitude.html.

Chambers D.W. (2011). Ethics fundamentals. *Journal of the American College of Dentists* 78(3): 41–46.

Garfunkel, A., and Cohen, D. (2018). Dental technology must not supersede centrality of the patient. *Compendium* 39(1). https://www.aegisdentalnetwork.com/cced/2018/01/dental-technology-must-not-supersede-centrality-of-the-patient.

Graskemper, J.P. (2009). Ethical advertising in dentistry. *Journal of the American College of Dentists* 76(1): 44–49.

Greco, P.M. (2012). When to say "I'm sorry." *American Journal of Orthodontics and Dentofacial Orthopedics* 141(6): 674–675. doi: 10.1016/j.ajodo.2011.11.010.

Greco, P.M. (2014). Ethics in orthodontics. No way out. *American Journal of Orthodontics and Dentofacial Orthopedics* 145(4): 421. doi: 10.1016/j.ajodo.2014.01.009.

Gross, R. (2001). *Decisions and Evidence in Medical Practice*. St. Louis, MO: Mosby.

Johnson, W., and Ridley, C. (2008). Taking the high ground. In: W. Johnson and C. Ridley, *The Elements of Ethics for the Professional*. New York: Palgrave Macmillan, pp. 1–2.

Leape, L.L. (2005). Understanding the power of apology: How saying I'm sorry helps heal patients and caregivers. *Focus on Patient Safety: Newsletter of the National Patient Safety Foundation* 8: 1–3.

Nash, D.A. (1994). A tension between two cultures … dentistry as a profession and dentistry as proprietary. *Journal of Dental Education* 58(4): 301–306.

National Geographic (n.d.) Seven wonders of the ancient world. https://education.nationalgeographic.org/resource/seven-wonders-ancient-world.

Saitta, N.M., and Hodge, S.D. (2011). To apologize for an unforeseen medical complication—a primer on apologies laws. *Pennsylvania Bar Association Quarterly July*: 93–110.

Scarlett, E. (1991). What is a profession? In: R. Reynolds and J. Stone (eds.), *On Doctoring*. New York: Simon & Schuster, pp.119–133.

Stiggelbout, A.M., Van der Weijden, T., De Wit, M.P. et al. (2012). Shared decision making: Really putting patients at the centre of healthcare. *BMJ Clinical Research* 344: e256. doi: 10.1136/bmj.e256.

Vincent C. (2003). Understanding and responding to adverse events. *New England Journal of Medicine* 348(11): 1051–1056. doi: 10.1056/NEJMhpr020760.

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