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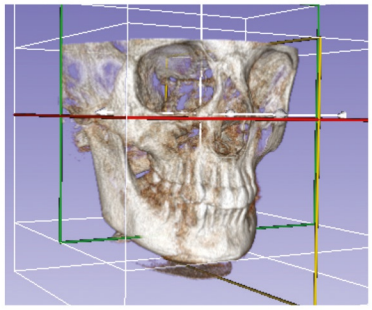

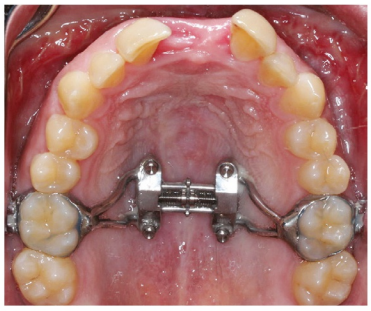

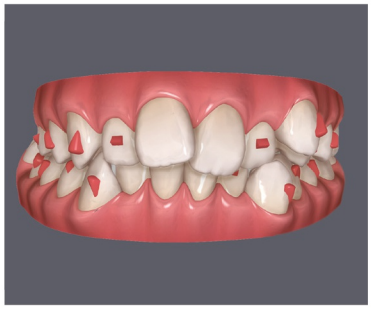

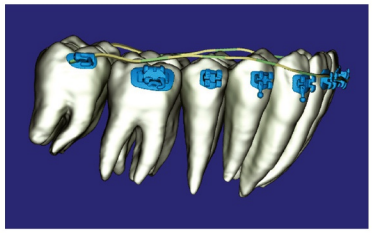

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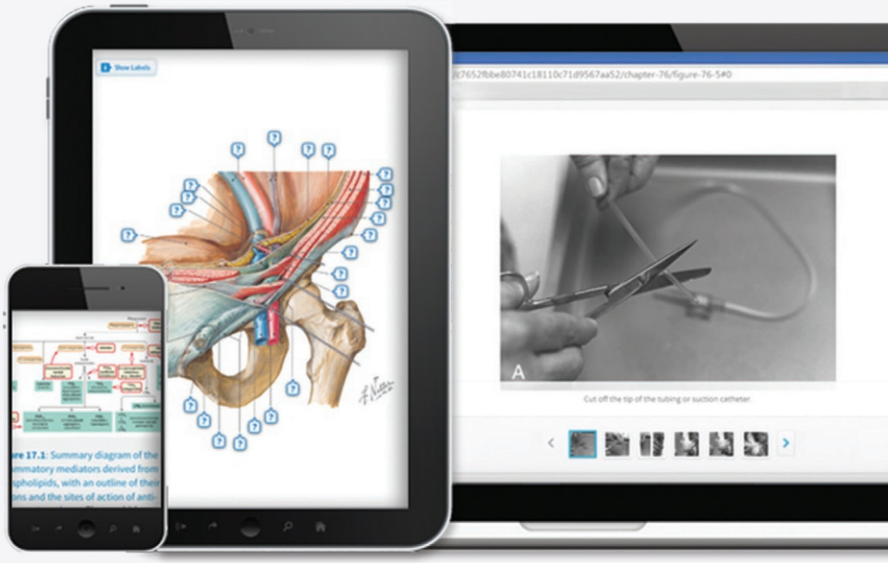

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DEDICATION

Robert L. Vanarsdall, Jr., DDS

It Is Never Too Late to Remember and Give Thanks

This 7th edition of *Orthodontics: Current Principles and Techniques* is dedicated to its long-time co-editor, Robert L. Vanarsdall, better known by his colleagues as "Slick." Slick passed away shortly after the publication of the 6th edition of this textbook, but his influence on the scope of this edition and indeed the specialty of orthodontics remains current today. For those who did not know Dr. Vanarsdall and even those who were privileged to know or even work with him, we want to share a picture of who Slick was and his manifold contributions.

Robert Lee Vanarsdall was born in 1930 in Crewe, a small town in south-central Virginia. Named after his father and carrying the historic name of a southerner, as a child and teen he demonstrated an outgoing nature and an affinity for being well dressed and polite. "Slick" was the name he reportedly was given by a local clothing store where he bought his clothes, always looking to be neat and stylish and becoming a trend setter with his peers. The name stuck, as did an expanded scope of leadership.

Slick graduated from the College of William and Mary and in 1962 married his college sweetheart, Sandra Hoffman. Slick's love for international travel developed after joining the United States Navy (1962), in which he served as a lieutenant, returning for his dental education and graduating from the Medical College of Virginia in 1970 with a DDS, but knowing he wanted to specialize. Dr. Vanarsdall often spoke of how "lucky" he was to be the first student at the University of Pennsylvania School of Dental Medicine to graduate with a combined orthodontic and periodontal specialty education in a then unique program developed by innovative dental educator and school dean, Dr. Walter Cohen. Slick subsequently was board certified in both Periodontics and Orthodontics, becoming an examiner for the American Board of Orthodontics.

On completion of his dual dental specialty education, Slick joined the Penn faculty initially as a teaching fellow and rose through the professorial ranks while further developing the postgraduate individual and combined orthodontic and periodontic specialty programs. He became chair of the Department of Periodontics and, later, the Department of Pediatric Dentistry. Slick directed the Department of Orthodontics for almost 30 years, serving as department chair until 2011. He continued to actively teach, practice, and lecture internationally until his passing.

During an academic career that spanned 44 years, Dr. Vanarsdall was a prolific writer with more than 100 papers and 12 book chapters. He served on multiple editorial boards and was editor-in-chief for the *International Journal of Adult Orthodontics and Orthognathic Surgery* for 17 years. In 1994, Slick joined Tom Graber as co-editor and a chapter author in the 2nd edition of this textbook published by Mosby-Elsevier. He continued in that role until the 6th edition published in 2017 (the initial text was published in 1969 by W.B. Saunders). Dr. Vanarsdall also was a co-editor and author in a comprehensive textbook on the use of implants for orthodontic anchorage, titled *Applications of Orthodontic Mini Implants,* with co-authors J. S. Lee, J. K. Kim, and Y. C. Park, all of whom remain recognized chapter authors in this 7th edition as well.

Dr. Vanarsdall was active in professional associations as a participant speaker and organizer. He lectured all over the world and was awarded every major honorary lecture. He chaired multiple local, national, and international professional meetings, including the 1994 and 2002 American Association of Orthodontists (AAO) Annual Sessions. He was a member of numerous committees and boards, including the AAO's Council on Scientific Affairs, for which he served as chair. An active contributor and member of the Eastern Component of the Edward H. Angle Society of Orthodontists, he served as its president from 2004 to 2005. Slick was the recipient of numerous national and international awards for his academic work, topped by the American Association of Orthodontists Foundation highest academic award, the Jarabak Memorial International Teachers and Research Award (2017).

Although Dr. Vanarsdall was an outstanding mentor to his students, he was even a better friend to them and his colleagues. Dr. David Musich, a longtime chapter author in this book, tells the story of receiving a patient transfer of a 16-year-old with an ankylosed/impacted canine and getting an offer of help from Slick. "This was her 4th surgery on that tooth. She was anxious—so was her mom. After 10 minutes of explanation and 35 minutes of gentle luxation, the tooth moved, and it was free to be moved into the arch. It was Slick's genuine compassion and caring spirit that allowed this young lady to finally have her canine positioned. As a clinician, he was a true artist and unique as a colleague." Important to note is that Dr. Vanarsdall flew halfway across the country just to help with this one patient and colleague. It was not unusual for Dr. Vanarsdall to share his expertise with colleagues and students, distant from the site and approbation of others.

What is extraordinary about the contributions of this dedicated teacher and clinical research scientist? Dr. Vanarsdall had the ability to come to clinical issues with an open mind. At a time when specialty orthodontics was directed at adolescents, he looked to how adult dental care could be enhanced, even in the face of periodontal concerns. In a specialty then focused on anteroposterior discrepancies, with diagnosis and treatment often driven by lateral cephalometric measures, he looked to enhanced diagnosis and therapeutics by way of the transverse dimension. He was one of the first to present patients treated with surgical arch expansion and many other clinical approaches we now use routinely. Lest we forget, he changed the way that the specialty of orthodontics is practiced today.

Author, clinician, teacher, scientist, innovator, researcher, lecturer, administrator, world traveler, practitioner, humanitarian, mentor, husband, father, friend. We all were bettered by Slick! It is never too late to remember and give thanks.

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PREFACE

Nothing is known in our profession by guess; and I do not believe, that from the first dawn of medical science to the present moment, a single correct idea has emanated from conjecture. . . .

Sir Astley Paston Cooper

Since the publication of the previous (6th) edition of *Orthodontics: Current Principles and Techniques* our specialty and the wider world have witnessed dramatic change, disruption, adaptation, and renewal. The 7th edition reflects this period of rich ingenuity and continues to be a valuable, comprehensive resource for the contemporary orthodontic specialty student and practitioner.

As in our previous editions, the goal is to target a readership of Orthodontic Residents and Specialist Orthodontic Practitioners. Excellent textbooks already exist to educate dental students in the fundamental knowledge and basic concepts and principles of orthodontics, which every dentist should have assimilated in dental school. Orthodontics, after all, is an integral part of dentistry that should be considered by generalists and other specialists in a team approach to oral health care.

We are delighted that the 7th edition continues to be used in Graduate Orthodontic programs throughout the world. This has been further facilitated by translation into multiple languages, permitting global distribution in educational settings and beyond. For graduate orthodontic programs and orthodontic specialist education, the 7th edition is available in an "eBook" format. Availability through a website and as a searchable reference text allows rapid access to clinical topics and access to fresh information in a fast-paced and rapidly changing technological world.

In this edition, we acknowledge the increasing focus on the expanding armamentarium at our disposal, including fixed sagittal correctors, bone-borne expanders, in-house aligners, autotransplantation, and computer-assisted diagnosis and treatment. Our aim has been to update the content to reflect contemporary orthodontic specialty practice, while retaining a strong theoretical and evidence-based underpinning. The opportunity to move some sections to an online format has allowed us to address more topics without substantially increasing the physical size of the book.

Given our expressed aim of providing a holistic review of our specialty from both clinical and theoretical perspectives, an overview of the history of orthodontics has been introduced. Classic chapters and case reports have been moved online, which allows us to more fully provide a historical perspective while focusing on current principles and techniques.

The pandemic-related shutdown in dental practices early in 2020 spawned creative new technology, including programs that allow us to virtually meet with patients and monitor their progress. The reintroduction of chairside practice in the summer of 2020 was accompanied with a keen focus on the generation, behavior, and mitigation of aerosols. A new chapter provides valuable insights into the topic of aerosols in orthodontic practice.

The accelerated development of new techniques and materials places ever-greater onus on the conduct and appreciation of high-quality, independent clinical trials. Moreover, the wider availability of information and ever-increasing pool of journal articles places a premium on the ability of both residents and seasoned practitioners to digest research findings and ascertain whether and when to implement new or revised treatment approaches. A new chapter dedicated to evidence-based orthodontics is a valuable resource for all. Likewise, Machine Learning and Artificial Intelligence are rapidly being integrated into orthodontics, enhancing our ability to predict, plan, and analyze tooth movement and soft tissue response. Increased use of computers for diagnosis, treatment planning, and robotics are certainly part of our future, and this is embraced in a new chapter on Artificial Intelligence and Big Data as applied to Orthodontics, as well as an updated chapter on Computer-Assisted Orthodontics.

We think that this 7th edition continues to recognize the global nature of the orthodontics specialty, which is reflected in a larger pool of international authors. Some of the topics covered by our international colleagues include autotransplantation, orthodontic-periodontic relationships, orthognathic surgery, interdisciplinary adult treatment, fixed functional appliances, biomaterials, and temporary anchorage devices.

The chapter on craniofacial dysmorphology and cleft lip and palate has been completely revised and updated with the inclusion of advanced methods of neonatal maxillary orthopedics for hospital-based orthodontists and residents enrolled in craniofacial fellowship programs. An aspect of interest for the orthodontist is the inclusion of a speech and language pathologist, describing the effects of adolescent growth and surgical maxillary advancement on velopharyngeal mechanisms. Likewise, the chapter on airway considerations in orthodontics has been revised to reflect advances in knowledge over the past 5 years.

In this new edition of the textbook we are delighted to welcome a new, talented editor and author, Padhraig Fleming. Padhraig is our first Europe-based co-editor. He has been Professor and Postgraduate Training Lead in Orthodontics at the Institute of Dentistry, Queen Mary University of London and in the summer of 2022 was appointed to a new position as Professor and Chair of Orthodontics, Dublin Dental University Hospital, Trinity College Dublin, Dublin, Ireland. He is also an Associate Editor of the *American Journal of Orthodontics and Dentofacial Orthopedics,* the *British Dental Journal,* and the *Journal of Dentistry and Progress in Orthodontics* and is on the editorial board of numerous other journals.

We are greatly indebted to each of our chapter contributors for their invaluable input. We sincerely hope that we have succeeded in doing full justice to the meteoric change that our specialty has witnessed over the past years while helping to perpetuate the fundamental principles and knowledge that we are certain will never lose relevance or import.

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The History of Orthodontics… From an Idea to a Profession

David L. Turpin and Norman Wahl

Today, the specialty of orthodontics is looked upon by the public with respect and even admiration. There are at least 30 English-language journals whose primary focus is orthodontics. Most orthodontists, though, know little about the struggles that took place when the profession was in its infancy. In the last half of the 19th century, orthodontics was not viewed as a specialty of dentistry, and Angle even speculated that it was destined to become a specialty of medicine. At that time the mechanisms of tooth movement were a complete mystery. We have certainly come a long way.

Some of the developments in our specialty are particularly impressive. For example, the perfection of fixed appliances was far ahead of the many contributions made in later years to assist with diagnosis and treatment planning. The use of enamel bonding has almost eliminated the need for metal bands, the application of orthognathic surgery has widened the envelope of correction, and a better understanding of the biology of tooth movement and growth have all had a profound impact on our work. One has to believe that the publication of scientific journals for the past 100 years has also played a major role in disseminating ideas and knowledge and in helping to bring many of these ideas to fruition.

In recognition of the rich history and ongoing improvements in our specialty, Norm Wahl and I were asked by the editors of this 7th edition to compile a history of orthodontics, starting from the middle of the 19th century. To tell this story, we highlight many of the careers of prominent educators and clinicians who have contributed to the development of orthodontia, or *orthodontics* as we now know it. We hope that the inclusion of this chapter will not only shed light on our profession's development but also serve as a pleasurable "read."

PRE-1900 DEVELOPMENT OF THE ORTHODONTIC SPECIALTY

At this time in history, many questioned whether teeth could be moved safely to new positions. Would the pulps remain vital? Would the uncompleted roots of growing teeth be bent? Would tooth longevity be affected? It would take pioneering dentists, working without the benefit of graduate training, to build the body of orthodontic knowledge brick by brick. Kingsley pioneered cleft-palate treatment. Case showed us the importance of facial esthetics. Dewey and Ketcham created the American Board of Orthodontics (ABO), the first certifying board in dentistry. But it was Edward H. Angle, the Father of Modern Orthodontics, who gave us our first school, journal, society, and practical classification of malocclusion.

THE PROFESSIONALIZATION OF ORTHODONTICS

Dentistry's first specialty organization, the Society of Orthodontists, was formed in 1900, and the first specialty journals began to appear. In the 1930s, creative thinkers in orthodontics began to more openly question the status quo. Apprenticeships had given way to formal instruction, and proprietary schools bowed to graduate university programs, including some taught or headed by women. Edward Angle was elected president of the society in 1900, and the first annual meeting was to be in St. Louis the following June. During its first year, the fledgling society claimed only 13 members.

THE AMERICAN BOARD OF ORTHODONTICS, ALBERT KETCHAM, AND EARLY 20TH-CENTURY APPLIANCES

Early in the past century, three events put Colorado in the orthodontic spotlight: the discovery—by an orthodontist—of the caries-preventive powers of fluoridated water, the formation of dentistry's first specialty board, and the founding of a supply company by and for orthodontists. Meanwhile, inventive practitioners were giving the profession more options for treatment modalities, and stainless steel was making

its feeble debut. Angle led the way, designing the expansion (E) arch around 1900, which was the precursor to our modern brackets.

MORE EARLY 20TH-CENTURY APPLIANCES AND THE EXTRACTION CONTROVERSY

The trying conditions of the Great Depression and World War II did not deter innovative orthodontists from adding new appliances to our armamentarium. Clinicians became fragmented into various "camps." Silas Kloehn's neck gear became a more patient-friendly version of extraoral anchorage, but it still had drawbacks. Angle's stranglehold on the specialty was finally broken when four of his disciples advocated extractions as a reasonable option to be considered in patients with crowding and/or protrusion.

THE CEPHALOMETER TAKES ITS PLACE IN THE ORTHODONTIC ARMAMENTARIUM

After World War II, cephalometric radiography came into widespread use, enabling orthodontists to measure changes in tooth and jaw positions produced by growth and treatment. Cephalometrics revealed that many malocclusions resulted from faulty jaw relationships, not just malposed teeth, and made orthodontists wonder if it was possible for jaw growth to be altered by orthodontic treatment.

FUNCTIONAL APPLIANCES TO MIDCENTURY

The history of functional appliances can be traced back to 1879, when Norman Kingsley introduced the "bite-jumping" appliance. In the early 1900s, parallel development began in the United States and Europe in fixed and functional techniques, respectively, but the Atlantic Ocean was a geographic barrier that restricted the early sharing of knowledge and experience in these philosophies.

THE GOLDEN AGE OF ORTHODONTICS

For orthodontists, the post–World War II era was characterized by the introduction of fluoridation, sit-down dentistry, and an increase in extractions. Postwar prosperity, the baby boom, and increased enlightenment of parents contributed to what was later called the "golden age of orthodontics." The subsequent clamor for more orthodontists led to a proliferation of graduate departments and inauguration of the American Association of Orthodontists (AAO) Preceptorship Program. There was also an increase in mixed-dentition treatment, requiring improved methods of analyzing arch lengths.

TWO CONTROVERSIES: EARLY TREATMENT AND OCCLUSION

From the beginning, orthodontists have been faced with the decision of when to start treatment. Until the late 20th century, this decision was based on clinical observation, the influence of strong leaders, and (after midcentury) the results obtained by what Europeans called "functional jaw orthopedics." Recent findings questioning the efficacy of early treatment have forced orthodontists to ask themselves whether their decision to "start early" is being influenced too heavily by practice-management considerations.

THE TEMPOROMANDIBULAR JOINT AND ORTHOGNATHIC SURGERY

The temporomandibular joint (TMJ) has always been the practitioner's no-man's land. Who's in charge here? The general dentist, the prosthodontist, the oral surgeon, the otolaryngologist, the psychiatrist, or the orthodontist? Theories about the cause of problems are as varied as the specialties involved.

SURGICAL ADJUNCTS TO ORTHODONTICS

Around 1970, after overcoming obstacles related to anesthesia, infection, and blood supply, orthognathic surgeons came into their own. The history of cleft lip and palate treatment has a much earlier beginning, because a deformed infant evokes a strong desire to intervene. Angle's belief that orthodontists can grow bone finally came to fruition with the advent of distraction osteogenesis, which developed from the limb-lengthening procedures of Gavriil Ilizarov in Russia.

SKELETAL ANCHORAGE

For many years, orthodontists have searched for a form of anchorage that does not rely on patient cooperation, although the answer already lay in the implants that dentists used to replace missing teeth and that oral surgeons used to hold bone segments together. Now these divergent lines have come together with titanium as the most biocompatible material in the form of stationary anchorage. State-of-the-art miniplate and microscrews—temporary anchorage devices (TADs)—now permit movements previously thought difficult or impossible.

LATE 20TH-CENTURY

Orthodontics continues to evolve. It has taken half a century for orthodontic bonding procedures to evolve from chemically cured acrylic to light-cured acrylic, and even having precisely placed adhesive when brackets are shipped from the manufacturer. The device that threatens to replace conventional brackets altogether—the aligner—also relies on bonded buttons, so it appears that some form of bonding will be with us for a while. The digital revolution has been occurring over the past 20 years, with the advent of digital photographs, two-dimensional (2D) and 3D imaging, intraoral scanning, and 3D printing.

As mentioned earlier, these advances have all been aided by our scientific journals. The current era of evidence-based research strives to make the orthodontic literature more accessible, useful, valid, and generalizable. Please visit the complete online chapter titled The History of Orthodontics in this 7th Edition of *Orthodontics: Current Principles and Techniques* to learn more about our profession's interesting journey over the past 150 years.

2

Craniofacial Growth and Development
Developing a Perspective

David S. Carlson and Peter H. Buschang

OUTLINE

This chapter is enhanced with the following electronic assets at www.expertconsult.com: Two tables.

An appreciation of the biological principles associated with growth and development, especially of the structures composing the craniofacial complex, is essential for attaining competency within the field of orthodontics. Particular emphasis for the advanced practice of orthodontics is placed on the hard tissues comprising the craniofacial regions, that is, the skeletal structures and the teeth, because these are the primary components of the craniofacial complex that the orthodontist addresses during treatment. Development, growth, and function of other craniofacial structures and tissues, such as muscles, neural tissues, and pharyngeal structures, as well as spaces such as the airway, are also of major interest to orthodontists. However, those elements are important primarily in terms of their influence—structurally, functionally, and developmentally—on the growth, size, and form of the skeletal elements of the face and jaws.

This chapter emphasizes postnatal growth, principally of the skeletal structures of the craniofacial complex, because of its importance in orthodontic treatment. Considerable attention is also given to prenatal development of craniofacial tissues and structures because it is critical for understanding postnatal growth. The reader is referred to a number of excellent references on developmental biology and human embryology for comprehensive reviews of early craniofacial development.[1,2]

SOMATIC GROWTH

The size and form of the craniofacial complex are major components of an individual's overall body structure. Moreover, the growth and maturation of the body as a whole, referred to generally as *somatic growth,* are highly correlated with those of the craniofacial complex. Therefore clinical evaluation of the status and potential for craniofacial growth, and thus of treatment planning in orthodontic patients, is highly dependent on an understanding of the somatic growth process.[3]

Differential Development and Maturation

In his classic work during the 1930s, Scammon[4] drew attention to the fact that the rate and timing of postnatal maturation, measured as a proportion of total adult size, vary widely among major systems of the human body (Fig. 2.1). In what has become known as "Scammon's curves," for example, maturation of the central nervous system (CNS) is shown to be completed primarily during the last trimester of gestation through age 3 to 6 years. As a result, the cranial vault, which houses the precociously developing and enlarging brain, is disproportionately large in the infant relative to the rest of the craniofacial region (Fig. 2.2). In contrast, the reproductive organs become mature a decade later, during adolescence.

The rate of general somatic growth and development, which includes the skeletal and muscular systems, is characterized by an S-shaped curve. The relative rate of growth is very high prenatally but then decreases during infancy and becomes even slower during childhood. The rate then accelerates greatly with the initiation of adolescence through the point of peak growth velocity, after which it slows once again and effectively stops altogether in adulthood. Development and growth of the craniofacial complex is intergraded between neural and somatic maturity patterns. The gradient moves from the cranium, which is the most mature, through the anterior cranial base, posterior cranial base and maxillary length, upper face height, corpus length, to

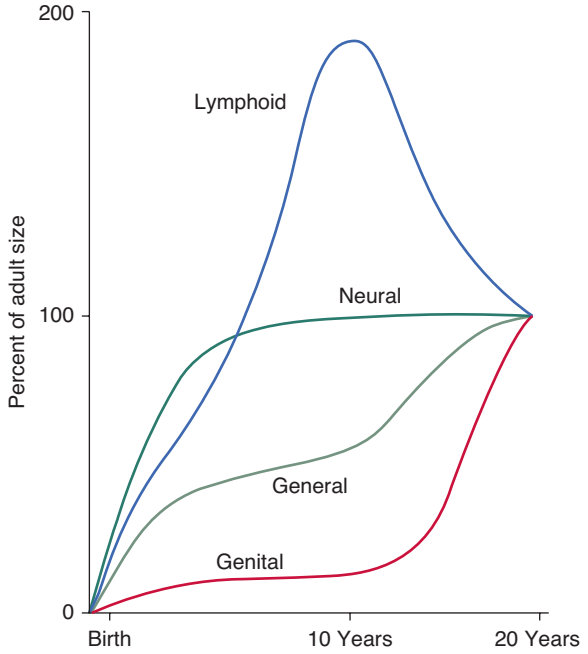

Fig. 2.1 Scammon's curves illustrating the fact that different systems of the body have different rates of development and come to maturity at different ages. (Adapted from Lowry GH. *Growth and Development of Children*. ed 6. Chicago: Year Book Medical Publishers; 1973.)

ramus height, which is the least mature and most closely approximates the general S-shaped pattern of general somatic maturation.[5]

Overall somatic growth, including the onset and end of puberty, is coordinated throughout the body by sex hormones and growth factors that are expressed differentially during the first two decades of postnatal life. However, the timing, rate, and amount of secretion of endocrine factors vary significantly between males and females and within each sex relative to chronologic age.

Variation in Rates of Growth during Maturation

Three episodes of relatively rapid growth have been documented for both general somatic and craniofacial growth. The greatest rates of growth occur prenatally and during infancy. The mid-childhood spurt takes place in approximately 50% of children between 6.5 and 8.5 years of age. The mid-growth spurt tends to occur more frequently and approximately 1 year later for boys than girls.[6] The more prominent adolescent growth spurt begins with the onset of puberty, at approximately 9 to 10 years of age in females and 11 to 12 years in males (Fig. 2.3). Female and male peak height velocities (PHV) are attained on average at 12 and 14 years of age, respectively, for North Americans and Europeans.[7] Females complete adolescence approximately 2 or more years ahead of males. The extra years of childhood growth before adolescence in males, as well as the slightly greater rates of adolescent growth and the slightly lengthier adolescent period, explain most of the sex differences in overall body size and craniofacial dimensions.

Because growth of craniofacial structures is correlated with general somatic growth, the timing of peak height velocity (PHV), which occurs at the pinnacle of the adolescent growth spurt, is especially useful for estimating peak maxillary and mandibular growth velocity. It has been shown that maxillary growth attains its maximum rate slightly before PHV, whereas the maximum rate of mandibular growth occurs just after PHV.[8,9]

The timing, rate, and amount of somatic growth are best determined by changes in overall height. Thus, height provides an important adjunct for cephalometric evaluations, especially during periods of rapid growth. Population-specific height percentiles make it possible to individualize craniofacial assessments. For example, if an individual's rate of somatic growth is particularly high or low, it is likely that his or her rate of craniofacial growth will be similarly high or low. Knowing a patient's height percentile also makes it possible to adjust measures of craniofacial size for the patient's body size. For example, if an individual is at the 90th percentile for body size, you would also expect his or her mandible to be larger than average. Height measurements are recommended because they are noninvasive, highly accurate, and simple to obtain at multiple occasions. Reference data for height are also typically based on larger samples of defined populations than are craniofacial reference data, which makes them more precise at the extreme percentiles.[10]

Assessments of maturation also provide critical information about the likelihood that the growth of craniofacial structures will continue and for how long or that growth has been completed. This is important because patients' maturational and chronologic ages should be expected to differ, often by more than 1 to 2 years, which confounds growth assessments necessary for orthodontic diagnosis and treatment planning. For this reason, it is always better to use the patient's skeletal age based on radiologic assessments of hand/wrist ossification to determine skeletal maturity, especially for determining whether the patient has entered adolescence, attained peak velocity, is past peak

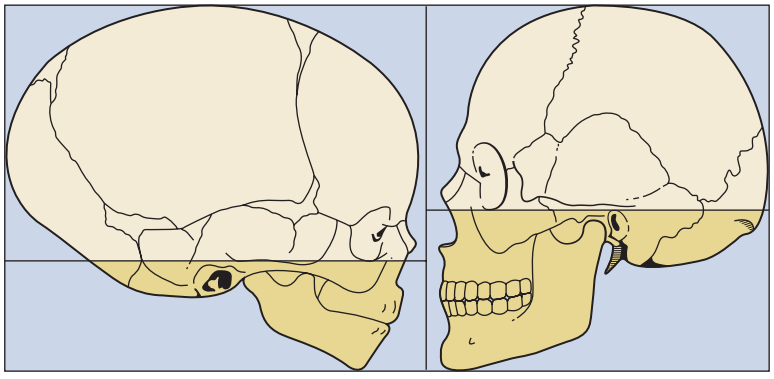

Fig. 2.2 Disproportions of the Head and Face in Infant and Adult. The neurocranium, which houses the brain and eyes is precocious in its development and growth and therefore is proportionately larger than the face during infancy and early childhood. (Adapted from Lowry GH. *Growth and Development of Children*. 6th ed. Chicago: Year Book Medical Publishers; 1973.)

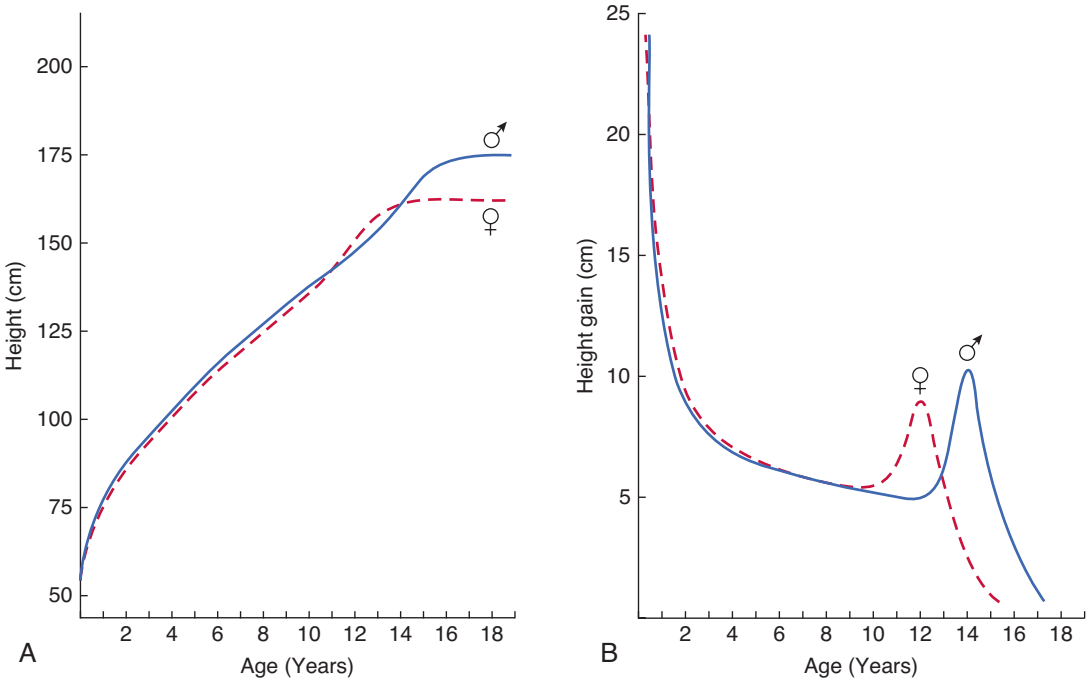

Fig. 2.3 Growth Velocity Curve (Growth per Unit of Time) for Skeletal Growth as General Measure of Human Ontogeny. Velocity of growth is characterized by decrease in growth rate beginning in the last trimester of prenatal development through maturation in the adult. During adolescence, hormonally mediated growth typically occurs to bring about a spurt in skeletal growth (peak height velocity). Pubertal growth spurt is characterized by considerable variability in onset and duration among individuals and according to sex. Onset of the pubertal growth spurt typically begins about age 10 in girls and lasts approximately 2 years. Boys have later onset (12 years); the entire pubertal period can last 4 to 6 years. (Adapted from Tanner JM, Whitehouse RH, Takaishi M. Standards from birth to maturity for height, weight, height velocity and weight velocity: British children, 1965. *Arch Dis Childh.* 41:454-471, 1966.)

growth, or is near the end of clinically meaningful growth.[11,12] Cervical vertebrae maturation provides another, albeit less precise, method to determine skeletal maturity.[13] Molecular assays are now being developed to provide more sensitive assessments to determine maturational status of skeletal growth.[14]

CRANIOFACIAL COMPLEX

The craniofacial complex comprises 22 separate bones that can be organized for heuristic purposes into relatively discrete anatomic and functional regions. Each of these regions has distinct mechanisms of development and growth, as well as different capacities for adaptation during growth (Fig. 2.4).

Structural Units

Desmocranium

The term *desmocranium* refers to the portion of the craniofacial skeleton that arises from a membrane of ectodermal, mesodermal, and neural crest origin that surrounds the proximal end of the notochord very early in development. As the brain develops and expands in utero, the desmocranium develops initially as a fibrous membrane covering of the brain that eventually will give rise to the bones of the cranial vault and fibrous joints, or sutures, as well as the dura mater over the brain and the periosteum overlying the bones of the cranial vault. In fact, in the absence of a brain, as with anencephaly, the desmocranial bones will fail to develop at all. Because the skeletal derivatives of the desmocranium have exclusively a membranous precursor, initial

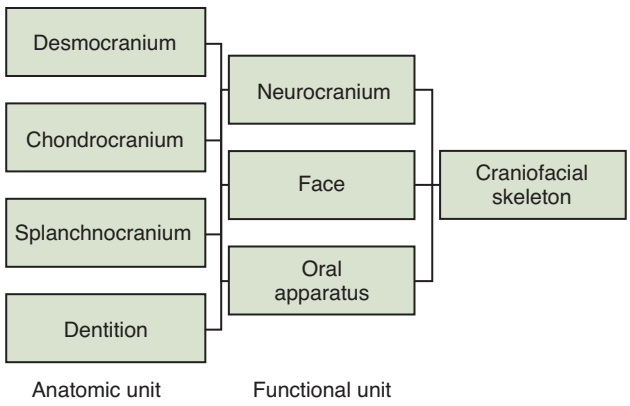

Fig. 2.4 Schematic of Organization of the Craniofacial Skeleton into Anatomic Regions and Overlapping Functional Regions.

morphogenesis and subsequent bone growth take place completely by intramembranous ossification.

Chondrocranium

The *chondrocranium* forms initially as part of the embryonic anlagen of primary cartilage that will become the cranial base, nasal septum, and nasal capsule. Like the desmocranium, the chondrocranium is also a derivative of the embryonic membrane surrounding the developing central nervous structures. However, the chondrocranium is

significantly less dependent on the presence of the brain for its initial formation and subsequent development. Growth associated with the derivative bones of the cranial base occurs by means of endochondral ossification.

Viscerocraniu

The *viscerocranium,* also referred to as the *splanchnocranium,* is composed of all those elements of the craniofacial complex that are derived from the first branchial arch and thus is of neural crest origin. These elements primarily include the bones of the midfacial complex and the mandible. Because the skeletal elements of the viscerocranium have no primary cartilaginous precursors, development and growth of its skeletal derivatives take place by intramembranous ossification that is also characterized by the presence of sutures and a specialized form of membrane-derived (secondary) cartilage at the mandibular condyles.

Dentition

The deciduous and permanent teeth are specialized anatomic components of the craniofacial complex that are composed of unique tissues and undergo a unique mechanism of development characterized by the interaction between ectodermal and mesenchymal tissues.

Functional Units

These four anatomic components can be combined organizationally into three overlapping and very broad functional units composing the craniofacial complex (Fig. 2.5).

Neurocranium

The *neurocranium* houses the brain and other elements of the CNS, such as the olfactory apparatus and auditory apparatus. As the brain rests on the cranial base and is covered by the cranial vault, development and growth of the neurocranium are characterized by a combination of membranous (desmocranium) and cartilaginous (chondrocranium) bone growth.

Face

The upper face may be defined as the region of the orbits of the eye. The midface, comprising primarily of the maxillae and zygomatic bones, is the region between the orbits and the upper dentition. Ectocranially, the bones of the face are composed externally of the intramembranously formed bones of the viscerocranium. However, the face also receives contributions from the chondrocranium as the cartilaginous nasal capsule and nasal septum. The lower face, comprising the mandible, develops entirely from the first branchial arch and thus is derived entirely as part of the viscerocranium. The mandible develops and grows by a specialized form of intramembranous formation of both bone and secondary cartilage.

Oral Apparatus

The oral apparatus is composed of the dentition and supporting structures within the upper and lower jaws. Thus the oral apparatus also is characterized by a unique morphogenesis of the teeth and a specialized form of intramembranous bone growth of the alveolar processes of the maxilla and mandible (viscerocranium). Development and growth of the skeletal structures comprising the oral apparatus are greatly influenced by the muscles of mastication and other soft tissues associated with mastication.

MOLECULAR BASIS OF CRANIOFACIAL DEVELOPMENT AND GROWTH

Patterning and subsequent formation of craniofacial tissues and structures have a complex, polygenic basis. For example, it has been shown that there are over 90 specific genes in which mutations will result in major disruptions of development, leading to severe craniofacial malformations.[15] Moreover, variations in craniofacial development and growth, from dysmorphologies to malocclusions, are multifactorial as a result of epigenetic mechanisms.[16,17] No genes are unique to the craniofacial complex. However, certain genes, especially those associated with developmental patterning of the head region and growth of cartilage, bone, and teeth, are of particular relevance for craniofacial development and growth and thus are of special importance for orthodontics. In addition, a number of genes of interest include those responsible for specific craniofacial deformities, such as craniosynostosis and facial clefts. The reader is referred to Hartsfield and Morford (see Chapter 3) for a comprehensive review of genetic mechanisms in the craniofacial region that are most important to orthodontics. A summary of the key genes associated with the patterning, development, and growth of the craniofacial region can be found in E-Table 2.1.

The key genes associated with craniofacial development may be organized informally into two broad yet overlapping groups based on their timing and patterns of expression and also their primary target tissues. First are those highly conserved genes, such as homeobox genes and transcriptions factors, that are responsible primarily for

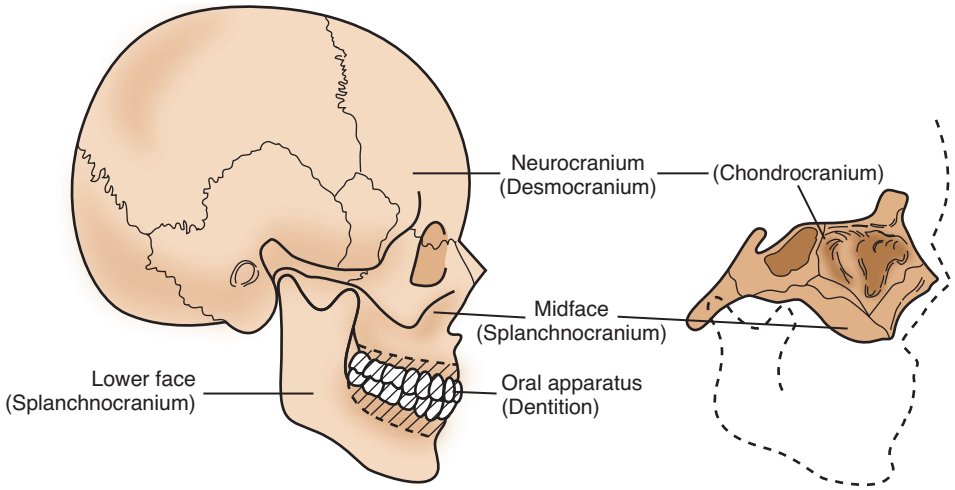

Fig. 2.5 Major Components of the Craniofacial Skeletal Complex.

TABLE 2.1 Comprising the Craniofacial Complex

Gene/Protein		General Role and Function	Significance for Craniofacial Development and Growth	References
Bmp-1 to *Bmp-9*	Bone morphogenetic protein 1-9	*Signaling molecule:* Skeletal differentiation, growth, repair	NCC and CF mesenchyme patterning; suture development; odontogenesis; nsCL/P	1-6
Dlx-1 to *Dlx-6*	Distal-less 1-6	*Homeobox:* Limb development; chondrogenesis; osteogenesis	Orofacial clefting	7-9
Efnb1	Ephrin B1	*Protein coding:* Cell division, adhesion	Craniofrontonasal syndrome; candidate for role in Class III malocclusion	1, 10-12
Fgf-1 to *Fgf-18*	Fibroblast growth factor 1-18	*Growth factors*: Differentiation and growth of multiple tissues and structures	CF ectoderm, NCC patterning; suture development; MCC growth; tooth induction; CL/P	1, 3, 4, 13-15
Fgfr-1 to *Fgfr-3*	Fibroblast growth factor receptor 1-3	*Transmembrane receptors*: Fgf receptor	Anterior cranial base growth; MCC growth; syndromic, nonsyndromic C-SYN; MX hypoplasia; CL/P	1, 3, 4, 15-17
GH	Growth hormone	*Peptide hormone-mitogen*: Cell growth and tissue regeneration	Growth of multiple CF tissues, structures; variations in MD growth, dentofacial treatment	13, 18
GHr	Growth hormone receptor	*Transmembrane receptor*: Receptor for GH	Polymorphisms associated with MD growth and MCC response to dentofacial treatment	19-21
Gli2 to *Gli3*	Zinc finger protein Gli2-3	*Transcription factor*: Regulates Ihh and Shh signaling	C-SYN; Greig cephalopolysyndactyly syndrome	1, 10, 22
Gsc	Goosecoid	*Transcription factor*: Dorsal–ventral patterning of NCC, head formation; rib fusion	Inner ear, cranial base, MX/MD anomalies	1, 8, 13, 23, 24
Hoxa1 to *Hoxa3*	Homeobox A1, A2, A3	*Homeobox*: Patterning of hindbrain rhombomeres and pharyngeal arches	Neural tube closure, 1st-2nd arch deformities	25, 26
Igf-1	Insulin-like growth factor 1	*Growth factor*: Mediator of GH; muscle, cartilage, and bone growth	MX/MD growth; suture development/growth; mediation of MCC to dentofacial treatment	3, 8, 13, 27-30
Ihh	Indian hedgehog	*Signaling molecule*: Endochondral and intramembranous ossification	Cranial base development; mediation of MCC growth during dentofacial treatment	31-33
L-Sox5	Long-form of Sox5	*Transcription factor*: Neurogenesis; chondrogenesis; type II collagen	Mediation of MCC growth during dentofacial treatment	34
Msx1 to *Msx2*	Muscle segment homeobox 1-2	*Homeobox*: Limb development; ectodermal organs	NCC proliferation, migration; odontogenesis; MD development; nsCL/P; Boston-type C-SYN	1, 3, 4, 8, 10, 35
Myo1H and *Myo1C*	Myosin 1H, Myosin 1C	*Protein coding*: Cell motility, phagocytosis, vesicle transport	Polymorphisms associated with MD prognathism	36, 37
Nog	Noggin	*Signaling molecule*: Patterning of the neural tube and somites	Head formation; neural tube fusion	4, 25, 26
Notch		*Transmembrane receptor*: Neuronal development; cardiac development; osteogenesis	MCC development	38
Osx	Osterix	*Transcription factor*: Osteoblast differentiation, mineralization; chondrogenesis	MCC differentiation, endochondral ossification; mediation of MCC growth during dentofacial treatment	39
Pitx1-2	Paired-like homeodomain 1-2	*Homeobox*: Left–right axis; left lateral mesoderm; skeletal development; myogenesis	MD development; role in Treacher-Collins syndrome; CL/P; odontogenesis	8, 13

Continued

TABLE 2.1 Comprising the Craniofacial Complex—cont'd

Gene/Protein		General Role and Function	Significance for Craniofacial Development and Growth	References
Prx-1Prx-2		*Homeobox*: Epithelial development in limbs and face	NCC patterning; malformations of 1st-2nd arch structures	8, 40, 41
PTHrP	Parathyroid-related protein	*Protein coding*: Endochondral bone formation	Development/growth of cranial base, MD, dental arches	42, 43
Runx2	Runt-related transcription factor	*Transcription factor*: Osteoblast differentiation; intramembranous and endochondral bone growth	Closure of fontanelles and sutures; ossification of cranial base, MX, and MCC; cleidocranial dysplasia	32, 43-46
Shh	Sonic hedgehog	*Transcription factor*: Development of limbs, midline brain, neural tube; osteoblastic differentiation; skeletal morphogenesis	Induction of frontonasal ectoderm; cranial base; fusion of facial processes; palatogenesis; odontogenesis; holoprosencephaly	1, 9, 33
Sho2		*Signaling molecule*: Development of digits; organization of brain, CF mesenchyme	Palatogenesis; TMJ development	6, 9, 38
Sox9		*Transcription factors*: Chondrogenesis; type II collagen; male sexual development	Cranial base; MCC growth; CL/P; Pierre-Robin sequence	38, 46-48
Spry 1-2	Sprouty	*Protein coding*: Mediates FGF signaling	MD/TMJ development	38, 48
Tcof1	Treacle	*Protein coding*: Early embryonic nucleolar-cytoplasmic transport	NCC proliferation, migration, survival; Treacher-Collins syndrome	38, 49
Tgf-β1 to *Tgf-β3*	Transforming growth factor-beta 1-3	*Growth factor*: Proliferation, differentiation, growth, function of multiple tissues	Palatogenesis; MD growth; suture development, maintenance, fusion; sCL/P	3, 24
Twist-1	Twist-related protein 1	*Transcription factor*: Skeletal development; syndactyly	MCC development; suture fusion; Saethre-Chotzen syndrome; facial asymmetry	9, 35, 38, 50, 51
Vegf	Vascular endothelial growth factor	*Growth factor*: Ingrowth of blood vessels	Chondrogenesis in cranial base, MCC	38, 45, 52
Wnt-1	Proto-oncogene protein Wnt 1	*Signaling molecule*: Cell fate, patterning during embryogenesis	MCC development/growth; MCC growth during dentofacial treatment	6, 32, 38, 53

CF, Craniofacial; *CPO,* cleft palate only; *CL/P,* cleft lip and palate; *C-SYN,* craniosynostosis; *MCC,* mandibular condylar cartilage; *MD,* mandible; *MX,* maxilla; *NCC,* neural crest cells; *nsCL/P,* nonsyndromal cleft lip and palate; *sCL/P,* syndromal cleft lip and palate; *TMJ,* temporomandibular joint.

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TABLE 2.1 Comprising the Craniofacial Complex—cont'd

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early pattern formation and differentiation of primary embryonic tissues and structures, including neural crest cells and head mesoderm. Mutation of those genes typically has a profound role in craniofacial dysmorphogenesis. The second group comprises genes such as growth factors and signaling molecules that are also responsible for mediating development, growth, and maintenance of the tissues and structures associated with the craniofacial complex both during embryogenesis and throughout postnatal development. Although mutations in this latter group of genes also are associated with craniofacial malformation syndromes, minor variants appear to be more common and may play a role in the development of more minor variations in growth. In addition, genes from both groups may be expressed reiteratively during development and growth, producing a highly complex matrix of interactions required for normal craniofacial morphogenesis. Adding to the complexity are the issues of wound healing, tissue regeneration, and repair—all processes important during orthodontic treatment—that can reinitiate the expression of genes required for early morphogenesis and postnatal growth.

Molecular research historically has focused on the role of specific genes critical for craniofacial morphogenesis during embryogenesis. The initial focus in that research typically has been on three areas: (1) naturally occurring genetic mutations associated with craniofacial dysmorphogenesis in humans; (2) development of genetically engineered animal models, typically the mouse, to produce loss of function of selected genes; and (3) mapping of gene expression in experimental animals through in situ hybridization and other biomarker approaches. More recently, significant progress has been made in the identification of gene variants (polymorphisms) that may be important for the origin of minor variations in craniofacial growth of potential relevance to orthodontic diagnosis and treatment. These genes and their variants could be significant for diagnosis and response to treatment of dentofacial deformities and minor malocclusions.[18] Significant advances in the genetic and epigenetic basis of craniofacial development, including the role of key genes in normal growth and orthodontic treatment, are expected to continue at a rapid pace.[19,20]

CRANIAL VAULT

Development of the Cranial Vault

The most prominent feature of the embryonic cephalic region at 6 to 7 weeks' gestation is the frontonasal prominence. The frontonasal prominence is a nonpaired structure that forms a dense desmocranial membrane, which covers the entire forebrain and extends laterally and inferiorly on each side of the developing head to meet the developing maxillary processes. The inner portion of the membrane contains neural crest cells and gives rise to the dura mater covering the brain. The outer portion of the desmocranial membrane, the *ectomeninx,* is composed of surface ectoderm, deep to which is the paraxial mesoderm. Patterning of the frontonasal prominence to form the cranial vault and elements of the nasal region is induced by expression of sonic hedgehog (Shh) and FGF-8.

By 8 weeks' gestation, initial blastemas of bone become apparent within the ectomeninx, first for the frontal bone and the squamous temporal bone and subsequently for the parietal bones and squamous portion of the occipital bone (Fig. 2.6). Over the ensuing 4 weeks, these condensations of bone steadily increase in size by radial expansion of newly differentiated skeletal tissue within the ectomeninx. As the development of new bone exceeds the rate of growth of the brain, the peripheral bone fronts become located closer and closer to each other, until they approximate each other as single-thickness plates of flat bones by about 12 weeks' gestation. At this point, the intervening fibrous tissue becomes highly cellular, and fibrous articulations, or *sutures,* are formed between the individual bone elements (Fig. 2.7).

Growth of the cranial vault bones represents a specialized form of intramembranous ossification that begins prenatally as blastemas of bone tissue that arise de novo within the middle layer of the desmocranial membrane covering of the brain. Once the skeletal elements as plates of bone become located close to each other, their fibrous connections become reorganized with the periosteum and the dura mater derived from the outer and inner layers of the desmocranial membrane, respectively, extending into the sutural articulations. The sutures then continue to support growth of the cranial vault through another specialized form of intramembranous osteogenesis similar to periosteal bone formation.[21-23]

Mechanisms of Suture Growth

Sutural bone growth can best be considered as a specialized form of intramembranous periosteal bone growth. Once formed, the bones of the cranial vault are enveloped, like all bones, in a skeletogenic membrane. On the external surface, this membrane is the periosteum. On the intracranial surface, the membrane is the dura mater, which is also derived from the embryonic ectomeninx and is skeletogenic. Viewed in cross section, the outer fibrous layer of periosteum (uniting layer) spans over the cranial suture and provides structural support to the suture and its two or more skeletal elements. The inner osteogenic

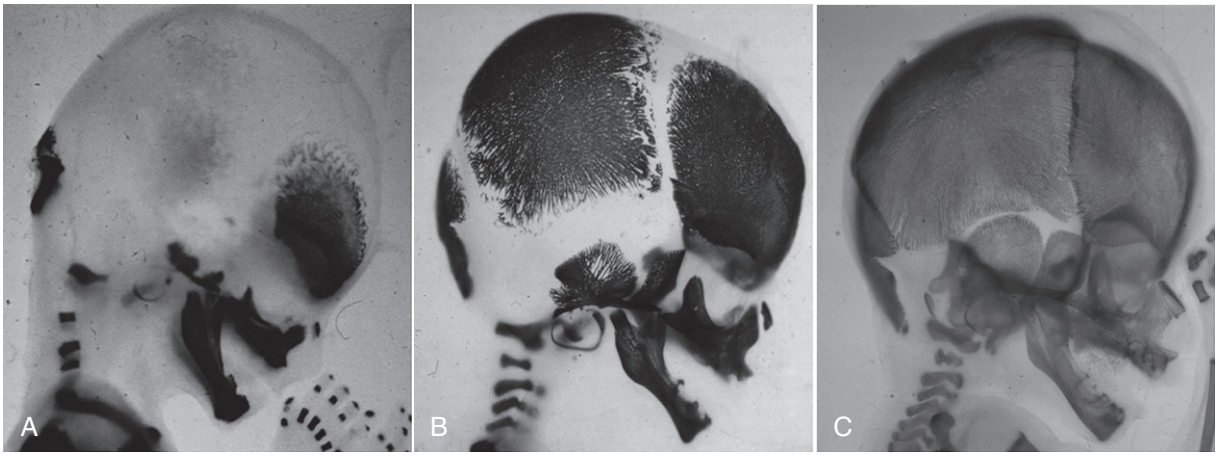


Fig. 2.6 Cleared and stained human fetuses indicating craniofacial skeletal structures at approximately 8 weeks' gestation **(A)**, 15 weeks' gestation **(B)**, and 18 weeks' gestation **(C)**.

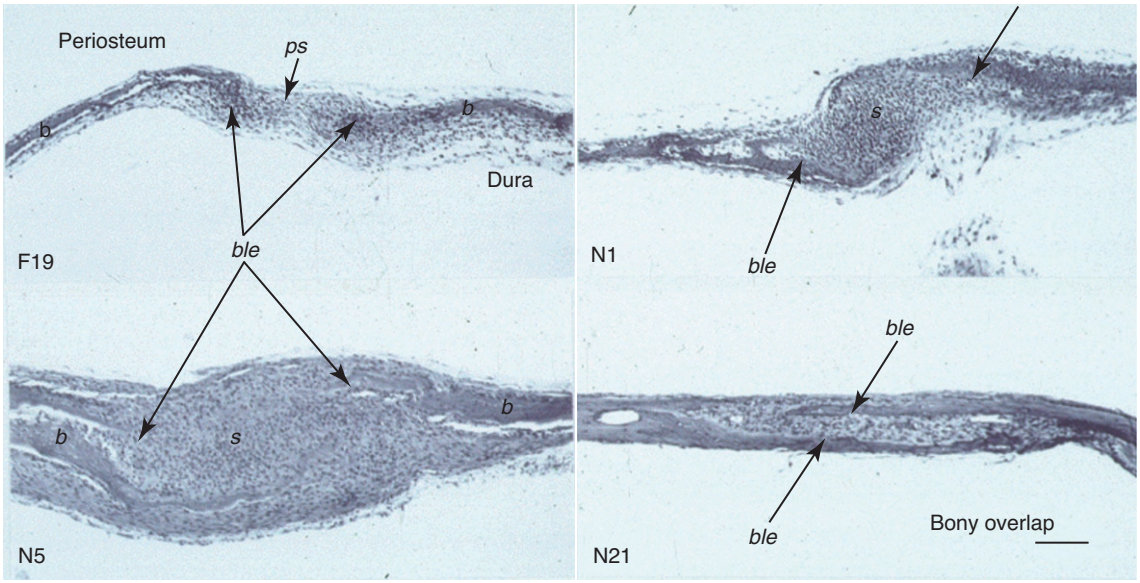


Fig. 2.7 Photomicrographs of hematoxylin and eosin–stained histologic sections through the coronal suture of normal rats at embryonic day 19 and postnatal days 1, 5, and 21. Bone *(b),* bone leading edge *(ble),* presumptive suture mesenchyme *(ps),* and suture *(s).* (From Opperman LA, Gakunga PT, Carlson DS. Genetic factors influencing morphogenesis and growth of sutures and synchondroses in the craniofacial complex. *Semin Orthod.* 2005;11(4):199-208.)

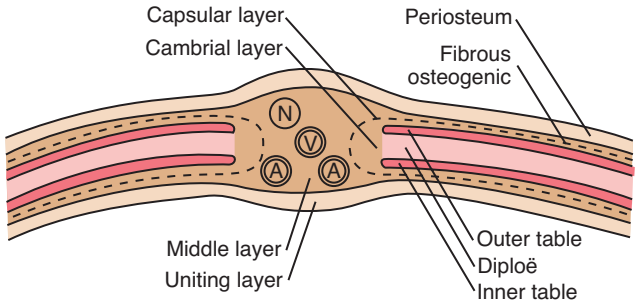


Fig. 2.8 Schematic representation indicating the relationship between the periosteum and dura mater as a mechanism for a specialized of intramembranous growth within the sutures of cranial vault bones. (Adapted from Pritchard JJ, Scott JH, Girgis FG. The structure and development of cranial and facial sutures. *J Anat.* 1956;90:73-86.)

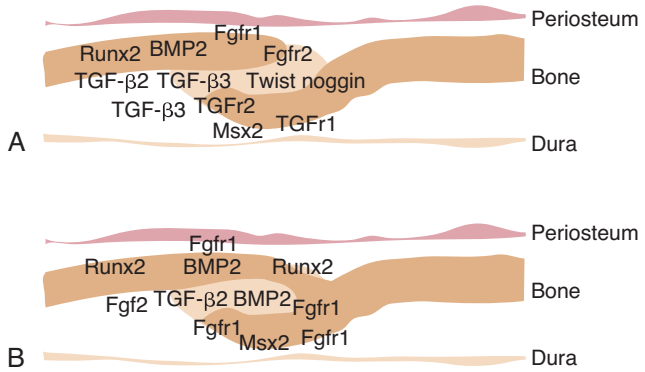


Fig. 2.9 Distribution of growth factors and transcription factors active during suture growth **(A)** and suture synostosis **(B).** (Adapted from Opperman LA, Gakunga PT, Carlson DS. Genetic factors influencing morphogenesis and growth of sutures and synchondroses in the craniofacial complex. *Semin Orthod.* 2005;11(4):199-208.)

layers of the periosteum and the dura reflect into the space between the two cranial vault bones and provide a source of new osteogenic cells (Fig. 2.8). As the bones of the cranial vault become separated because of expansion of the brain and intracranial contents, the osteogenic cells form skeletal tissue and thus provide a mechanism for maintaining relatively close contact through the intervening suture.

The molecular basis of the development and growth of the sutures of the cranial vault has received considerable attention, principally because of the number of naturally occurring and engineered genetic mutations characterized by craniosynostosis (see Wilkie and Morriss-Kay,[15] Rice,[24] and Chai and Maxson[25] for comprehensive reviews). Studies have shown a complex pattern of gene expression within the sutural blastema associated with the periosteal reflection and intracranial dura mater. Secretion of soluble factors by the dura mater in response to growth signals from the expanding underlying brain is essential for normal cranial suture morphogenesis and maintenance of cranial sutures as patent bone-growth sites through complex tissue interactions and feedback between dura mater, bone fronts, and sutures. Both sutures and the dura mater also contain growth factors, such as several members of the family of transforming growth factor-beta 1 (*TGF-β1*, *TGF-β2*, *TGF-β3*), bone morphogenetic protein 2 (*BMP2*), *BMP7*, fibroblast growth factor 4 (*FGF-4*), insulin-like growth factor 1 (*IGF-1*), and sonic hedgehog (*Shh*) (Fig. 2.9).[26,27] Overexpression of transcription factors *Runx2* and *Msx2* and haploinsufficiency of Twist[28] and Noggin[29] are also associated with suture obliteration, and loss of function of *Gli3* results in premature synostosis.[30] Genetic analysis of naturally occurring craniosynostosis in humans has shown that mutations of genes for fibroblast growth factor receptors 1, 2, and 3 (*FGFR-1, FGFR-2,* and *FGFR-3*) and in *MSX2*[31] and *TWIST*[32,33] genes are also associated with premature suture fusion.

Development and growth of the cranial vault as a whole, and development and growth of bone at the sutural articulations, are primarily dependent on the expansion of the brain and other intracranial

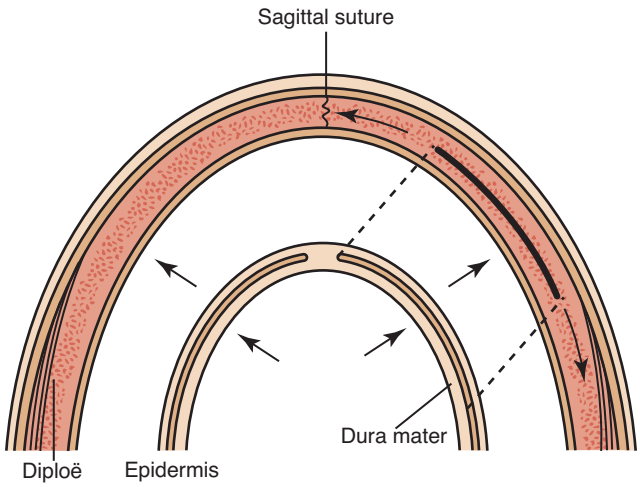


Fig. 2.10 Schematic diagram indicating the relationship between expansile growth of the brain as a stimulus for compensatory growth of sutures of the cranial vault. (Adapted from Moss ML. The functional matrix. In: Kraus B, Reidel R, eds. *Vistas Orthod.* Philadelphia: Lea & Febiger; 1962;85-98.)

contents.[34] Furthermore, it has been clearly demonstrated that sutures are secondary, compensatory, and adaptive sites of bone growth that normally respond to biomechanical forces. As the brain expands during prenatal development and during the first decade of life postnatally, forces are created within the neurocranium that cause the bones of the cranial vault to expand outward, which tends to separate them from each other at the sutural boundaries (Fig. 2.10). Under normal conditions, the cellular and molecular substrate associated with the dura mater, the periosteum, and the suture respond to this biomechanical displacement in the same manner in which periosteum throughout the skeletal system responds—by initiating and maintaining osteogenesis within the sutures to maintain the proximity of the adjoining skeletal structures. When the biological substrate of the suture is abnormal, however, as in the case of many genetic syndromes such as Crouzon syndrome, Apert syndrome, and Jackson-Weiss syndrome, for example, each of which is associated with mutations of *FGFR-2,* premature craniosynostosis may result.[35,36] The opposite condition, reduced suture growth, and prolonged patency, as seen in cleidocranial dysostosis, may occur with abnormalities associated with growth factors, including in particular Runx2, which are necessary for normal suture fusion.

Postnatal Growth of the Cranial Vault

Because of the very precocious nature of prenatal and early postnatal human brain development, the cranial vault is disproportionately large relative to the rest of the face and body. At birth, the cranial vault is initially characterized by the presence of all of the cranial vault bones. At that time, all the major sutural fibrous articulations between the bones of the cranial vault are present, including the metopic suture between the right and left frontal bone. In addition, there typically are four larger remnants, known as *fontanels,* of the desmocranial membrane in areas where the pace of bone growth has not been sufficient to approximate the bones of the cranial vault to form a suture (Fig. 2.11).

During the first 24 months after birth, growth of the cranial vault bones proceeds rapidly enough to close the fontanels as each complex of cranial vault bones becomes organized through interlocking sutures. The metopic suture normally fuses to form a single frontal bone within the first year of life, although the suture may appear to persist for up to 8 years of age or even throughout life in a small percentage of individuals. The cranial vault will continue to enlarge primarily as a result of compensatory growth of the sutural bone fronts stimulated by expansion of the brain. By 4 years of age, the brain and the associated cranial vault will have achieved approximately 80% of adult size; by age 10, the brain and cranial vault have attained 95% of their adult size. Throughout this time of very rapid expansion, the remaining sutures of the cranial vault normally remain patent and actively growing to keep pace with the brain as it expands in size.

Osteogenesis at cranial sutural bone fronts may continue for the first two decades of life. However, by the end of the second decade of life, bone growth at cranial sutures has slowed and the potential for growth of cranial sutures has greatly diminished. Also at that time, the sutures will begin the normal process of bony closure, or *synostosis,* when the potential for sutural growth ceases altogether.

The cranial sutures normally lose the capacity for growth by the end of the second decade of life, and virtually all become synostosed during the lifespan. Normal suture closure is initiated along the endocranial surface. Initially, this is characterized by bridging of bone across the suture and eventually through modeling of bone, leading to complete obliteration of the suture. Cessation of growth at cranial sutures typically begins around age 25 for the sagittal suture and may be extended for 2 to 3 additional years for the coronal suture.

Despite the fact that the major cranial sutures stop growing by the third decade of life, some enlargement of the cranial vault overall typically occurs throughout the lifespan as a result of periosteal deposition

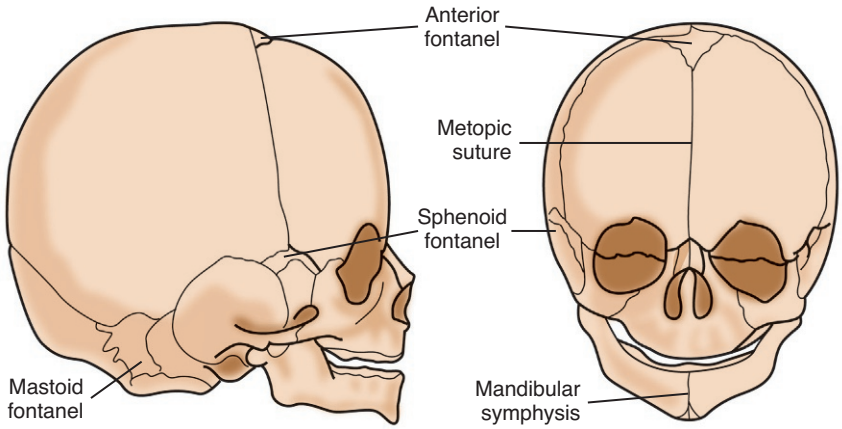


Fig. 2.11 Lateral and Frontal Views of the Neonate Skull Indicating the Location of Sutures and Fontanels. (Adapted from Sicher H, DuBrul EL. *Oral Anatomy.* 5th ed. St. Louis: Mosby; 1970.)

along the ectocranial surface. Certain specific areas of the cranial vault, such as the glabellar and nuchal regions, may exhibit slightly greater periosteal growth as a secondary sex characteristic in males.

CRANIAL BASE

Development of the Cranial Base

The ectomeningeal membrane that surrounds the developing brain in the cranial base region gives rise to a number of paired cartilaginous elements that form the embryonic chondrocranium. The first of the cartilage anlagen to form arises from neural crest cells at about 6 weeks' gestation as the parachordal cartilages, which surround the proximal end of the notochord and give rise to the anterior cranial base. The posterior component of the cranial base is derived primarily from mesoderm to form the basioccipital bone.[37] Development of the chondrocranium then progresses rostrally to the otic capsule, which will form the petrous portion of the temporal bone; the postsphenoid, presphenoid, alisphenoid, and orbitosphenoid cartilages of the sphenoid bone; and the nasal capsule and mesethmoid, which will form the ethmoid bone, inferior turbinate, and nasal septum. By 8 weeks' gestation, the separate cartilage elements have merged to form a single plate of primary hyaline cartilage, the *basal plate,* extending from the foramen magnum rostrally to the tip of the nasal cavity (Fig. 2.12).

More than 110 separate centers of ossification form in the basal plate, beginning with the parachordal cartilages and continuing rostrally through the sphenoid complex around 9 to 16 weeks, to the ethmoid region as late as 36 weeks. As these centers of ossification arise within the chondrocranium, segments of intervening cartilage form synchondroses (Fig. 2.13). The principal cranial base synchondroses that are most relevant for understanding craniofacial growth are the spheno-occipital synchondrosis, between the body of the sphenoid and the basioccipital bone, and the sphenoethmoidal synchondrosis, between the sphenoid and ethmoid bones. The greater wing of the sphenoid bone and the squamous portion of the occipital bone develop and grow by intramembranous ossification.

Mechanism of Synchondrosal Growth

Cranial base synchondroses are temporary cartilaginous joints located between bones of endochondral origin and growth. Synchondroses can best be considered as homologous to the epiphyseal growth plates of long bones. Functionally, both provide a mechanism for rapid endochondral growth of bone in a manner that is capable of overcoming biomechanical loads, thus exhibiting tissue-separating capabilities. Developmentally, cranial base synchondroses and epiphyseal plates of long bones synostose and become obliterated when the skeletal element achieves its mature size and shape. This typically occurs at the end of puberty for epiphyseal growth plates but varies from the end of the juvenile period through the end of puberty for the major cranial base synchondroses.

Cranial base synchondroses and epiphyseal growth plates are both derived from the primary hyaline cartilage that arises as part of

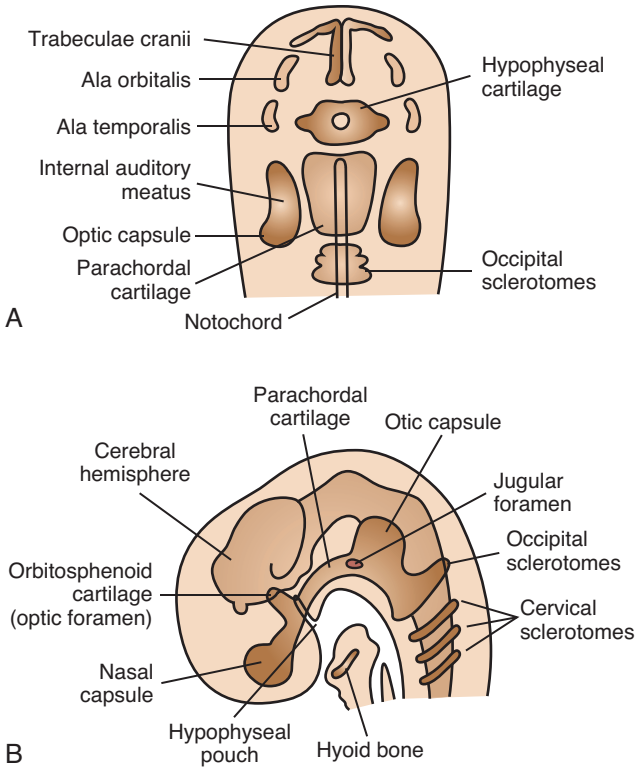


Fig. 2.12 Schematic Representation of the Cartilaginous Basal Plate Comprising the Embryonic Chondrocranium. A, Dorsoventral view. B, Lateral view.

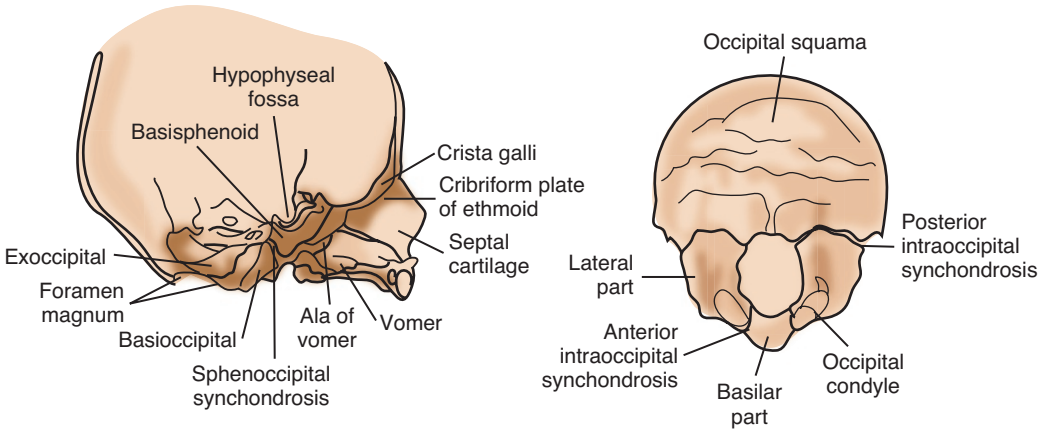


Fig. 2.13 Drawing of sagittal and basal views of the neonatal skull indicating spheno-occipital synchondrosis and intraoccipital synchondroses. The sphenoethmoidal synchondrosis will arise between the sphenoid and ethmoid bones. (Adapted from Bosma JF. Introduction to the symposium. In: Bosma JF, ed. *Development of the Basicranium*. Bethesda, MD: US Department of Health, Education, and Welfare; 1976:3-28.)

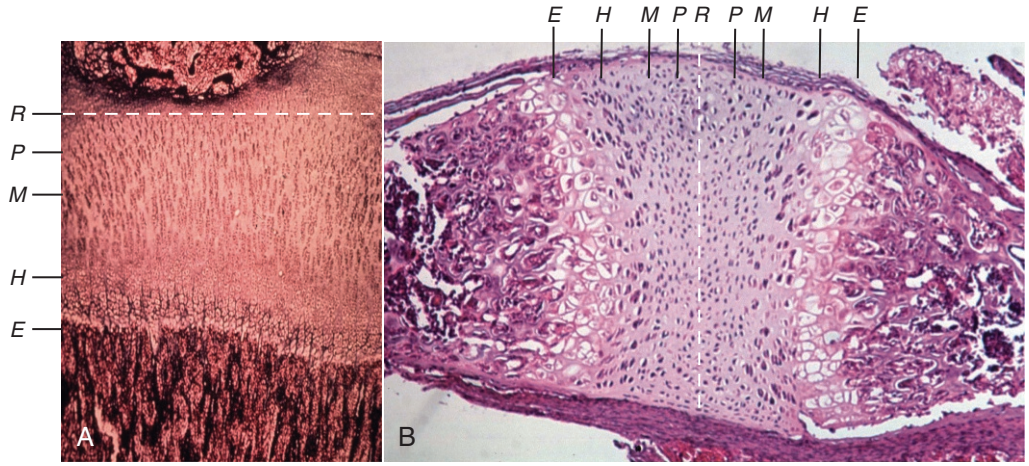


Fig. 2.14 Histologic comparison between the cartilages within a growing epiphyseal plate (A) and cranial base synchondrosis (B) (hematoxylin and eosin–stained). *R,* Resting zone *(dashed line); P,* proliferating zone; *M,* maturational zone; *H,* hypertrophic zone; *E,* zone of endochondral ossification.

the embryonic cartilaginous anlagen. Like endochondral bones and growth plates throughout the body, growth of synchondroses is controlled principally by expression of Indian hedgehog gene (Ihh) and sonic hedgehog (Shh).[38,39] The significance of *FGFR-3* for growth of the anterior cranial base is also indicated by mutations associated with achondroplasia.

Histomorphologically, both cranial base synchondroses and epiphyseal growth plates, are characterized by primary chondrocytes that are distributed into zones that are highly typical for growth plate cartilage (Fig. 2.14). However, a major difference between epiphyseal growth plates in long bones and cranial base synchondroses is that synchondroses are "bidirectional." Thus each cranial base synchondrosis effectively has two back-to-back growth plates with a shared region of newly forming cartilage in the center and bone at each end. Growth plates are unidirectional.

The primary hyaline cartilage of the cranial base is the same as that found throughout the embryonic cartilaginous anlage that characterizes all the other cartilaginous bones throughout the body. It is well known that growth of tissues derived from the primary embryonic cartilaginous anlagen tends to be relatively resistant to all but very extreme external influences. Growth of cartilage-derived skeletal elements throughout the body tends to be relatively resistant to environmental and other factors and instead is regulated to a large extent by intrinsic, genetically regulated growth factors and cell-signaling molecules.[40] The same is true for the cranial base synchondroses. However, it is important to note that the growth of both epiphyses and synchondroses can be significantly affected by such epigenetic factors as disease, malnutrition, and undernutrition, as well as other conditions that affect production and expression of endocrine factors responsible for bone growth.

The cartilage cells within both epiphyseal growth plates and cranial base synchondroses are characterized by extensive amounts of extracellular matrix that are secreted by and separate the cartilage cells. This matrix makes the cartilage very dense and strong but also flexible relative to bone and thus better able to absorb mechanical forces without directly affecting the cells and potentially altering growth. Because there are no vessels within cartilage extracellular matrix, all nutrients, growth factors, and cell-signaling molecules must diffuse through the matrix to reach the chondrocytes. The matrix thus "buffers" the chondrocytes from extrinsic mechanical forces and many soluble molecules that might provide information about the external environment.[41] As a result, cartilage growth in general, and endochondral ossification from primary hyaline cartilage in particular, tend to be more rigidly programmed genetically than intramembranous bone growth associated with periosteum, such as occurs in the desmocranium and viscerocranium.

This difference in the mechanisms of growth between bone formed by means of intramembranous ossification and bone derived from endochondral ossification can be summarized through the concepts of skeletal *growth centers* versus skeletal *growth sites*.[42] Development and growth of the skeletal tissues derived from primary cartilage are significantly more intrinsically regulated and less dependent for their expression on epigenetic factors. In particular, *growth centers* have what has been described as "tissue-separating capabilities," emphasizing the capacity to grow and expand despite the presence of mechanical forces that would seem capable of inhibiting or restricting skeletal growth. Thus epiphyseal and synchondrosal cartilage are referred to as *growth centers*. In contrast, a *growth site* is an area of skeletal growth that occurs secondarily and grows in compensatory fashion to growth and function in a separate but proximate location. Growth sites have no tissue-separating capabilities but rather respond more readily to factors extrinsic to their specific area. Periosteal bone growth associated with muscle function is one obvious example of a growth site. Sutural bone growth is another example of a class of growth sites because of its association with bones of intramembranous origin and its clear connection to periosteal bone growth.

Postnatal Growth of the Cranial Base

Late prenatal and overall postnatal growth of the cranial base is related directly to growth of the synchondroses. There are four principal growth-related cranial base synchondroses that separate the bones of the cranial base at birth. The intersphenoid synchondrosis, between the presphenoid and basisphenoid, fuses around the time of birth in humans and thus does not contribute to postnatal growth. The anterior and posterior intraoccipital synchondroses stop growing around 3 to 5 years of age (Fig. 2.15). The sphenoethmoidal synchondrosis, which lies between the sphenoid and the ethmoid bones, is most active with respect to growth of the cranial base through approximately 7 to 8 years of age in humans. At that time, the sphenoethmoidal synchondrosis loses its cartilage phenotype and becomes a suture. Once that transition occurs, growth of the anterior cranial base is essentially complete. As a result, the anterior wall of the sella turcica, which is

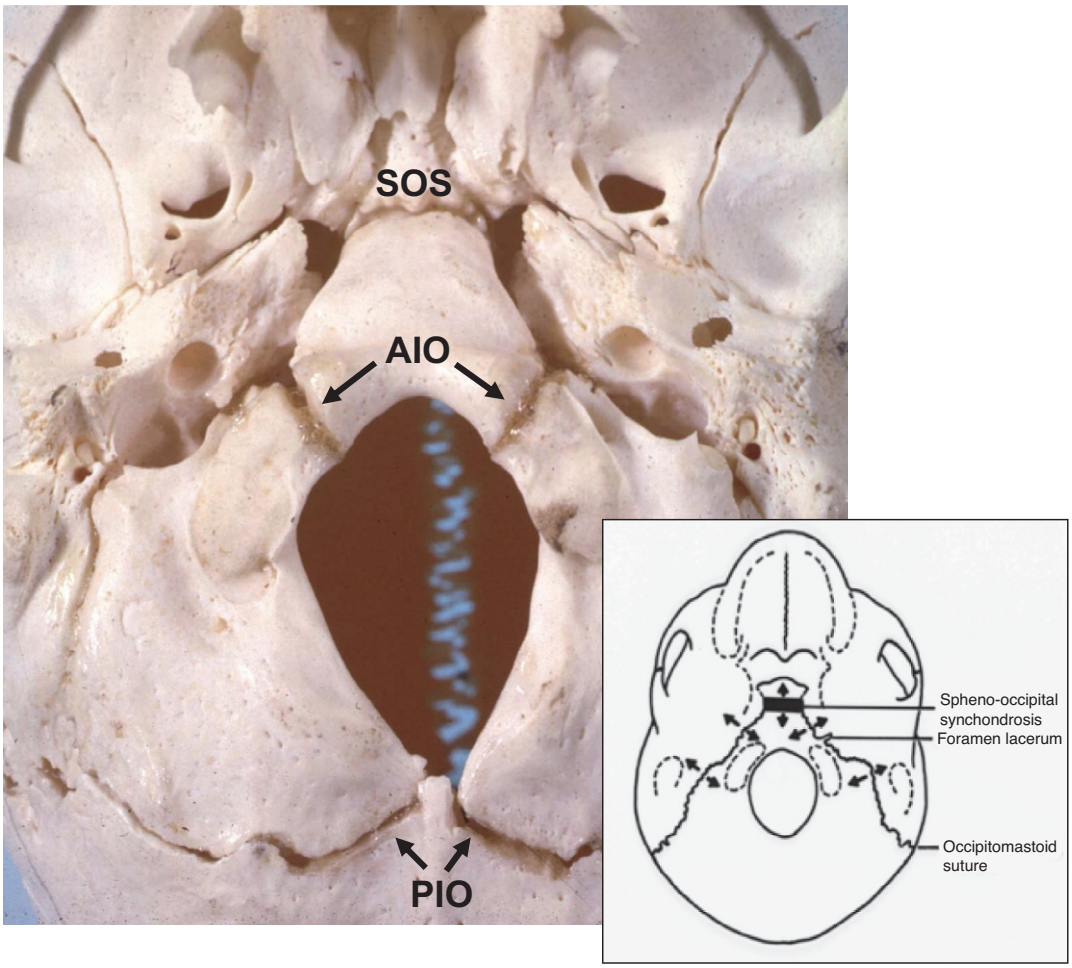


Fig. 2.15 Basal view of a young child showing the anterior (AIO) and posterior (PIO) intraoccipital synchondroses, as well as the spheno-occipital synchondrosis *(SOS)*.

located on the body of the sphenoid; the greater wing of the sphenoid; the cribriform plate; and the foramen cecum are commonly used after age 7 as stable reference structures for analyses of serial lateral radiographic cephalograms.

The spheno-occipital synchondrosis, between the body of the sphenoid and occipital bones, is most prominent throughout the period of active craniofacial growth and fuses shortly after puberty (see Fig. 2.15). Once synostosis occurs, growth of the cranial base, especially in the anteroposterior direction, is essentially over. Subsequent changes in the form of the cranial base, such as in the angulation of the basioccipital bone relative to the anterior cranial base, for example, must come about as a result of bone modeling.

During the early postnatal years, the cranial base undergoes a dramatic shift in its growth pattern (Fig. 2.16). Anterior (nasion-sella) and posterior (sella-basion) cranial base lengths, as well as cranial base angulation (nasion-sella-basion), exhibit greater growth changes during the first 2 to 3 postnatal years than any time thereafter. For example, cranial base angulation decreases more than twice as much during the first 2 postnatal years than between 2 and 17 years of age, primarily as a result of differential growth of the spheno-occipital synchondrosis. Growth continues after 2 years of age, but the changes are smaller and steadier.

Between birth and 17 years of age, the anterior cranial base grows approximately 36% (males) to 53% (females) more than the posterior cranial base, with most of the differences occurring during the first few years.[43] It is important to understand that the anterior cranial

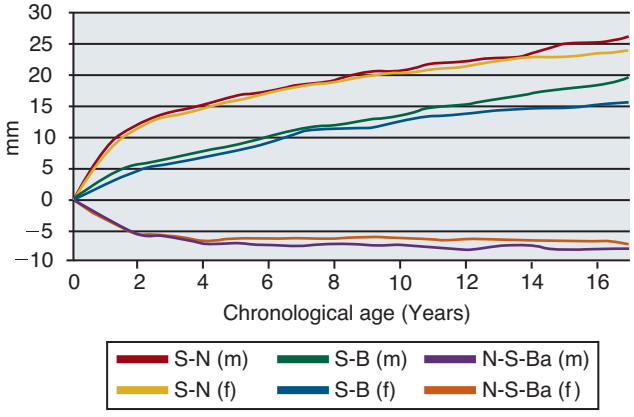


Fig. 2.16 Male *(m)* and Female *(f)* Cranial Base Growth Changes From Birth Through 17 Years of Age. (Data from Ohtsuki F, Mukherjee D, Lewis AB, et al. A factor analysis of cranial base and vault dimensions in children, *Am J Phys Anthropol.* 1982;58(3):271-279.)

base grows more and is also more mature (i.e., closer to its adult size) than the posterior cranial base throughout the postnatal growth. Longitudinal analyses have shown that the anterior cranial base has already attained 86%–88% of its adult size by 4.5 years of age, whereas the posterior cranial base has attained only about 80%–84% of its adult size (Fig. 2.17). The relative maturity differences between the anterior

and posterior cranial base lengths are maintained throughout postnatal growth.

Anterior and posterior cranial base lengths increase because of bony deposition, as well as growth at the spheno-occipital and sphenoethmoidal synchondroses. Postnatally, the posterior cranial base becomes longer primarily due to growth at the spheno-occipital synchondrosis. Histologic studies have shown that the spheno-occipital synchondrosis fuses at approximately 16 to 17 years in females and 18 to 19 years in males.[44] Radiographically, the spheno-occipital synchondrosis shows active growth until approximately 10 to 13 years of age, at which time closure starts superiorly and continues inferiorly around 11 to 14 years in females and 13 to 16 years in males.[45,46]

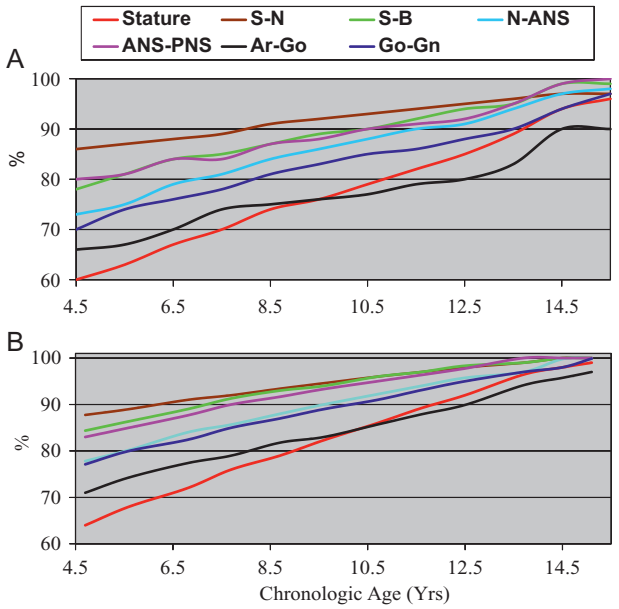


Fig. 2.17 Craniofacial Growth Maturity Gradient of (A) Males and (B) Females. (Adapted from Buschang PH, Baume RM, Nass GG. A craniofacial growth maturity gradient for males and females between 4 and 16 years of age. *Am J Phys Anthrop.* 1983;61:373-382.)

Because both landmarks are commonly used to describe the growth of the anterior cranial base, it is important to distinguish the changes that occur at nasion from those that occur at foramen cecum. After fusion of the sphenoethmoidal synchondrosis, which occurs at approximately 7 to 8 years of age, increases in the distance between sella and foramen cecum are due primarily to the posterior and inferior drift of the sella turcica. The distance sella-nasion, on the other hand, continues to increase primarily as a result of bony apposition on the outer surface of the frontal bone associated with the development of the frontal sinus (the earliest pneumatization of the frontal sinus occurs around 2 years of age). The anterior cranial fossa continues to expand slightly, and the frontal sinus becomes more prominent. As a result, the frontal bone and root of the nose become more anteriorly located. Ford[47] estimated that the frontal bone drifts anteriorly approximately 7 mm between the time that the sphenoethmoidal synchondrosis fuses and adulthood.

MIDFACE/NASOMAXILLARY COMPLEX

The midface, or nasomaxillary complex, is composed of the paired maxillae, nasal bones, zygomatic bones, lacrimal bones, palatine bones, and, within the nasal cavity, the turbinates and vomer. Prenatally, human fetuses also have left and right premaxillary bones; however, these normally fuse with the maxillae within 3 to 5 years after birth (Fig. 2.18).

The midface is connected to the neurocranium by a circummaxillary suture system and, toward the midline, by the cartilaginous nasal capsule, nasal septum, and vomer (Fig. 2.19). There is also an intermaxillary suture system composed of the midpalatal, transpalatal, intermaxillary, and internasal sutures. With the exception of the inferior turbinates, all the bones composing the midface are formed intramembranously from a connective tissue mass.

Development of the Midface

The midface has both viscerocranial and chondrocranial components. The chondrocranial component comprises principally of parasagittal extensions of the cartilaginous anterior cranial base as the nasal septum and cartilaginous nasal capsule into the nasal region. The viscerocranial

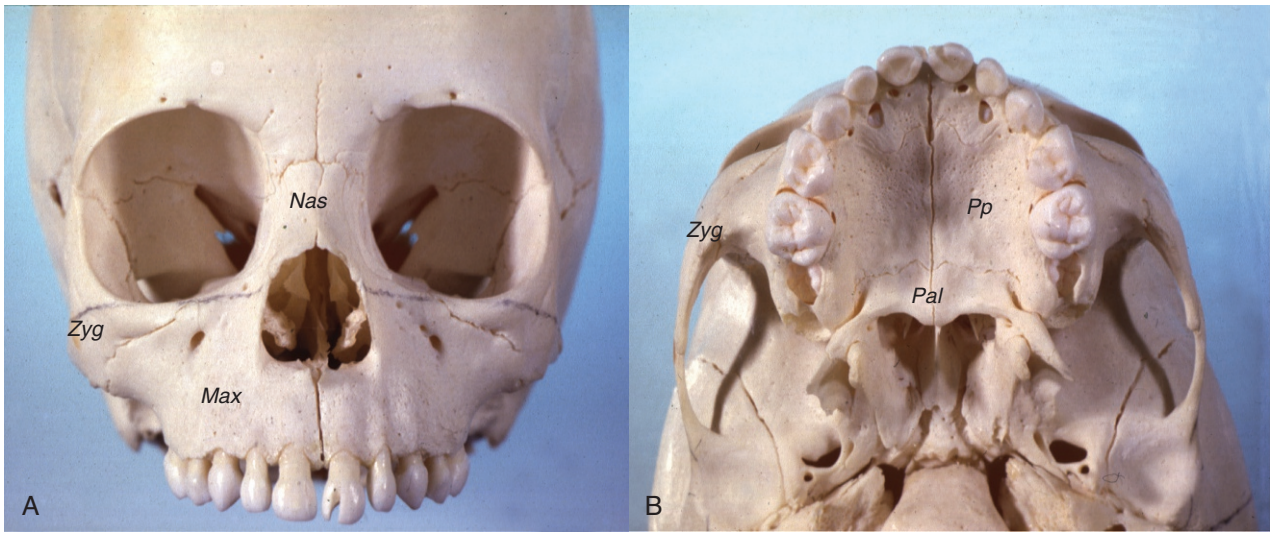


Fig. 2.18 A, Frontal and (B) basal views of a juvenile human indicating the bones comprising the midface. *Max,* Maxilla; *Nas,* nasal bones; *Zyg,* zygomatic bones; *Pal,* palatine bones; *Pp,* palatal processes of the maxillary bones.

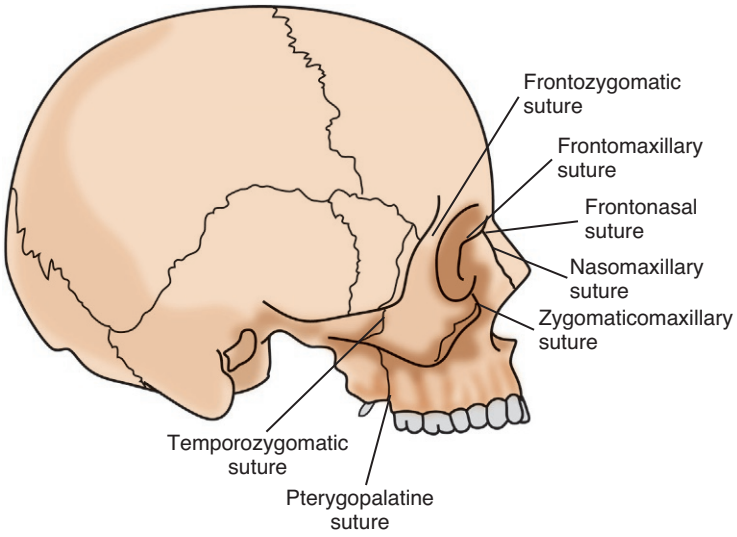


Fig. 2.19 Location of the Circummaxillary Suture System Articulating the Midface with the Neurocranium.

component is derived from two embryonic structures. The first is an inferior extension of the frontonasal prominence, which extends toward the oral opening, or stomodeum, to form nasal structures and the philtrum of the upper lip. The second is the paired maxillary processes of the first branchial arch. Differential growth of the right and left maxillary processes results in their apparent migration medially until they come into contact with the medial nasal process of the frontonasal prominence.

The skeletal elements comprising the midfacial complex arise almost exclusively from neural crest cells within the maxillary process of the first branchial arch. The primary palate, which gives rise to the four maxillary incisors, is derived from the frontonasal prominence. Only the facial ethmoid and inferior turbinate are derived from the cartilaginous component of the midface. Like the bones of the cranial vault, because the bones composing the nasomaxillary complex have no cartilaginous precursors, they rely on intramembranous ossification for their development. However, the exact process by which initial bone formation occurs differs from that of the cranial vault bones. Whereas the bones of the cranial vault arise within a desmocranial membrane, centers of ossification for the nasomaxillary bones develop as blastemas directly within the mesenchyme of the first branchial arch. These blastemas of bone are then surrounded by a periosteum that provides the source of new osteoblastic cells and thus for enlargement of the skeletal element. Molecular signaling mechanisms associated with the development, growth, and maintenance of the facial sutures are dependent on the presence of the nasal capsular cartilage, which appears to play a role similar to the dura mater in sutures of the cranial vault in the expression of *TGF-β1*, *TGF-β2*, *TGF-β3*, and *Msx2*.[48] It has also been shown that *Fgf8* plays a significant role in the integration and coordination of the frontonasal prominence with the nasal and optic regions.[49]

Virtually all of the major centers of ossification within the midface can be seen at approximately 7 to 8 weeks' gestation. At 6 weeks' gestation, the palatal shelves, which are mesenchymal tissue extensions of the embryonic maxillary processes of the first branchial arches, elevate within the oral cavity, where they will give rise to the hard and soft palates. The palatal shelves begin to ossify at 7 to 8 weeks' gestation, with the two bone fronts of the palatal processes each extending medially to form the secondary palate, composed of processes from the maxillary bones and from the palatine bones, as they meet in the midline, where they form the midpalatal suture.

The molecular mechanisms associated with the development of the palate are among the most studied in all of craniofacial growth and development because of the obvious problem of cleft lip and palate, which is the most common craniofacial deformity (~1:1000 for children of European descent).[50,51] Genes that have been identified specifically for a significant role in the genesis of cleft lip and palate now include isoforms of *BMP, Dlx, Fgf-8, Msx, Pitx, Sho2, Shh, Sox9,* and *TGF-β*, among others. It is also well documented that epigenetic factors, such as anoxia resulting from cigarette smoking and alcohol use, have a major impact on nonsyndromal cleft lip and palate.

Development of the nasomaxillary complex proceeds laterally and anteroposteriorly with expansion of the brain and cranial cavity and expansion of the oral cavity and oronasal pharynx. Also throughout the fetal period, anterior and inferior growth of the nasal septal cartilage, which is an extension of the anterior cranial base, is most prominent. The cartilaginous nasal capsule, which envelops the nasal cavity laterally, is primarily structural and contributes little to the overall growth of the nasomaxillary complex other than possible expression of growth factors that support the facial sutures (Fig. 2.20). Thus the primary factors influencing the growth of the nasomaxillary complex from the late embryonic period and throughout the fetal period and the juvenile period postnatally are an expansion of the brain and cranial vault and growth of the anterior cranial base, including in particular anterior and inferior growth of the nasal septum, as well as expansion of the nasal cavity and oronasal pharynx.

Postnatal Growth of the Midface

At the time of birth, the midface is well developed but diminutive relative to the neurocranium. The circummaxillary and intermaxillary sutures are all present and active as sites of bone growth. The nasal capsule and midline nasal septum are still primarily cartilaginous and continuous with the rest of the chondrocranium from the anterior cranial base. The septum is also very actively growing by means of interstitial cartilaginous growth, leading to significant anterior and vertical growth of the midface, especially during the first 3 to 4 years of life.

With the exception of the nasal septum, postnatal development of the nasomaxillary complex occurs by intramembranous ossification. Growth at the circummaxillary and intermaxillary sutures occurs in response to midfacial displacements, the result principally of growth of the anterior cranial base and nasal septum. Inferior, anterior, and lateral displacements of the midface result in concomitant compensatory sutural growth to account for the majority of vertical, anteroposterior, and transverse changes that occur during both childhood and

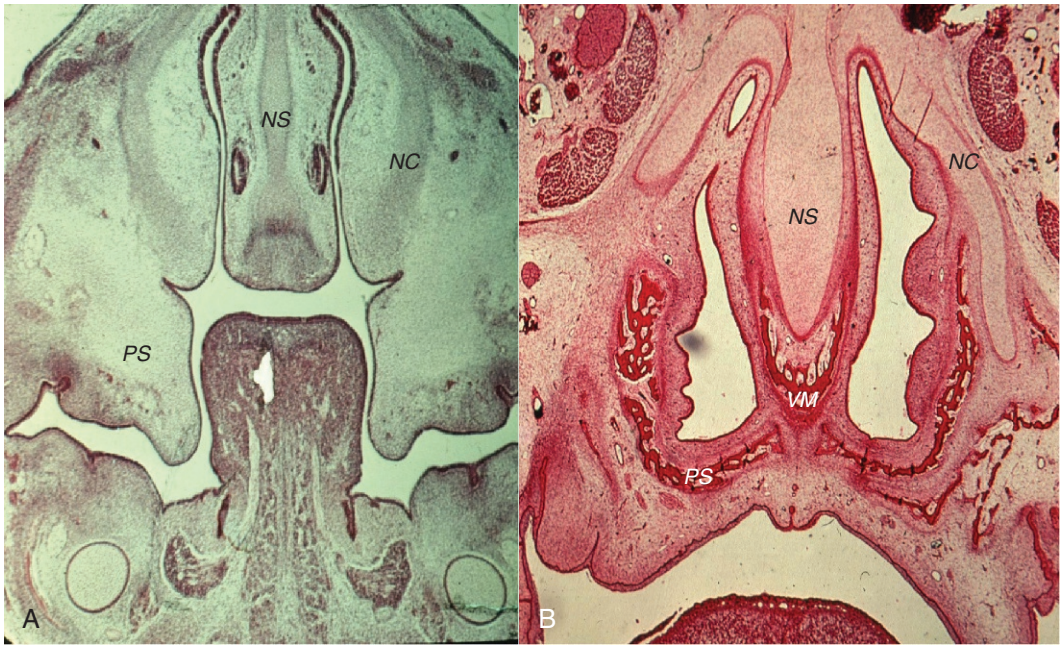


Fig. 2.20 Frontal histologic sections of human fetuses at approximate ages of 5 weeks' gestation **(A)** and 11 weeks' gestation **(B)** (hematoxylin and eosin–stained). *NC,* Nasal capsular cartilage; *NS,* nasal septal cartilage; *V,* vomer; *PS,* palatal shelves.

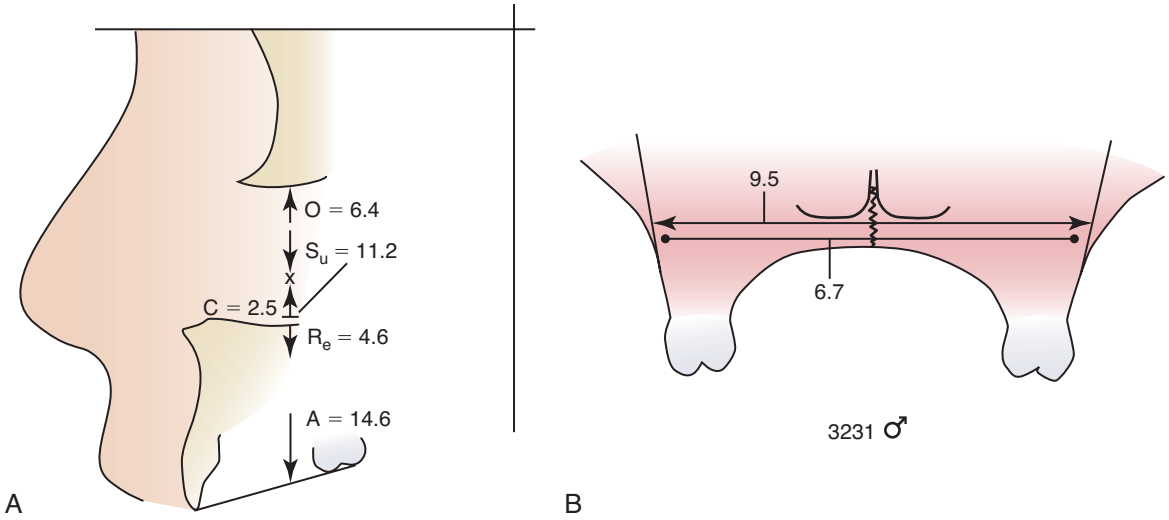


Fig. 2.21 **A,** Sutural displacement *(S_u),* apposition of the orbital floor *(O),* resorption of the nasal floor *(R_e),* apposition at the infrazygomatic crest *(C),* and dentoalveolar development *(A)* from 4 years of age through adulthood in nine boys. **(B)** Width changes (mm) of the maxilla and lateral implants between 3.9 and 17.7 years of age. (From Björk A, Skieller V. Postnatal growth and development of the maxillary complex. In: McNamara JA Jr, ed. *Factors Affecting the Growth of the Midface,* Ann Arbor, MI: Center for Human Growth and Development, Michigan Craniofacial Growth Series; 1976:61-100.)

adolescence (Fig. 2.21). Along with displacements, extensive surface modeling takes place over the entire nasomaxillary complex, especially along its posterior and superior aspects.

As long as the midface undergoes displacement, sutural growth occurs, with the amounts of bony apposition being related directly to amounts of sutural separation. Growth continues until the sutures are no longer separating. The premaxillary/maxillary suture fuses at approximately 3 to 5 years of age.[52] The midpalatal and transpalatal maxillary sutures, which are the major intermaxillary growth sites associated with transverse and anteroposterior maxillary growth, have been reported to close between 15 and 18 years of age[53] and 20 to 25 years of age,[54] respectively, depending on the criteria on which closure is based. More recent studies suggest only limited amounts of sutural obliteration (i.e., the development of bony bridges, or spicules, running across the suture after growth has ceased) in adult midpalatal sutures.[55,56] The increasing complexity that characterized sutures during childhood and adolescence appears to be functionally related rather than age related.[57] Although data are limited, it appears that closure of the circummaxillary sutures occurs somewhat later than closure of the intermaxillary sutures.

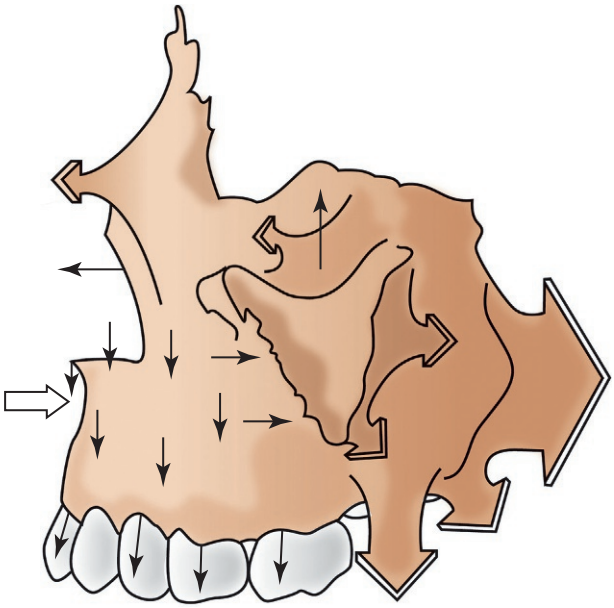


Fig. 2.22 Maxillary remodeling, with the sizes of the arrows indicating relative amounts of change and with *dark* and *light arrows* indicating resorption and apposition, respectively. (Redrawn from Enlow DH, Bang S. Growth and remodeling of the human maxilla. *Am J Orthod.* 1965;51:446-464.)

The midface undergoes a complex modeling pattern throughout childhood and adolescence (Fig. 2.22).[58] As the midface is displaced anteriorly, compensatory bony deposition occurs along the posterior margin of the maxillary tuberosity, resulting in an increase in the length of the entire maxilla and of the dental arches.[59] The posterior maxilla is a major modeling site that accounts for most of the increases in maxillary length. The anterior periosteal surface of the maxilla is slightly resorptive, while the buccal surfaces undergo substantial bony deposition. From the sagittal perspective, the area of the anterior nasal spine drifts inferiorly; the A-point also drifts inferiorly and slightly posteriorly. For every 4 mm that the posterior nasal spine drifts posteriorly, it drifts approximately 3 mm inferiorly. Associated with inferior displacement of the midfacial complex, bony resorption occurs along the floor of the nasal cavity, whereas apposition occurs on the roof of the oral cavity (i.e., palate) and orbital floor. Implant studies suggest that for every 11 mm of inferior midfacial displacement, the orbital floor drifts superiorly 6 mm and the nasal floor drifts inferiorly 5 mm.[60] Thus midfacial height increases because of the combined effects of inferior cortical drift and inferior displacement (see Fig. 2.21). The height of the midface is further increased by continued development of the dentition and alveolar bone. The lack of naturally stable structures on the surface of the midfacial complex makes superimposition difficult.

The width of the midface at the time of birth is proportionately large because of the precocious development of the eyes, which are the central features of the neonatal midface. Growth in width during the first 2 to 3 years after birth is associated with expansion of the brain laterally and anteroposteriorly, which brings the eyes laterally with it. As this occurs, the sutures separating the two halves of the frontal bone (metopic suture), the two nasal bones (internasal suture), the two maxillae (intermaxillary suture), and the two palatine bones (midpalatal suture) are positioned to respond by secondary, compensatory bone formation. It has been estimated that the midalveolar and bijugale widths of the maxilla increase approximately 5 and 6 mm, respectively, between 7.6 and 16.5 years of age; rates of growth in width diminish slightly with increasing age.[61]

At the same time that the midface is increasing in width, it is increasing even more dramatically in depth (anteriorly) and height (vertically). The midface increases most in height, next in depth, and least in width. As the brain and eyes grow anteriorly relative to the middle cranial base, the orbits increase in depth and the anterior cranial base lengthens, primarily as a result of growth at the sphenoethmoidal synchondrosis. Concomitantly, the nasal septum grows vertically as the midface is displaced inferiorly relative to the anterior cranial base. The combination of these two growth processes—growth in a vertical direction associated with interstitial cartilaginous growth within the nasal septum and growth in an anterior direction associated with interstitial cartilage growth within both the nasal septum and synchondroses of the cranial base—results in the typical downward and forward growth of the entire midface relative to the anterior cranial base. Surface deposition cannot account for the downward and forward midfacial growth that occurs during childhood and adolescence.

The age of approximately 7 years is something of a benchmark for growth of the midface. Growth of the CNS—the brain and eyes—is essentially complete at about 7 years of age. Concomitantly, the cartilage of the sphenoethmoidal synchondrosis ossifies and a suture is formed between the sphenoid and ethmoid bones at about that time. As a result, a relatively stable anterior cranial base is established extending from the sella turcica to the foramen cecum. Also at about 7 years of age, the growth of the cartilages of the nasal capsule and nasal septum changes significantly. The cartilaginous nasal capsule becomes ossified, and the nasal septum, which remains cartilaginous throughout life in humans, decreases significantly in growth activity. Despite these important developmental changes in the growth processes of the midface, downward and forward skeletal growth continues to be significant over the next decade or so, particularly in males during adolescence.

Growth of the nasomaxillary complex continues throughout childhood and adolescence, with substantially greater vertical than anteroposterior growth potential (Fig. 2.23). By 4.5 years of age, palatal length (anterior nasal spine–posterior nasal spine) and anterior facial height

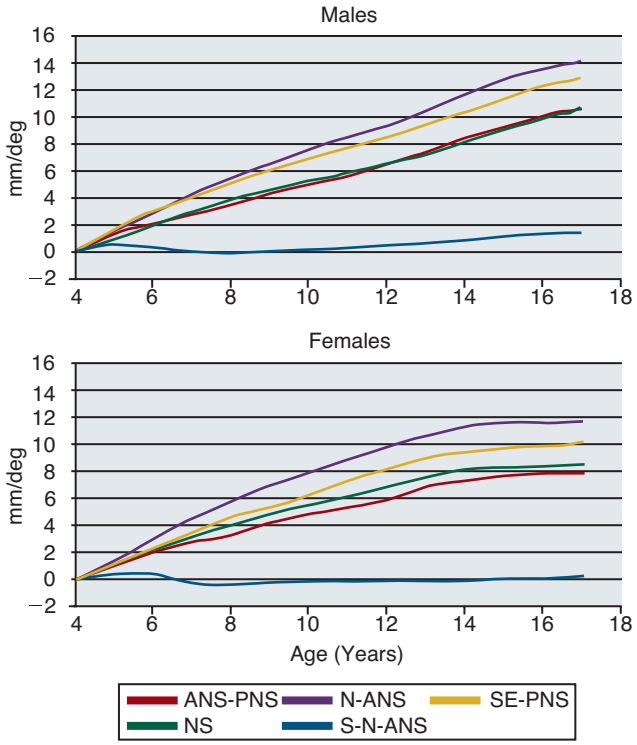
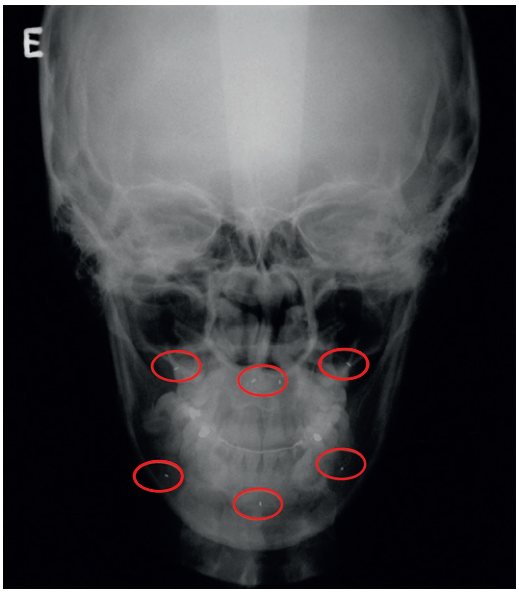


Fig. 2.23 Maxillary Growth Changes between 4 and 17 Years of Age of Males and Females. (Adapted from data provided by Bhatia SN, Leighton BC. *A Manual of Facial Growth: A Computer Analysis of Longitudinal Cephalometric Growth Data.* New York: Oxford University Press; 1993.)

(nasion–anterior nasal spine) have attained approximately 80% and 73% of their adult size, respectively (see Fig. 2.17). In terms of absolute growth, midfacial heights should be expected to increase 10 to 12 mm in females and 12 to 14 mm in males between 4 and 17 years of age. Palatal length should be expected to increase 8 to 10 mm over the same period. Because nasion drifts anteriorly at approximately the same rate as the midface is displaced anteriorly, the sella-nasion-anterior (SNA) nasal spine angle shows little or no change during childhood or adolescence. Although vertical maxillary growth rates peak during adolescence, at approximately the same time as stature, anteroposterior maxillary growth remains more or less constant, with no distinct adolescent spurt.

Because the displacements are not parallel, the midface undergoes varying amounts of vertical and transverse true rotation. True rotation is independent of surface modeling and refers to changes that occur over time in the positions of basal bone; it is commonly assessed with metallic implants placed into the mandibles and maxillae of growing children.[62] From the sagittal perspective, most children undergo true forward or counterclockwise (subject facing to the right) rotation of the midface, due to greater inferior displacement of the posterior than anterior maxilla. The true rotation that occurs tends to be covered up or hidden by the resorption that occurs on the nasal floor. For example, true forward rotation is associated with greater resorption in the anterior than posterior aspect of the nasal floor. Because of greater transverse displacements posteriorly than anteriorly, the midfacial complex also exhibits transverse rotation around the midpalatal suture (Fig. 2.24). As a result, there is greater sutural growth in the posterior than anterior aspect of the midpalatal suture. Cephalometric analyses using metallic implants have shown that the posterior maxilla expands approximately 0.27 to 0.43 mm/yr, with greater expansion occurring during childhood than during adolescence.[60]



References	Ages (Years)	*Mx*	*Md*
Björk and Skieller, 1977	4-21	.42	N/A
Korn and Baumrind, 1990	8.5-15.5	.43	.28
Gandini and Buschang, 2000	13.9-16.7	.27	0.19
Iseri and Solow, 2000	7-12	N/A	.22
	13-18	N/A	.13

Fig. 2.24 Transverse expansion (mm/yr) of metallic bone markers inserted into the maxillary *(Mx)* and mandibular *(Md)* basal structures.

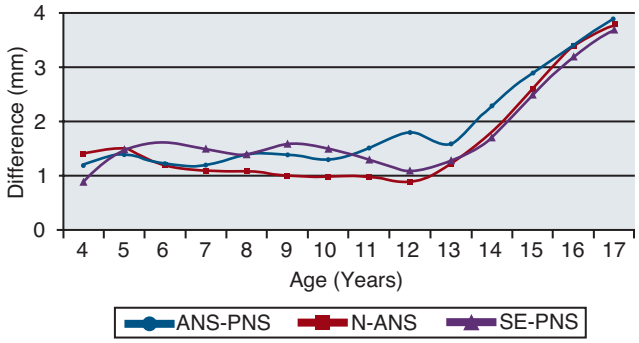


Fig. 2.25 Sex Differences (Male Minus Female) in Maxillary Size. (Adapted from data provided by Bhatia SN, Leighton BC. *A Manual of Facial Growth: A Computer Analysis of Longitudinal Cephalometric Growth Data.* New York: Oxford University Press; 1993.)

There are definite sex differences in maxillary postnatal growth (Fig. 2.25), with males being larger and growing more than females. Size differences, averaging between 1 and 1.5 mm, are small but consistent during infancy and childhood. Sexual dimorphism increases substantially throughout the midfacial complex during adolescence, with differences of approximately 4 mm in maxillary length (anterior nasal spine to posterior nasal spine [ANS-PNS]) and upper facial height (nasion to anterior nasal spine [N-ANS]) at 17 years of age. Males also have significantly wider midfaces than females, with differences approximating 5 to 7 mm during late adolescence.[63] The primary reason that adult males are larger than adult females is the extra 2 years of childhood growth that males have; males enter the adolescence phase of growth at approximately 12 years of age, whereas females enter around 10 years. Males are also larger than females because they experience a more intense adolescent spurt, but this contributes less to the sex differences observed.

MANDIBLE

Development of the Mandible

The mandible develops bilaterally within the mandibular processes of the first branchial arch. Each embryonic mandibular process contains a rodlike cartilaginous core, Meckel's cartilage, which is an extension of the chondrocranium into the viscerocranium. Throughout its course, distally Meckel's cartilage is accompanied by the mandibular division of the trigeminal nerve (cranial nerve V), as well as the inferior alveolar artery and vein. Proximally, Meckel's cartilage articulates with the cartilaginous cranial base in the petrous region of the temporal bone, where it gives rise to the malleus and incus bones of the inner ear.

By 6 weeks' gestation, a center of ossification appears in the perichondrial membrane lateral to Meckel's cartilage.[46] It is critical to note that ossification of the mandible takes place in membrane *lateral* and *adjacent* to Meckel's cartilage, and *not within* Meckel's cartilage itself (Fig. 2.26). Therefore it is clear that the mandible develops and subsequently grows by means of intramembranous ossification and not through endochondral ossification and replacement of Meckel's cartilage. The only portion of the developing lower jaw that appears to be derived from endochondral ossification of Meckel's cartilage is the mental ossicles, which are two very small sesamoid bones that are

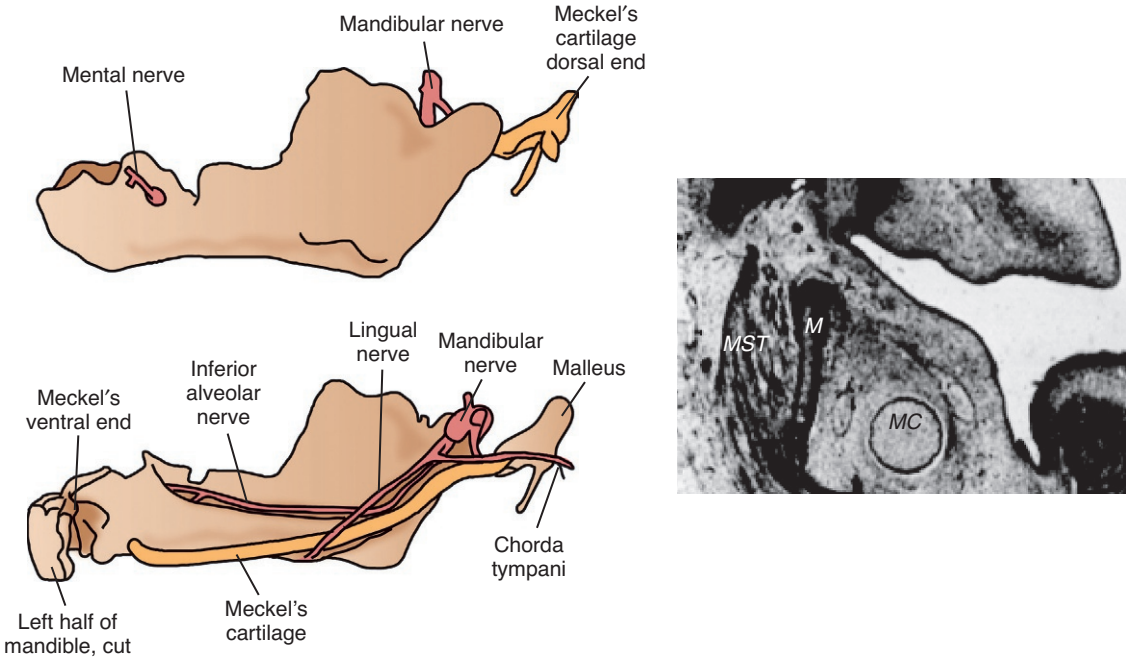


Fig. 2.26 Drawings of a Fetal Mandible with Lateral *(top left)* and Medial *(bottom left)* Views. *Right,* Photomicrograph of coronal view of human fetus indicating Meckel's cartilage medial to the mandible *(M). MST,* Masseter muscle. (Drawings adapted from Warwick R, Williams PL, eds. *Gray's Anatomy*. 35th ed. Philadelphia: WB Saunders; 1973.)

formed in the inferior aspect of the mandibular symphysis.[65] These bones are no longer present at the time of birth.

Intramembranous ossification of the body of the mandible proceeds distally toward the mental symphysis and proximally up to the region of the mandibular foramen. As it does so, Meckel's cartilage begins to degenerate and involute as the inferoalveolar neurovascular bundle becomes progressively enveloped by the intramembranously developing mandibular bone. Meckel's cartilage completely disappears by approximately 24 weeks' gestation, remaining in remnant form as the dense sphenomandibular ligament and giving rise to the malleus and incus ear ossicles.

Initial evidence of the formation of the temporomandibular joint (TMJ) is seen on expression of the Barx-1 homeobox gene. By approximately 8 weeks' gestation, the condylar process appears as a separate carrot-shaped blastema of cartilage extending from the ramus proximal to the mandibular foramen and extending up to articulate with the squamous (membranous) portion of the developing temporal bone. Formation of the joint cavity between the condylar process and the squamous portion of the temporal bone is essentially completed as the TMJ by about 12 weeks' gestation (Fig. 2.27).

Because the cartilage composing the mandibular condyle arises "secondarily" within a skeletogenic membrane and apart from the primary embryonic cartilaginous anlagen, it is referred to as a *secondary cartilage* (Fig. 2.28). Secondary cartilage is a unique type of skeletal tissue that has the characteristics of both intramembranous bone and certain histologic and functional features of hyaline growth cartilage. Secondary cartilage is formed in areas of precocious stresses and strains within intramembranous bones, as well as in areas of rapid development and growth of bone.[65,66] Within the craniofacial complex, the angular and the coronoid processes of the mandible also may exhibit the presence of secondary cartilage because these are sites of very rapid bone growth associated with the function of the muscles of mastication. In addition, secondary cartilage may be found in areas

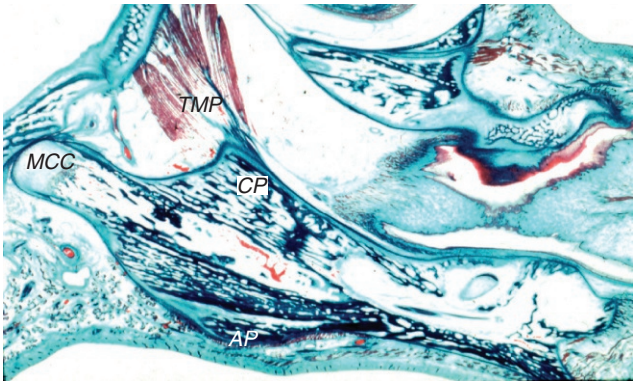


Fig. 2.27 Parasagittal histologic section of human fetus (~12 weeks' gestation) (hematoxylin and eosin–stained). *MCC,* Mandibular condylar cartilage; *CP,* coronoid process; *AP,* angular process; *TMP,* temporalis muscle.

of sutures characterized by rapid intramembranous bone growth and biomechanical load associated with separation and bending at the articular surfaces.

At birth, the two halves of the mandible are separated in the midline by a fibrous articulation, the mental symphysis, which will fuse by the end of the first year of life. Each half of the mandible is characterized anatomically by (1) a *condyle* and *condylar process,* which articulates with the temporal bone to make up the TMJ; (2) a *ramus,* which extends roughly vertically–inferiorly from the condylar process and provides insertions for the muscles of mastication; and (3) a *corpus,* or body, which extends roughly horizontally–anteriorly to provide a base for the mandibular dental arch and house the inferior alveolar–neurovascular bundle. Each of these anatomic structures also can be considered in terms of overlapping functional units (Fig. 2.29). The mandibular condyle and condylar processes obviously are essential for

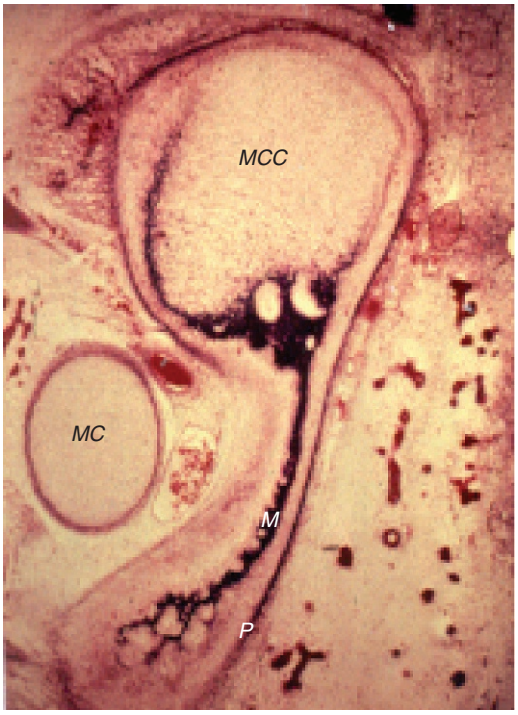


Fig. 2.28 Frontal histologic section of a human fetus (~8 weeks' gestation) (hematoxylin and eosin–stained). The bone comprising the body and ramus of the mandible *(M)* originates in the membrane lateral to Meckel's cartilage *(MC)*. The periosteal membrane enveloping the mandible gives rise secondarily to the mandibular condylar cartilage *(MCC)*.

normal articular function of the TMJ and movements of the mandible, while at the same time playing a significant role in mandibular growth for most of the first two decades of life.[67] Variation in the function of the TMJ, such as might occur in association with differences in mastication, jaw movements, and jaw position, for example, is highly likely to affect its growth and form. The gonial region of the mandible, at the inferior aspect of the ramus, is related to the function of the masseter and medial pterygoid complex of muscles, and the coronoid process is primarily related to the temporalis muscle. Variation in the growth and form of each of these regions is due in large part to variation in the function of the muscles of mastication. The alveolar process of the mandible functions to provide support for the dentition. Finally, the body of the mandible, extending from the mandibular foramen to the mental process, provides support and structural connection between the various functional components of the mandible.

Growth of the Mandibular Condyle

Just as a suture can be considered to be a specialization of an osteogenic membrane (i.e., periosteum and dura mater), the condylar cartilage can also best be considered to be a specialization of periosteum. As with sutures, growth of the mandibular condyle tends to be relatively highly responsive to mechanical, functional, and hormonal stimuli both at the time of development and throughout the growth period, similar to intramembranous bone development elsewhere.

Histomorphology of the Growing Condyle

A number of similar but somewhat different terms have been used to describe the histomorphology of the growing mandibular condyle.[68] These are summarized according to their equivalencies in E-Table 2.2.

The secondary cartilage composing the condyle during growth can be divided into two general layers: an articular layer and a growth layer. The more superficial *articular layer* is continuous with the outer fibrous layer of the bilaminar periosteum, encapsulating the condylar neck and temporal bone, respectively. Deep to the articular layer is a subarticular *growth layer*. The growth layer of the condylar cartilage is organized into an additional series of layers or zones typical of growing cartilage that blend into each other (Fig. 2.30). Each of these zones is present in the neonate and remains in the condyle through maturity. However, their absolute and relative size as well as their growth-related activity may vary considerably, depending on the overall rate and amount of condylar growth and on the functional requirements placed on the condyle and TMJ.[69,70]

Articular layer. The articular layer of the joint surface of the mandibular condyle and temporal portion of the TMJ consist of an avascular dense fibroelastic connective tissue whose collagen fibers are oriented parallel to the articular surface. The articular layer varies in thickness along the condylar head and temporal joint surface, increasing in thickness in the superior aspect of the condyle and on the articular eminence of the glenoid fossa, where compressive forces associated with mastication are greatest.[71] The fibrous articular layer of the mandibular condyle and that found in the glenoid fossa and articular eminence are identical functionally to the articular cartilage found in the diarthroidial joints of the postcranial long bones, but their origin and histologic composition are completely different. Articular cartilage is derived from the primary cartilaginous anlagen at the ends of long bones; the articular tissue of the TMJ is a specialization of the fibrous layer of periosteum that covers the mandible and temporal bone.

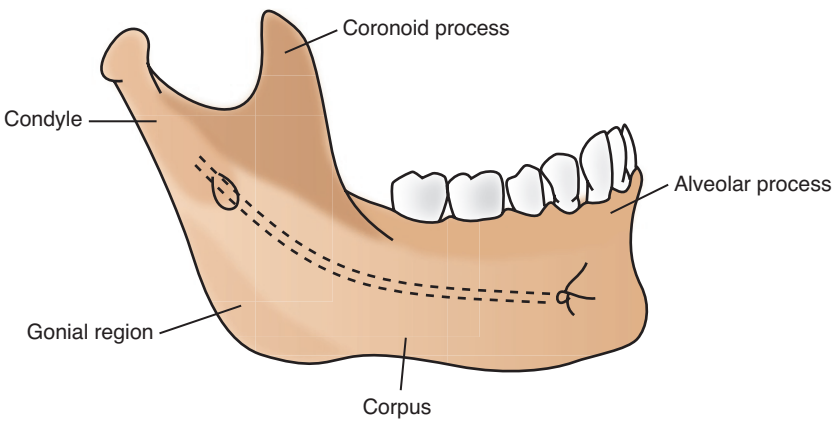


Fig. 2.29 Major Functional Units of the Mandible.

TABLE 2.2 Comparison of Terminology Used to Describe the Histomorphology of the Condylar Cartilage

Blackwood[1]	Durkin et al.[2]	Wright and Moffett[3]	Petrovic et al.[4]	Thilander et al.[5]	Carlson et al.[6]	Luder[7]
Articular zone	Resting surface articular layer	Articular layer	Fibrous capsule	Surface articular layer	Fibrous articular tissue	*Perichondrium* articular layer
	Transitional or proliferative layer	Proliferative layer	Prechondroblastic layer	Proliferative layer	Prechondroblastic (proliferative) layer	Polymorphic cell layer Flattened cell layer (1 and 2)
Intermediate zone	Hypertrophic cartilage	Zone of matrix production	Zone of maturation Functional chondroblasts	Hypertrophic zone (nonmineralized)	Chondroblastic zone (maturation and hypertrophy)	Hyaline cartilage Flattened cell layer (3)
Hypertrophic cartilage	Erosion zone	Zone of cell hypertrophy	Hypertrophic chondroblasts	Hypertrophic zone (mineralized)		Upper hypertrophic cell layer
		Zone of calcification and resorption	Zone of erosion Degenerating chondroblasts			Lower hypertrophic cell layer
	Subchondral bone		Zone of endochondral ossification		Zone of endochondral ossification	

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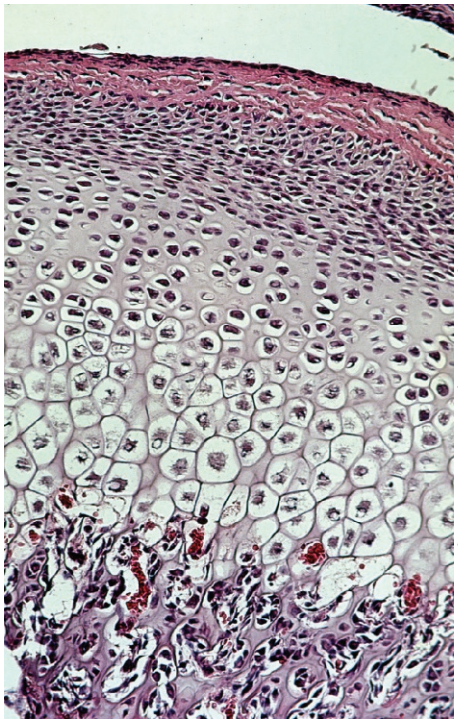


Fig. 2.30 Histologic section indicating the various layers of the secondary cartilage in a growing mandibular condyle (hematoxylin and eosin stain).

Growth layer. The growth layer immediately deep to the articular layer comprises of a series of cellular zones representing the various stages of chondrogenesis in secondary cartilage. The *proliferative,* or *prechondroblastic, zone* immediately deep to the articular layer is continuous with the osteogenic layer of the periosteal membrane along the condylar neck.[72,73] Its outer portion is composed of undifferentiated mesenchymal cells that differentiate into skeletoblastic stem cells or prechondroblasts. Morphologically, this zone appears as densely packed with spindle-shaped cells that increase in size and become increasingly separated as a result of production of intercellular matrix within the inner region of the proliferative zone. The newly formed cartilage cells in the proliferative zone express type I collagen, which is characteristic of bone and underscores the fact that the source of these cells is a periosteal-like membrane. Recent studies of gene expression in the proliferative zone demonstrate that the prechondroblastic layer is also characterized by high expression of *FGF-13*, *FGF-18*, *TGF-β2*, *IGF-1*, and vascular endothelial growth factor.[74,75]

The *zone of maturation* contains larger, spherical, maturing chondrocytes arranged in an apparently random fashion. These cartilage cells undergo very few mitoses, which is atypical for cartilage cells found in a growing epiphyseal plate. In addition, there is significantly less extracellular matrix in the mandibular condylar cartilage than is found in the growth plates of developing long bones, which are composed of primary cartilage. Cartilage cells within the zone of maturation are capable of switching their phenotype to express type II collagen, which is typically expressed by primary cartilage in growing epiphyses in response to biomechanical load.

Cartilage cells in the *zone of hypertrophy* become progressively larger through osmotic activity and absorption of water. Their nuclei become pyknotic and their cytoplasm is increasingly evacuated as the cells are about to be encroached upon by the osteoblasts from the endosteal region of the condyle. Genes for procollagen, aggrecan, Sox9, and Ihh are highly expressed in the chondroblastic layer.[74]

The *zone of endochondral ossification* is characterized by the initiation of mineralization of the intercellular matrix within the distal-most three to five layers of hypertrophying cells. This matrix is subsequently eroded away by osteoclastic activity and replaced by bone. The process of endochondral ossification associated with the condylar cartilage is identical to the process that takes place in the primary cartilage of long bone epiphyses.

Age-Related Changes in the Mandibular Condyle

Detailed histologic analysis of human autopsy specimens of the human TMJ has demonstrated progressive changes in the thickness and presumed growth activity of the condyle cartilage throughout development.[76-79] These changes appear to be coordinated with functional changes associated with occlusal development.[80,81] In general, the combined growth-related layers of the condylar cartilage begin as a relatively thick structure in the neonate (1.25–1.5 mm thick) but become much thinner (0.3 mm) by the mixed dentition stage. The cartilage remains generally thin but well defined and actively growing in the permanent dentition stage until, by age 20 to 30 years, the cartilage essentially disappears and the condyle is capped by a bony plate. Even in adults, however, it is not unusual to see areas of hyaline cartilage ("cartilage islands") deep to the articular layer in the condyle.

The subarticular region of the temporal component of the TMJ has the same tissue layers as the condyle; however, they are substantially less prominent. Morphologically, the temporal component of the TMJ in the neonate is essentially flat, and the articular disc interposed between the condyle and temporal bone is highly vascular. During the period of the primary dentition, at approximately 3 years of age, the temporal surface takes on its characteristic S-shaped contour, and the articular disc becomes avascular in its central region. Thereafter, the temporal surface of the TMJ grows more slowly, with the mandibular fossa becoming deeper as the articular eminence becomes steeper; this happens primarily through the process of bone deposition on the articular eminence and, to a lesser extent, by resorption of bone in the posterosuperior region of the fossa, as well as endosteal deposition in the superior aspect of the fossa. This increase in the contour of the temporal component of the TMJ normally continues until the fourth decade of life.

In summary, the mandibular condylar cartilage is a secondary cartilage that in subadult individuals serves both as a site of growth and as a place of articulation. Thus, it displays functional characteristics of both a growth plate and an articular cartilage, but it differs from both in fundamental aspects of its development and structure throughout ontogeny. Its most superficial layers are not cartilaginous in phenotype but rather are perichondrial in origin. Importantly, the chondrocytes of the mandibular condylar cartilage are derived by mitosis in cells that are themselves not chondrocytes, similar to embryonic cartilage but not to the growth plate in which the cells that proliferate are chondrocytes. Finally, the prechondrogenic phenotype of these dividing cells in the mandibular condylar cartilage can be readily modulated to a preosteogenic phenotype by changes in the periarticular environment. Taken together, these features define a tissue with structural and growth characteristics that are consistent with the concept of an adaptive, compensatory growth site and set it apart from primary cartilaginous growth centers.

Mechanisms of Condylar Growth

The mandibular-condylar cartilage was initially considered to be a growth center with an intrinsic capacity for tissue-separating growth. However, it is now generally understood that growth of the mandibular-condylar cartilage is highly adaptive and responsive to growth in adjacent regions, particularly the maxilla. Numerous

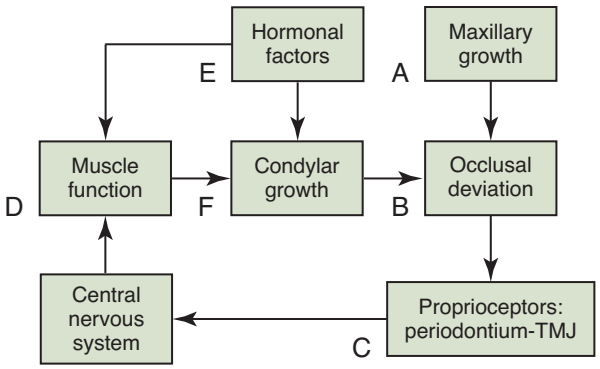


Fig. 2.31 Simplified Explanation of Petrovic's "Servosystem Hypothesis of Mandibular Growth." Independent growth of the maxilla *(A)* creates a minor occlusal deviation between the upper and lower dentition *(B)*. This occlusal deviation is perceived by proprioceptors *(C)*, which provide a signal to the muscles responsible for jaw protrusion to be tonically more active *(D)*, which causes the mandibular condyle to become slightly more anteriorly located within the temporomandibular joint, thus stimulating condylar growth *(F)*. Muscle function and the adaptive capacity of the condyle for growth are enhanced by expression of hormonal factors *(E)*, and thus condylar growth may vary depending on the maturational and hormonal status of the individual. (Adapted from Carlson DS. Theories of craniofacial growth in the postgenomic era. *Semin Orthod.* 2005;11(4):172-183.)

experimental studies were conducted over the past several decades to assess the role that function and jaw position, in particular, might play in influencing the postnatal growth of the mandibular condyle. For example, a number of studies involving anterior postural change of the mandible using rats[82,83] and primates[84] as experimental animals demonstrated significant increases in the overall length of the mandible. From these experiments, Petrovic et al. developed a "cybernetic" model of mandibular growth regulation referred to as the "servosystem hypothesis of mandibular growth" (Fig. 2.31).[85,86]

There has been a significant expansion of knowledge concerning the molecular biology and cellular dynamics associated with growth of the condylar cartilage. It has been shown, for example, that FGF and IGF are present in the matrix and cell surfaces of the condylar cartilage and that they vary according to their specific location, much like in sutures. Less is known of the presence or importance of TGF-β or other growth factors, and knowledge of hormonal influences on growth of the condylar cartilage is even more rudimentary and somewhat contradictory.[87-89]

Several studies have begun to explore the molecular basis for the effect of mandibular function and position on mandibular growth by using appliances that replicate the effects (e.g., increased mitotic activity, cartilage thickness) reported previously.[90-93] Fuentes et al.[94] used a novel incisor-borne appliance that prompted a crossbite in growing rats and produced a differential change in proliferation and cartilage thickness between the crossbite and noncrossbite sides. In animals wearing the appliance, gene expression for *IGF-1* and *FGF-2* and their receptors in condylar cartilage was altered from that in control rats. The changes in gene expression, which typically preceded the changes in mitotic activity and cartilage thickness, were in most instances opposite in direction between the crossbite and noncrossbite sides. Using a similar design, Hajjar et al.[95] found that rats fitted with an incisor-borne appliance that prompted anterior displacement of the mandible exhibited increased expression of both *IGF-I* and *IGF-II* mRNA and protein in the mandibular condylar cartilage. Rabie et al.[90,96] and Tang et al.[97] demonstrated that the expression of *Sox9*, type II collagen, and Indian hedgehog (*Ihh*) was increased in the condylar cartilage and glenoid fossa of rats wearing the appliance for 1 to 2 weeks.

In general, these findings parallel the findings discussed previously for development of the sutures of the cranial vault. These similarities between the condylar cartilage and sutures should not be surprising given the periosteal origin of both suture mesenchyme and the secondary cartilage of the mandibular condyle.

Postnatal Growth of the Mandible

At birth, the ramus of the mandible is quite short, both in absolute terms and in proportion to the mandibular corpus. During postnatal development, the ramus becomes much more prominent, particularly in height but also in width. At the same time, the corpus increases in length, providing the necessary space for development and eruption of the mandibular dentition. Associated with these early postnatal changes in the absolute and relative sizes of the mandible are decreases in the gonial angle between the ramus and corpus and increases in the angle between the two corpora.

The mandible has the greatest postnatal growth potential of any component of the craniofacial complex. Growth changes that occur are closely associated with the functional processes that comprise the mandible, including the gonial process, coronoid process, alveolar process, and bony attachments of the suprahyoid muscles, which are all major sites of postnatal modeling. Although condylar growth is often assumed to be the mandible's primary growth site, it is important to note that the entire superior aspect of the ramus displays approximately the same amount of growth.

Viewed in its lateral projection, the posteroinferior and superior border of the ramus, including the condyle, and the posterosuperior aspect of the coronoid process are depository throughout the period of active growth. The anterior and lower borders (extending approximately to the first molars) of the ramus of the mandible are resorptive. Resorption of bone continues to occur along the anterior border of the ramus, resulting in a longer corpus and increased space for the development and eruption of the mandibular dentition (Fig. 2.32).[98] Within the corpus, the greatest growth changes are appositional growth of the

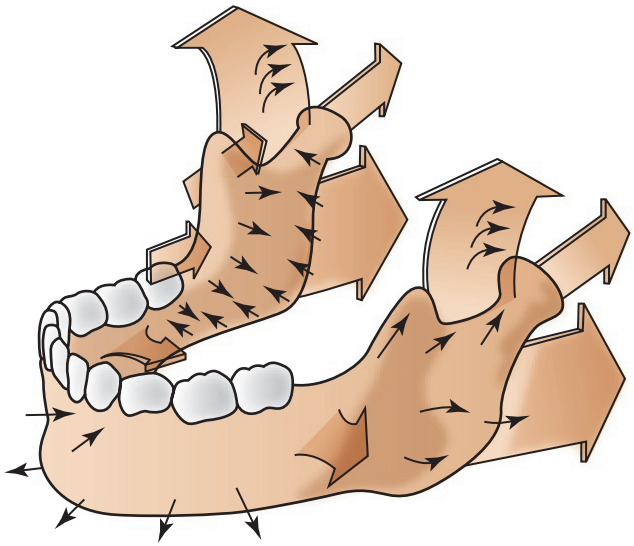


Fig. 2.32 Mandibular remodeling, with the sizes of the arrows indicating relative amounts of change and with *dark* and *light arrows* indicating resorption and apposition, respectively. (Adapted from Enlow DH, Harris DB. A study of the postnatal growth of the human mandible. *Am J Orthod.* 1964;50:25.)

alveolar bone associated with dental development and eruption. The symphysis, especially the superior aspect, becomes wider because of superior and posterior drift of its posterior aspect (Fig. 2.33).[99] There is resorption on the anterior aspect of the symphysis above the bony chin. The cortical region at or just above the chin is the only place on the entire surface of the mandible that remains stable (i.e., does not model) during postnatal growth, which is why it serves as an important site for superimposing successive radiographs. The inferior aspect of the anterior corpus tends to be depository, but the amounts of bone added are limited and variable.

Widening of the body of the mandible occurs through deposition of bone along the buccal surface and transverse rotation of the right and left corpora. The mandible also widens as a result of bony deposition along its posterior surface, which, because of its posterolateral orientation, produces a longer and wider body. Growth in width of the superior aspect of the ramus is somewhat more complex as a result of the substantial increases in height that occur. Viewed in a coronal projection, the superior aspect of the ramus and coronoid process are canted somewhat mediolaterally. As the mandibular corpus and inferior aspect of the ramus increase in width by deposition along the buccal surface, the buccal surface of bone on the superior aspect of the ramus is resorptive, whereas the lingual and superior surfaces of bone are depository.

The greatest postnatal changes in mandibular growth also occur during infancy, with overall length (condylion to gnathion [Co–Gn]) increasing 15 to 18 mm during the first year, 8 to 9 mm during the second year, and then slowing down to increase approximately 5 mm during the third year. During these early years, condylar growth and modeling of the superior aspects of the ramus are directed posteriorly and superiorly, with roughly equal amounts of growth in each direction. This orientation is important because it rapidly increases corpus length to make room for the rapidly developing dentition. After the first few postnatal years, growth of the condyle and superior ramus slows down dramatically and changes orientation toward a predominant superior direction.

By 4.5 years of age, ramus height has attained approximately 64% and 70% of its adult size for males and females, respectively (see Fig. 2.17). Corpus length (Go-Gn) closely approximates the maturity pattern of midfacial height; it remains more mature than ramus height throughout postnatal growth. This supports the general principle that the vertical aspects of craniofacial growth are less mature and have greater postnatal growth potential than the anteroposterior aspects. Total mandibular length (condylion to menton [Co-Me]) undergoes the greatest increases in length (~25 and 30 mm for females and males, respectively) between 4 and 17 years of age, followed by corpus length (gonion to pogonion [Go-Pg]; approximately 18 and 22 mm for females and males, respectively) and ramus height (condylion to gonion [Co-Go]; approximately 14 and 17 mm for females and males, respectively) (Fig. 2.34). During later childhood and adolescence, the condyle shows substantially greater amounts of superior than posterior growth. For every 1 mm of posterior growth, there is 8 to 9 mm of superior growth. It has been estimated that the condyles of females and males grow 2 to 2.5 and 2.5 to 3.0 mm/yr, respectively, during childhood and adolescence, with the greatest rates occurring during the adolescent spurt (Fig. 2.35). The coronoid process and sigmoid notch follow similar growth patterns. Because of the resorption of bone that normally occurs in the gonial region, ramus height (measured from gonion to condylion) substantially underestimates the actual amount of growth that occurs at the condyle. There is approximately 1 mm of resorption at gonion for every 3 mm of superior condylar growth.[100] Between 7 and 15 years of age, biantegonial and bigonial widths increase approximately 10 12 mm, respectively.[61,63] Importantly, mandibular width continues to increase throughout childhood and adolescence. Although an adolescent spurt in vertical mandibular growth certainly occurs, a

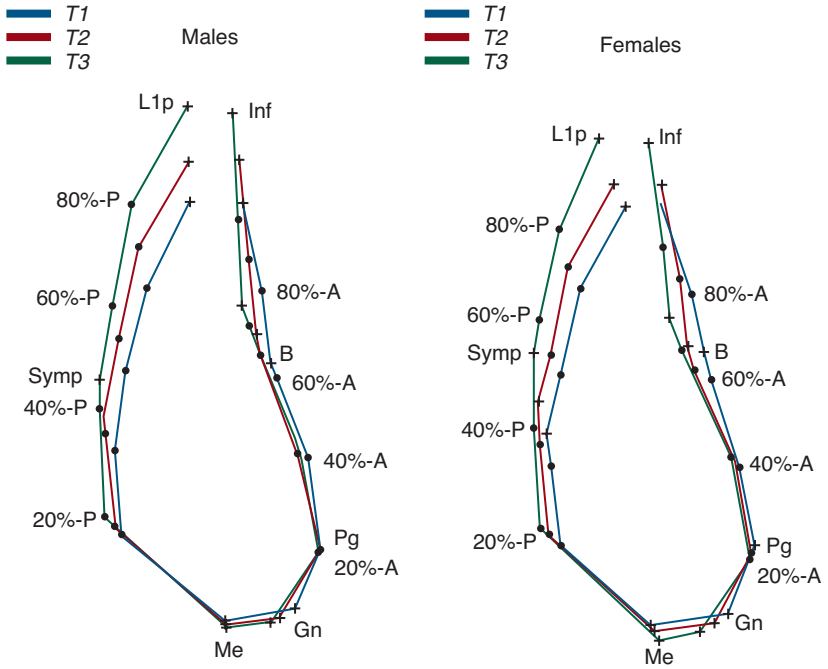


Fig. 2.33 Remodeling Changes of the Symphysis between 6 *(T1),* 10 *(T2),* and 15 *(T3)* Years of Age. *Gn,* Gnathion; *Inf,* infradentale; *Me,* menton; *Pg,* pogonion; *Symp,* posterior symphysis. (Adapted from Buschang PH, Julien K, Sachdeva R, et al. Childhood and pubertal growth changes of the human symphysis. *Angle Orthod.* 1992;62:203-210.)

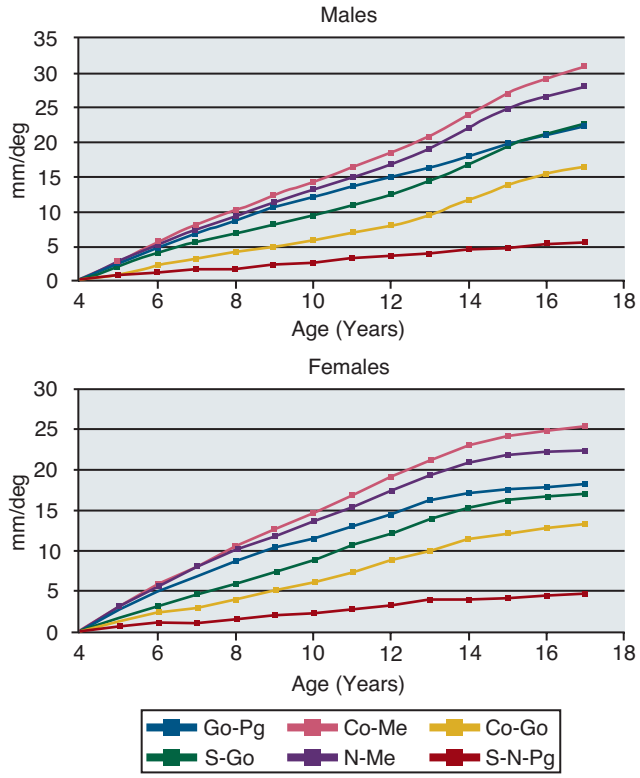


Fig. 2.34 Mandibular growth changes between 4 and 17 years of age of males and females. (Adapted from data provided by Bhatia SN, Leighton BC. *A Manual of Facial Growth: A Computer Analysis of Longitudinal Cephalometric Growth Data*. New York: Oxford University Press; 1993.)

pronounced spurt for the anteroposterior and transverse growth has not been established.

The mandible undergoes substantial amounts of true vertical rotation and more limited, but definite, transverse rotation. Although the maxilla exhibits more transverse rotation, the mandible exhibits more vertical rotation than the maxilla. The typical pattern of vertical rotation is forward (counterclockwise with the subject facing to the right), as a result of greater inferior displacements of the posterior than anterior aspects of the mandible.[101] Rates of vertical mandibular rotation have been estimated to range between 0.4 and 1.3 degrees/yr, with significantly greater rates of rotation during childhood than adolescence (Fig. 2.36). Although relatively few (< 10%) children are "true" posterior rotators, up to 25% of adolescents have been reported to be posterior rotators.[80] Greater amounts of true mandibular rotation occur during the transition to the early mixed dentition than at any time thereafter.[102,103]

The mandible also rotates transversely because of greater expansion of the posterior than of the anterior aspects of the two corpora. This type of rotation has been demonstrated repeatedly in subjects with metallic implants and represents expansion of basal bone. It has also been shown that, when viewed from frontal projects, the right and left mandibular nerves are displaced laterally throughout growth. Transverse rotation is also age related, with greater amounts occurring during childhood than adolescence. The posterior aspect of the mandible expands approximately 65% to 70% as much as the posterior maxilla expands at the posterior aspect of the midpalatal suture (see Fig. 2.20).

As in the rest of the craniofacial complex, sex differences in mandibular growth are evident at the earliest ages and become pronounced during adolescence. At birth, males have significantly larger mandibles than do females. Sex differences, which are greatest for overall length, followed by corpus length and ramus height, respectively, range from 0 to 2 mm between 1 and 12 years of age, when males initiate their adolescent phase of growth. Mandibular dimorphism increases to 4 to 8 mm by the end of the adolescent growth phase (Fig. 2.37). There are no sex differences in vertical rotation during childhood or adolescence.

In summary, the mandible increases in size as a result of the combined processes of proliferation of secondary cartilage at the condyle and differential formation and modeling of bone along the entire surface of the mandible, particularly along its superior and posterior aspects. Growth of the mandible is expressed in a downward and forward direction relative to the cranium and cranial base. The mandible is typically displaced downward more than the maxilla, with the resulting space being taken up by the erupting dentition. Because of the geometry of the craniofacial complex, normal, coordinated growth of the jaws and a normal relationship of the associated occlusal arches require that the relative rate and amount of growth of the maxilla and mandible differ.

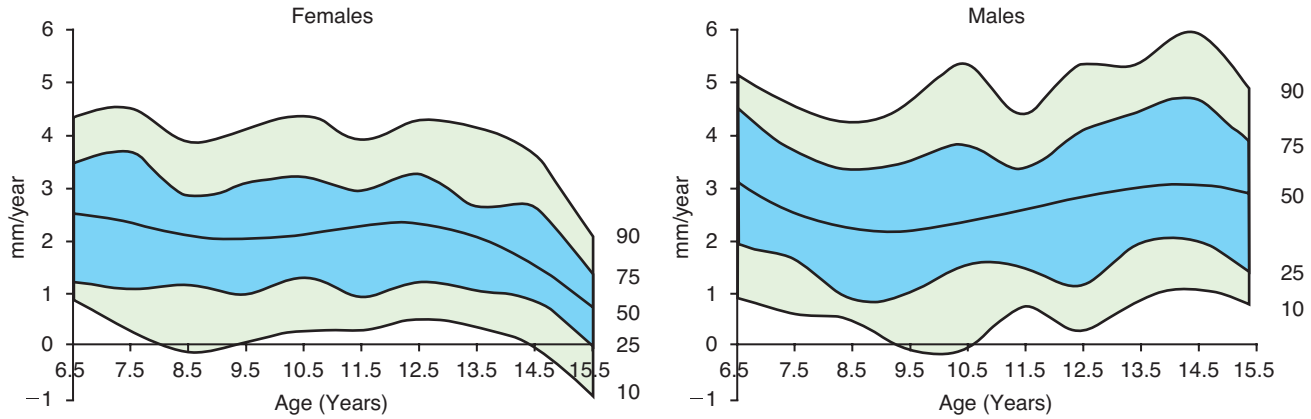
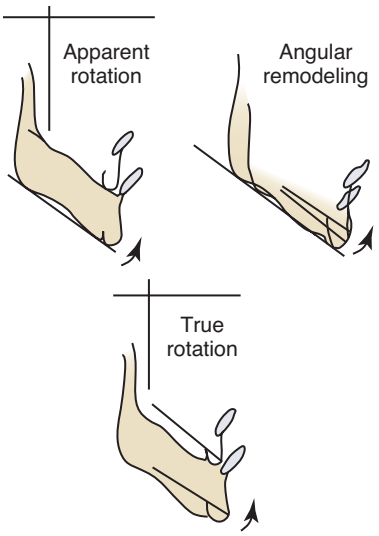


Fig. 2.35 Percentile Curves for Condylar Growth of Females and Males. (Adapted from Buschang PH, Santos Pinto A. Condylar growth and glenoid fossa displacement during childhood and adolescence. *Am J Orthod Dentofac Orthop*. 1998;113:437-442.)



References	Ages	deg/yr
Odegaard, 1970	7-14	0.8
Lavergne and Gasson, 1977	7-19	0.9
Skieller et al., 1984	Adolescence	1.0
Spady et al., 1992	Childhood	0.9
	Adolescence	0.4
Miller and Kerr, 1992	5-10	1.3
	10-15	0.8
Karlsen, 1995	6-12 (high angle)	0.7
	6-12 (low angle)	1.3
	12-15 (high angle)	0.7
	12-15 (low angle)	1.3
Wang et al., 2009	5.6-8.5	1.3
	8.5-15.5	0.7

Fig. 2.36 True Mandibular Rotation (Degrees per Year) During Childhood and Adolescence.

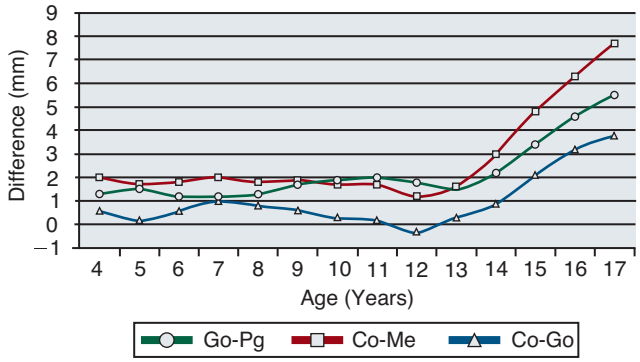


Fig. 2.37 Sex Differences (Male Minus Female) in Mandibular Size. (Adapted from Bhatia SN, Leighton BC. *A Manual of Facial Growth: A Computer Analysis of Longitudinal Cephalometric Growth Data.* New York: Oxford University Press; 1993.)

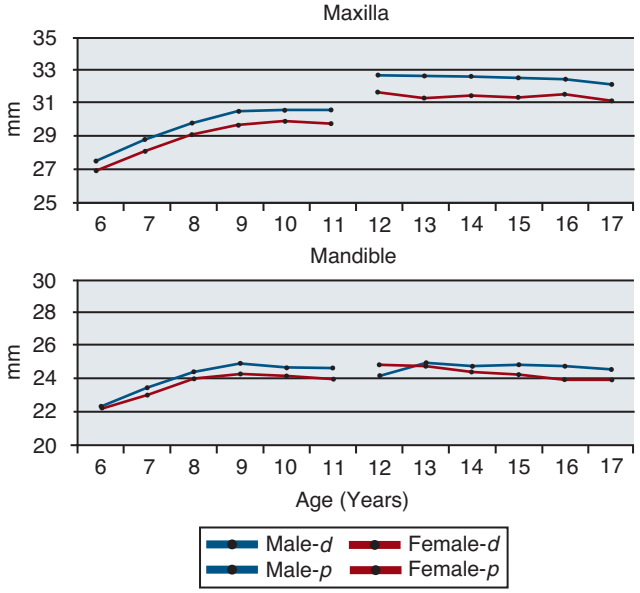


Fig. 2.38 Maxillary and mandibular intercanine widths of males and females based on measurements taken from the deciduous *(d)* and permanent *(p)* canines. (Data from Moyers RE, van der Linden PGM, Riolo ML, et al. *Standards of Human Occlusal Development*. Ann Arbor, MI: Center for Human Growth and Development; 1976.)

ARCH DEVELOPMENT, TOOTH MIGRATION, AND ERUPTION

The oral apparatus is the region of the craniofacial complex that holds the greatest potential for adaptive changes. Dental arch width and perimeter change dramatically, especially during the transitions to the early mixed and permanent dentitions.[104] Maxillary intercanine width increases approximately 3 mm during the transition to the early mixed dentition and an additional 2 mm with the emergence of permanent canines (Fig. 2.38).[105] Mandibular intercanine width increases approximately 3 mm during initial transition but shows little or no change with the eruption of the permanent canines. Intermolar widths progressively increase during childhood and adolescence, approximately 4 to 5 mm for the maxilla and 2 to 3 mm for the mandible between 6 and 16 years of age (Fig. 2.39). Maxillary arch depth (incisors to molars) decreases slightly during the transition to the early mixed dentition, increases 1 to 2 mm with the emergence of permanent incisors, and then decreases approximately 2 mm with loss of the deciduous first and second molars. Mandibular arch depth decreases slightly during the transition to mixed dentition, maintains its dimension during most of the mixed dentition, and then decreases 2 to 3 mm with the loss of the deciduous first and second molars. Maxillary arch perimeter from first molars to first molars increases 4 to 5 mm during early mixed dentition and then decreases approximately 4 mm during late mixed dentition, resulting in only a slight overall increase between 5 and 18 years of age (Fig. 2.40). Mandibular arch perimeter, from first molar to first molar, on the other hand, increases approximately 2 mm during early mixed dentition and decreases 4 to 6 mm during late mixed dentition, resulting in overall decreases of 3.5 and 4.5 mm in males and females, respectively. Most of the dental arch changes represent dentoalveolar compensations associated with incisor liability during the early mixed dentition, Leeway space during the late mixed dentition, and growth changes.

Perhaps most important from a clinical perspective, the teeth continue to migrate and erupt throughout childhood and adolescence, even after they have attained functional occlusion. The posteruptive movements of teeth are directly related to the spaces created by growth displacements and movements of other teeth. Dentoalveolar

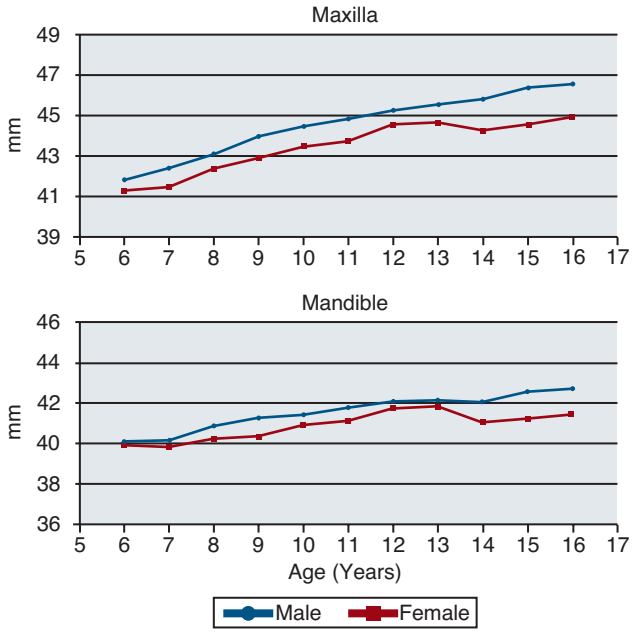


Fig. 2.39 Maxillary intercanine width of males and females based on measurements taken from the deciduous and permanent canines. (Data from Moyers RE, van der Linden PGM, Riolo ML, et al. *Standards of Human Occlusal Development*. Ann Arbor, MI: Center for Human Growth and Development; 1976.)

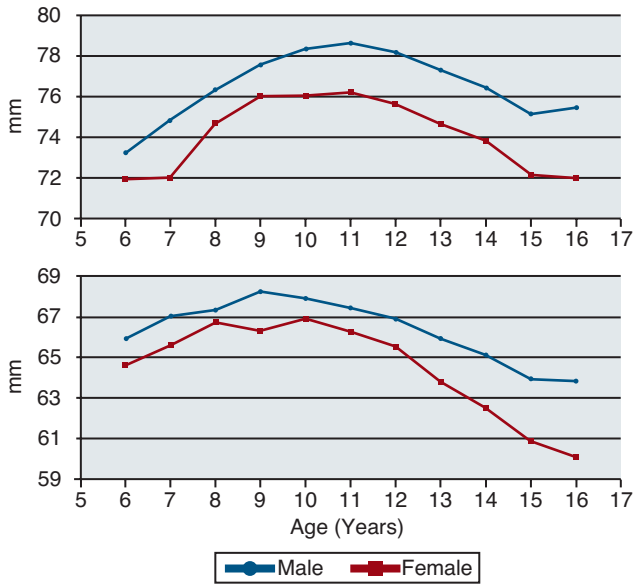


Fig. 2.40 Maxillary and Mandibular Arch Perimeter of Males and Females. (Data from Moyers RE, van der Linden PGM, Riolo ML, et al. *Standards of Human Occlusal Development*. Ann Arbor, MI: Center for Human Growth and Development; 1976.)

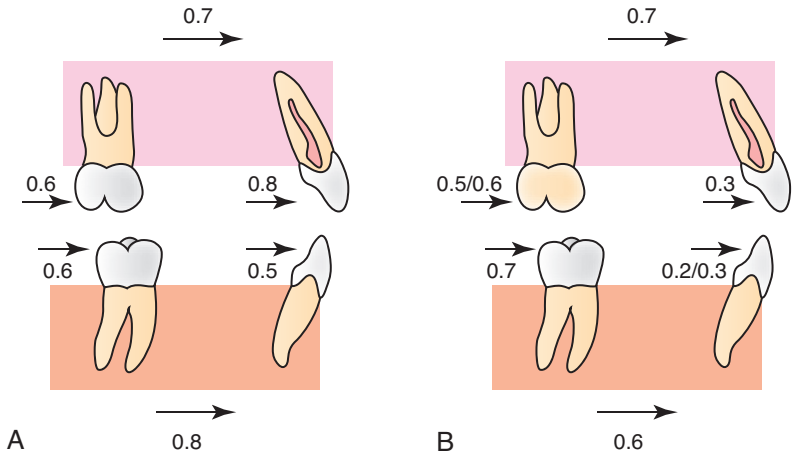


Fig. 2.41 Approximate maxillary and mandibular AP displacements and tooth migration (mm/yr) during (A) childhood and (B) adolescence (female/male).

compensation is the mechanism that coordinates their eruption and migration relative to their jaw bases; it maintains the relationships of teeth within and between the upper and lower dental arches. Dentoalveolar compensation depends on a normal eruptive system, dental equilibrium, and influences of neighboring teeth.[105] During childhood, the maxillary incisor drifts anteriorly at a greater rate than the maxillary molar (0.8 vs. 0.6 mm/yr, respectively), which accounts for the arch-depth increases evident with the eruption of the incisors (Fig. 2.41). In contrast, the mandibular molars drift anteriorly at a slightly greater rate than the incisors. Between 10 and 15 years of age, the molars (0.5–0.7 mm/yr) show significantly greater amounts of anterior drift than the incisors (0.3 mm/yr).

Substantial amounts of eruption occur throughout growth. During childhood, the maxillary first molars and incisors erupt at a rate of approximately 1.0 mm/yr, whereas their mandibular counterparts erupt at a rate of approximately 0.5 mm/yr (Fig. 2.42). During adolescence, the maxillary molars and incisors erupt at rates of 1.2 to 1.4 mm/yr and 0.9 mm/yr, respectively. The mandibular molars and incisors erupt at a rate of 0.5 to 0.9 mm/yr, with little or no differences between incisor and molar eruption. The amounts of eruption that occur are associated closely with the inferior displacements of the midface and, especially, the mandible.

During childhood, there is little or no evidence of sexual dimorphism in the migration and eruption of teeth. In contrast, there is a relatively high degree of dimorphism during adolescence in mandibular eruption, with boys showing almost twice as much eruption as girls. The maxillary teeth show only limited sex differences, pertaining primarily to the molars.

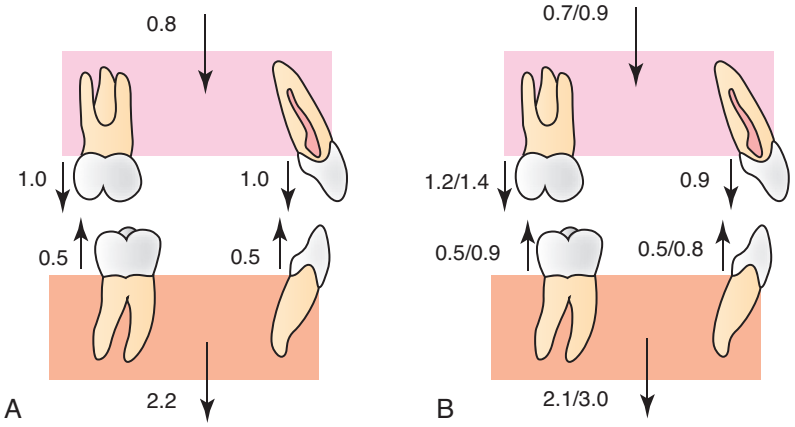


Fig. 2.42 Approximate maxillary and mandibular vertical displacements (mm/yr) and tooth eruption during (A) childhood and (B) adolescence (female/male).

ADULT CHANGES IN CRANIOFACIAL FORM

The size and shape of the craniofacial complex continue to change throughout a considerable part of adulthood. Over 90% of the 70 cephalometric distances and 70% of the 69 angles evaluated by Behrents[106] showed changes after 17 years of age; 61% of the distances and 28% of the angles showed changes after 35 years of age. In particular, the mandibular plane angle increases in adult females and decreases in adult males, which explains why males 25 to 46 years of age exhibit greater chin projection than females, who undergo increases in the angle Nasion-Sella-Gnathion (NSGn).[107]

Adult soft tissues undergo the more pronounced changes than the skeletal structures. The nose grows substantially during adulthood, with the tip moving down and forward approximately 3 mm after 17 years of age. Males exhibit significantly more nasal growth than females. Upper lip length increases (~2–3 mm) in both males and females after 17 years of age, resulting in decreases in upper incisor display over time. Lower lip length also increases, but less than upper lip length. The lips straighten and flatten during adulthood, but the most pronounced changes occur after 50 years of age. The soft tissue profile angle increases over time, with smaller increases when the nose is included than when it is excluded. Adult profile changes are limited to 2 to 3 degrees and 4 to 6 degrees when the nose is included and excluded, respectively.

POSTNATAL INTERRELATIONSHIPS DURING CRANIOFACIAL GROWTH

Postnatal craniofacial growth follows a gradient of relative growth that ranges between the neural and general somatic patterns. Vertical growth and modeling of the viscerocranium, as well as dental eruption, exhibit mid-childhood and pubertal growth spurts. Anteroposterior growth and tooth migration, which do not exhibit mid-childhood or pubertal growth spurts, change more or less regularly—except for the accelerated migration associated with the loss of teeth—throughout childhood and adolescence.

Generally, most displacements and rotations of the maxillomandibular complex are controlled epigenetically through growth of the chondrocranium, soft tissue growth, and expansion of the oronasal capsule. The cartilaginous growth centers play a particularly important role in the primary displacement of the chondrocranium, as well as in the secondary displacement of the viscerocranium. The anterior displacement of the midface has been associated with growth of the anterior cranial base and expansion of the anterior cranial fossa; mandibular displacements are more closely associated with growth of the posterior cranial base and middle cranial fossa. Anteroposterior length changes of the anterior cranial base, measured from sella to foramen cecum, coincide closely with expansion of the frontal lobes and growth at the sphenoethmoidal synchondrosis. Angular changes of the cranial base have been associated with growth gradients within the synchondroses, complex interactions with the growth of the brain, as well as facial growth. The cranial base angle decreases as a result of greater chondrogenesis in the superior than in the inferior aspects of the sphenoethmoidal and, especially, spheno-occipital synchondroses. Changes in cranial base angulation also appear to be related to changes in brain size, especially to the dramatic changes that occur during the first 2 postnatal years.

Cranial base growth influences the displacement and rotation of the viscerocranium. Growth of the posterior cranial base (i.e., spheno-occipital synchondrosis) is directly related to inferior and posterior displacements of the glenoid fossa; growth of the anterior cranial base is associated with midfacial displacement. Consequently, cranial base growth changes partially explain individual and population differences in anteroposterior skeletal relationships. Most studies show that individuals with larger cranial base angles and/or larger anterior and posterior cranial base lengths tend to be retrognathic (i.e., Class II), whereas those with the smaller lengths and angles tend to be prognathic (i.e., Class III).

Structures within the midfacial complex also affect its displacement and rotation. Growth of the eyeball is associated with both the anterior and lateral displacements of the midface, which explains why enucleation of the eyeball results in anterior and lateral growth deficiencies of the midface.[108] The nasal septum also plays important roles in nasomaxillary growth, displacement, and rotation. However, although the anterior cranial fossa, cranial base, eyeball, and nasal septum play important roles in the early displacement and rotation of the midface, their growth potentials are limited after 7 to 8 years of age. Soft tissue growth and other factors leading to the expansion of the oronasal capsule are relatively more important in explaining the midfacial rotation and displacement during later childhood and adolescence.

In turn, mandibular displacement and rotation are greatly influenced by midfacial displacement and rotation, growth of the posterior cranial base, soft tissue growth, expansion of the oronasal capsule, and development of occlusion. Posture appears to have a profound effect on mandibular growth and remodeling. There is also a direct relationship

between the true rotation of the maxilla and mandible. Both jaws usually rotate forward; individuals showing greater amount of forward rotation of the maxillary also tend to show greater forward rotation of the mandible (Fig. 2.43). Midfacial growth and the associated changes in the position of the maxillary dentition are also thought to play an important role in mandibular growth displacements. Major insults to maxillary growth can inhibit mandibular growth. Cranial growth disturbances can also influence mandibular growth indirectly through their effects on the midface and on the positional changes of the glenoid fossa, especially during infancy and early childhood. For example, it has been shown that craniosynostosis, if left untreated for a sufficiently long period, can produce significant asymmetry of the mandible.

The anterior and, especially, inferior displacements of the maxilla and mandible have direct effects on the growth at the sutures, condylar growth, modeling patterns, dental eruption, and dental migration. Although there is an upper threshold, the amount of bony apposition that occurs at sutures is related to the amount of sutural separation. For example, larger expansion forces produce greater sutural separation, which in turn results in greater sutural bone formation (Fig. 2.44). Such growth potential is essential during periods of greater sutural separation, which require concomitantly greater bone formation. The condyle also undergoes a growth spurt that closely coincides with the increased rates of inferior displacement of the mandible that occur during adolescence.[109] Because the mandible's modeling patterns are directly related to the amounts of vertical and horizontal displacement that take place,[110] individuals with greater inferior displacement show greater superior drift of bone along the entire surface of the ramus (i.e., greater apposition superiorly and greater resorption along the lower border) than do individuals who undergo less inferior displacement. Because of the close association between mandibular displacement and rotation, individuals showing greater or lesser amounts of anterior displacement of the mandible tend to exhibit lesser or greater amounts of posterior drift of the superior aspect of the ramus, respectively. The amounts of inferior displacement of the mandible that occur are also positively related to the amount of eruption that occurs, especially of the posterior teeth. Importantly, it is the displacement that determines the amounts of eruption that occur during growth, rather than vice versa. Displacements of the mandible also influence the anteroposterior compensations of the teeth. Individuals showing relatively greater anterior displacement of the mandible than maxilla tend to exhibit greater mesial displacement of the maxillary molars and counterclockwise rotation of the occlusal plane; those who undergo relatively greater anterior maxillary displacements display greater mesial displacement of the mandibular molars and minimal mesial displacement of maxillary molars.

The morphologic correlates with true rotation are numerous and hold important clinical implications.[111] Vertical rotation has been related to changes in tooth position, with true forward rotators showing greater amounts of lower incisor proclination during eruption; backward rotators show retroclination of the incisors and loss of arch space. True rotation is also related to the modeling pattern that occurs on the lower mandibular border; subjects who undergo greater amounts of true forward rotation also exhibit the greatest amounts of posterior resorption and anterior bony deposition. Ramus modeling in general depends on the rotational pattern of the mandible. Individuals who undergo greater amounts of true forward rotation also exhibit greater amounts of condylar growth, oriented in a more superoanterior direction (Fig. 2.45). Perhaps the most important clinical correlate is the relationship between true rotation and chin position. Most mandibles are displaced back during growth because of greater posterior

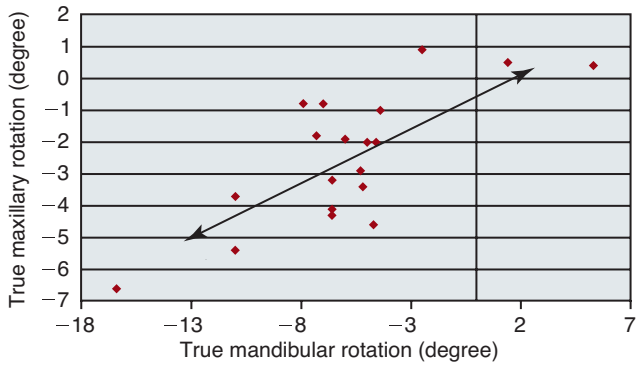


Fig. 2.43 Relationship of True Mandibular and True Maxillary Rotation (r = .75). (Data from Björk A, Skieller V. Facial development and tooth eruption. An implant study at the age of puberty. *Am J Orthod.* 1972;62:339–383.)

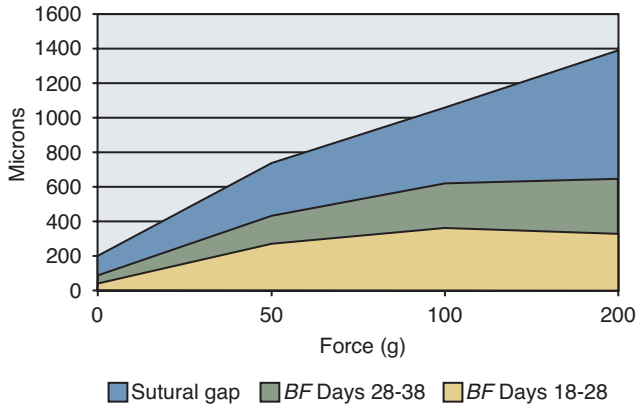


Fig. 2.44 Relationships of Bone Formation *(BF),* Sutural Gap Width, and Amounts of Force Applied to Separate Sutures.

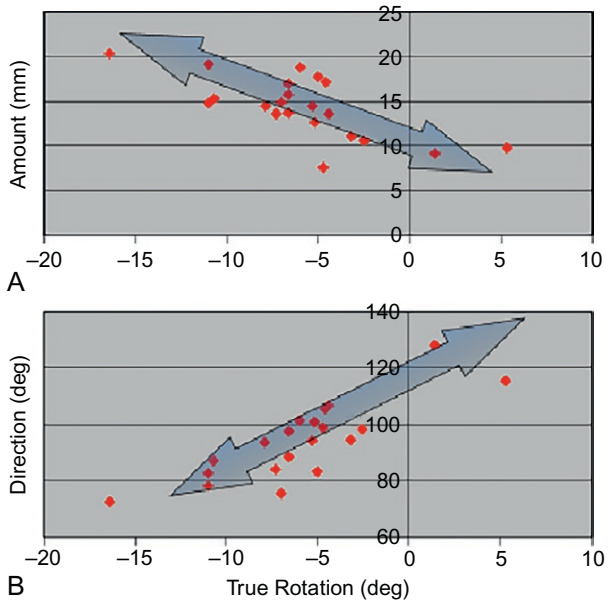


Fig. 2.45 Relationships between true mandibular rotation and **(A)** the total amount of condylar growth and **(B)** the direction of condylar growth. (Data from Björk A, Skieller V. Facial development and tooth eruption. An implant study at the age of puberty. *Am J Orthod.* 1972;62:339-383.)

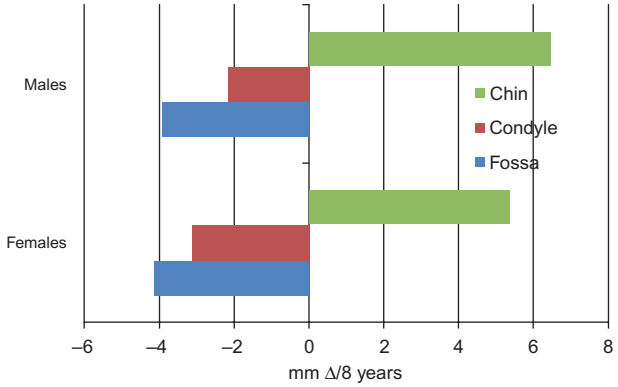


Fig. 2.46 Anteroposterior changes in chin, condylar and glenoid fossa positions in untreated children and adolescents showing backward displacement of the mandible and forward rotation of the chin.

displacement of the glenoid fossa than posterior condylar growth (Fig. 2.46). However, the chin typically comes forward as a result of true mandibular forward rotation. True rotation of the mandible explains more of the individual variation in chin position than condylar growth or changes in glenoid fossa position.

SIGNIFICANCE OF UNDERSTANDING CRANIOFACIAL GROWTH FOR ORTHODONTICS

To be most effective as clinicians, it is essential that orthodontists understand the development, growth, and adaptive potentials of the craniofacial structures. Along with orthodontic biomechanics, knowledge of how the craniofacial complex develops and grows provides the foundation for understanding the cause of the various dental and skeletal malocclusions, the best of all possible treatment approaches, and how patients might be expected to respond after treatment. A thorough understanding of growth provides the basis for knowing which craniofacial components should be expected to respond to treatment and how great the response might be expected to be. Because a structure's response potential to stress is directly related to its relative growth potential, and the vertical aspects of the mandible have the greatest relative growth potential, it follows that skeletal malocclusions might be expected to relate to vertical mandibular growth. Class II and Class III skeletal malocclusion both pertain primarily to the mandible.[112,113] These individuals are often retrognathic as a result of limited true forward rotation of the mandible, which is in turn related to deficient inferior growth displacement of the posterior mandible and/or excessive inferior displacement of the anterior aspect of the mandible.

Knowledge of growth is also important because, whenever possible, orthodontists should try to mimic growth when planning treatment. An understanding of growth provides the biological limits within which treatments can be performed. As previously indicated, the viscerocranium is made up almost entirely of intramembranous bone and is predominantly under epigenetic and environmental control. It is programmed to adapt, and adaptation should be expected whenever it is stressed. The biological system cannot distinguish between stresses imposed by the orthodontist and those imposed during normal growth; it simply responds depending on its growth potential. Continuing with the previous example, individuals who exhibit good growth patterns tend to be true forward rotators with condyles that grow in a more anterior direction. Based on this knowledge, hyperdivergent retrognathnic patients would best be served by treatments that focus on rotating the mandible rather than stimulating or redirecting condylar growth in a posterior direction.[114]

Finally, an understanding of growth makes it possible to estimate morphologic changes that should be expected to occur during and after orthodontic treatment. Unless it is intentionally disrupted, an individual's growth path before treatment might be expected to continue during and after treatment. Knowing how the maxilla and mandible rotated and/or were displaced during treatment provides an understanding of the modeling and consequent shape changes that might be expected to occur. Moreover, vertical growth after treatment is problematic in terms of posttreatment crowding, because of its relationship with tooth eruption. It has been shown that the best predictors of mandibular crowding of the permanent dentition, both after treatment and without treatment, are the inferior displacement of the mandible and superior eruption of the incisors.[86]

As understanding of craniofacial development, growth, and adaptation continues to improve in the future, orthodontists can look forward to even more therapeutic advances that can be used to influence growth and posttreatment stability. This understanding will facilitate greater clinical control of craniofacial growth changes and compensatory adaptation of tissues after treatment. Understanding normal craniofacial growth and especially that of the complex network of underlying molecular factors responsible for craniofacial growth and treatment will also be of immeasurable benefit in assisting the orthodontist in understanding what may or may not be possible, not only with respect to diagnosing a patient's underlying abnormality but also in determining the best treatment approach for its correction.[17,18,115-120]

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