# ORTHODONTICS

## CURRENT PRINCIPLES AND TECHNIQUES

SIXTH EDITION

GRABER · VANARSDALL · VIG · HUANG

ELSEVIER

Expert CONSULT Built with inkling | E books

# Any screen. Any time. Anywhere.

Activate the eBook version of this title at no additional charge.

Expert Consult eBooks give you the power to browse and find content, view enhanced images, share notes and highlights—both online and offline.

## Unlock your eBook today.

1. Visit **expertconsult.inkling.com/redeem**
2. Scratch off your code
3. Type code into "Enter Code" box
4. Click "Redeem"
5. Log in or Sign up
6. Go to "My Library"

It's that easy!

Scan this QR code to redeem your eBook through your mobile device:

Place Peel Off Sticker Here

**For technical assistance:**
**email expertconsult.help@elsevier.com**
**call 1-800-401-9962 (inside the US)**
**call +1-314-447-8200 (outside the US)**

ELSEVIER

# ORTHODONTICS

## CURRENT PRINCIPLES AND TECHNIQUES

SIXTH EDITION

**Lee W. Graber, DDS, MS, MS, PhD**

**Robert L. Vanarsdall, Jr., DDS**

**Katherine W.L. Vig, BDS, MS, D Orth, FDS RCS**

**Greg J. Huang, DMD, MSD, MPH**

# ORTHODONTICS

## CURRENT PRINCIPLES AND TECHNIQUES

**SIXTH EDITION**


Lee W. Graber, DDS, MS, MS, PhD
Secretary General, World Federation of Orthodontists
Past President, American Association of Orthodontists
Past President, World Federation of Orthodontists
Private Practice, Glenview and Vernon Hills, IL

Katherine W.L. Vig, BDS, MS, D Orth, FDS RCS
Othodontic Faculty, Harvard School of Dental Medicine, Boston, MA
Professor Emeritus and Former Chair of Orthodontics
The Ohio State University, College of Dentistry, OH
Past President, American Cleft Palate-Craniofacial Association

Robert L. Vanarsdall Jr., DDS
Professor and Chair Emeritus
Department of Orthodontics
School of Dental Medicine
University of Pennsylvania
Philadelphia, PA

Greg J. Huang, DMD, MSD, MPH
Professor and Chair
Department of Orthodontics
School of Dentistry
University of Washington
Seattle, WA



ELSEVIER

ELSEVIER

3251 Riverport Lane
St. Louis, Missouri 63043

ORTHODONTICS: CURRENT PRINCIPLES AND TECHNIQUES,
SIXTH EDITION ISBN: 978-0-323-37832-1



**Notices**

Knowledge and best practice in this field are constantly changing. As new research and experience broaden our understanding, changes in research methods, professional practices, or medical treatment may become necessary.

Practitioners and researchers must always rely on their own experience and knowledge in evaluating and using any information, methods, compounds, or experiments described herein. In using such information or methods they should be mindful of their own safety and the safety of others, including parties for whom they have a professional responsibility.

With respect to any drug or pharmaceutical products identified, readers are advised to check the most current information provided (i) on procedures featured or (ii) by the manufacturer of each product to be administered, to verify the recommended dose or formula, the method and duration of administration, and contraindications. It is the responsibility of practitioners, relying on their own experience and knowledge of their patients, to make diagnoses, to determine dosages and the best treatment for each individual patient, and to take all appropriate safety precautions.

To the fullest extent of the law, neither the Publisher nor the authors, contributors, or editors, assume any liability for any injury and/or damage to persons or property as a matter of products liability, negligence or otherwise, or from any use or operation of any methods, products, instructions, or ideas contained in the material herein.

Previous editions copyrighted 2012, 2005, 2000, 1994, 1985

**Library of Congress Cataloging-in-Publication Data**
Names: Graber, Lee W., editor. | Vanarsdall, Robert L., editor. | Vig, Katherine W. L., editor. | Huang, Greg J., editor.
Title: Orthodontics : current principles and techniques / [edited by] Lee W. Graber , D.D.S., M.S., M.S., Ph.D., President, American Association of Orthodontists, Past President, World Federation of Orthodontists, Private Practice, Vernon Hills, IL, Robert L. Vanarsdall Jr, DDS, Professor and Chair, Department of Orthodontics, School of Dental Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, Katherine W.L. Vig, BDS, MS, D Orth, FDS RCS, Professor Emeritus and Former Chair of Orthodontics, The Ohio State University, College of Dentistry, Past President, American Cleft Palate-Craniofacial Association, Greg J. Huang, DMD, MSD, MPH, Professor and Chair, Department of Orthodontics, School of Dentistry, University of Washington. University of Washington.
Description: Sixth edition. | St. Louis, Missouri : Elsevier, [2017] | Revison of: Orthodontics / Thomas M. Graber, Brainerd F. Swain. 1985. | Includes bibliographical references and index.
Identifiers: LCCN 2016027994 (print) | LCCN 2016028815 (ebook) | ISBN 9780323378321 (hardback : alk. paper) | ISBN 9780323444323 (Online)
Subjects: LCSH: Orthodontics.
Classification: LCC RK521 .G673 2017 (print) | LCC RK521 (ebook) | DDC 617.6/43–dc23
LC record available at https://lccn.loc.gov/2016027994

*Content Strategist:* Kathy Falk
*Associate Content Development Specialist:* Laura Klein
*Content Development Manager:* Jolynn Gower
*Publishing Services Manager:* Hema Rajendrababu
*Project Manager:* Srividhya Vidhyashankar
*Design Direction:* Ashley Miner

Printed in United States of America

Last digit is the print number: 9 8 7 6 5 4 3 2 1

# DEDICATION: TO ORTHODONTIC EDUCATORS AND RESIDENTS


Every text that is conceived, written and published starts with a purpose. Although this is the sixth edition of Orthodontics: Current Principles and Techniques, the concept of this multi-authored graduate level textbook started in the late 1960's with work that culminated in the 1969 publication of *Current Orthodontic Concepts and Techniques*. Why do a graduate level textbook? The answer was very simple: The principal editor and author Tom Graber, when interviewed later in life said it best—"There was a need." "The need" was defined by a widely held perception that there was a lack of supportive materials for clinicians teaching in orthodontic specialty education programs. Indeed, many of those who served as instructors and lecturers were private practice clinicians with little or no background in professional education.

The authors sought to provide a vehicle for educators to meld the then existing scientific basis of orthodontics with clinical practices in a manner that could be universally used. Course outlines that followed the textbook chapters as well as supportive slides were made available to help good clinicians become better teachers. A secondary but no less important goal for the textbook was to provide an organized platform by which practicing orthodontists could be updated on current concepts within the specialty. Tom Graber championed the need for continuing professional education and often cited G.V. Black, the father of modern dentistry, who had stated, "The professional person has no right to be other than a continuous student." The focus of the authors and editors who participated in the 1969 orthodontic text—and those who now do so in what is the eight iteration[1] has remained the same. We want to support orthodontic educators, the residents they teach and the "continuous students" orthodontic specialists must become.

With these thoughts as a background, it is to the educators and the orthodontic residents of the past, present and future we wish to dedicate the sixth edition. They embody the purpose of this text, because it is from their efforts our supportive science and clinical practice has grown and on their shoulders that rides the future development of our dental specialty.

---

[1]This is the sixth edition of the current series, with the title of the textbook and publisher changed in 1985. The first edition of the current series was the third for the text and included a change in title and publisher.

Pictures shown are from top row left: Edward H. Angle and the Class of 1900 of the Angle School of Orthodontia, from American Journal of Orthodontics and Dentofacial Orthopedics, 148:2, cover, 2015; Charles H. Tweed (glasses and bow tie) demonstrating patient at 1940's meeting (courtesy Rolf G. Behrents); Lysle E. Johnston lecturing to residents on cephalometrics (courtesy Rolf G. Behrents); Robert L. Vanarsdall lecturing to residents on three dimensional imaging, 2016. Bottom picture is of resident attendees and faculty at the Graduate Orthodontic Residents Program outside the American Association of Orthodontists building, St. Louis, 2015 (courtesy Rolf G. Behrents).

# LIST OF CONTRIBUTORS


**Adrian Becker, BDS, LDS, DDO**
Clinical Associate Professor Emeritus
Orthodontics
Hebrew University-Hadassah School of Dental Medicine
Jerusalem, Israel

**Erika Benavides, DDS, PhD**
Clinical Associate Professor
Periodontics and Oral Medicine
University of Michigan
Ann Arbor, Michigan

**Philip Edward Benson, PhD FDS (Orth)**
Professor of Orthodontics
Academic Unit of Oral Health and Development, School of Clinical Dentistry
University of Sheffield
Sheffield, United Kingdom

**Ignacio Blasi, Jr., DDS, MS**
Diplomate, American Board of Orthodontics
Private practice
Tysons Corner, Virginia

**Charles J. Burstone, DMD, MS, PhD†**
Professor, Emeritus
Orthodontics
University of Connecticut Health Center
Farmington, Connecticut

**Peter H. Buschang, PhD**
Regents Professor & Director of Orthodontic Research
Orthodontics
Texas A&M University Baylor College of Dentistry
Dallas, Texas

**Tamer Büyükyilmaz, DDS, MSD, PhD**
Private practice
Adana, Turkey

**David S. Carlson, PhD**
Regents Professor
Biomedical Sciences
Texas A&M University Baylor College of Dentistry
Dallas, Texas

**Lucia Cevidanes, DDS, MS, PhD**
Assistant Professor
Orthodontics and Pediatric Dentistry
University of Michigan
Ann Arbor, Michigan

**Stella Chaushu, DMD, PhD**
Professor and Chair
Orthodontics
Hebrew University-Hadassah School of Dental Medicine
Jerusalem, Israel

**Peter D. Chemello, DDS**
Private practice, Northwest Oral and Maxillofacial Surgery
Arlington Heights, Illinois

**Clark D. Colville, DDS, MS**
Assistant Clinical Professor
Orthodontics
University of Texas School of Dentistry
Houston, Texas
Clinical Advisory Board
Invisalign
Santa Clara, California

**Hali Dale, HON.B.Sc, DDS**
Diplomate, American Board of Orthodontics
Private Practice
Toronto, Ontario

**Jack G. Dale†, BA, DDS**
Postdoctoral Fellowship in Orthodontics
Harvard University
Cambridge, Massachusetts
Associate Professor
Faculty of Toronto
Toronto, Canada
Chairman
Charles H. Tweed Foundation
Tucson, Arizona
Private Practice
Toronto, Canada

**Dwight Damon, DDS, MSD**
Private practice
Spokane, Washington

**M. Ali Darendeliler, BDS, PhD, Dip Orth, Certif Orth, Priv. Doc, MRACDS (Ortho), FICD**
Professor and Chair
Orthodontics
University of Sydney
Sydney, NSW, AUS
Head of Department
Orthodontics
Oral Health Services and Sydney Dental Hospital, Sydney LHD
Sydney, Australia

**Hakan El, DDS, PhD**
Associate Professor
Orthodontics
Hacettepe University
Sihhiye, Ankara, Turkey

**Theodore Eliades, DDS, MS, Dr Med Sci, PhD, FIMMM, FRSC, FInstP**
Professor and Director
Clinic Orthodontics and Paediatric Dentistry, Center of Dental Medicine
University of Zurich
Zurich, Switzerland

**Norah Lisa Flannigan, BDS, MDETSCI, PhD, MFDSRCPS MORTHRCS, FDS (ORTH), RCS**
Senior Lecturer
Orthodontics
The University of Liverpool
Liverpool, England
Honorary Consultant
Orthodontics
Liverpool University Dental Hospital
Liverpool, England

**Thomas M. Graber†, DMD, MSD, PhD, OdontDr, DSc, ScD, MD, FDSRCS (Eng)**
Director, Kenilworth Dental Research Foundation
Clinical Professor, Orthodontics, University of Illinois, Chicago, Illinois
Former Professor and Chair, Section of Orthodontics, Pritzker School of Medicine, University of Chicago, Chicago, Illinois
Former Editor-in-Chief, World Journal of Orthodontics
Editor-in-Chief Emeritus, American Journal of Orthodontics and Dentofacial Orthopedics

**Dan Grauer, DDS, PhD**
Assistant Professor
Orthodontics
University of Southern California
Los Angeles, California
Private Practice
Santa Monica, California


† Deceased.

**Nigel W.T. Harradine, BDS, MB BS, LMCC, FDS RCS (London), FDS RCS (Edin), MSc (Orth)**
Senior Clinical Lecturer
Child Dental Health
University of Bristol
Bristol, United Kingdom
Consultant Orthodontist
Child Dental Health
Bristol Dental Hospital
Bristol, United Kingdom

**James Kennedy Hartsfield, Jr., DMD, MS, MMSc, PhD**
Professor and E. Preston Hicks Endowed Chair in Orthodontics and Oral Health Research
Oral Health Science
University of Kentucky College of Dentistry
Lexington, Kentucky
Adjunct Professor of Orthodontics and Oral Facial Genetics
Orthodontics and Oral Facial Genetics
Indiana University School of Dentistry
Indianapolis, Indiana
Adjunct Professor of Medical and Molecular Genetics
Medical and Molecular Genetics
Indiana University School of Medicine
Indianapolis, Indiana
Adjunct Clinical Professor of Orthodontics
Orthodontics
University of Illinois
Chicago, Illinois

**Nan E. Hatch, DMD, PhD**
Associate Professor of Dentistry
Lysle E Johnston, Jr. Collegiate Professor of Orthodontics
Chair, Orthodontics and Pediatric Dentistry
University of Michigan
Ann Arbor, Michigan

**Sarandeep S. Huja, DDS, PhD**
Professor and Division Chief, Orthodontics and Director of Graduate Studies, Dentistry
College of Dentistry, Division of Orthodontics
University of Kentucky
Lexington, Kentucky

**Donald R. Joondeph, BS, DDS, MS**
Professor Emeritus and Former Chair
Orthodontics
University of Washington
Seattle, Washington

**Jung Kook Kim, DDS, MS, PhD**
Adjunct Associate Professor
Department of Orthodontics
School of Dental Medicine University of Pennsylvania
Philadelphia, Pennsylvania
Clinical Professor
Department of Orthodontics
College of Dentistry Yonsei University
Seoul, South Korea

**Herbert A. Klontz, DDS, BA, MS**
Clinical Associate Professor
Orthodontics
College of Dentistry
University of Oklahoma
Oklahoma City, Oklahoma

**Jong Suk Lee, DDS, MS, PhD**
Adjunct Assistant Professor
Orthodontics
School of Dental Medicine
University of Pennsylvania
Philadelphia, Pennsylvania
Clinical Professor
Orthodontics
College of Dentistry Yonsei University
Seoul, South Korea

**Robert M. Little, DDS, MSD, PhD**
Professor Emeritus
Orthodontics
University of Washington
Seattle, Washington

**John B. Ludlow, DDS, MS, FDS RCSEd**
Adjunct Professor
Diagnostic Sciences
University of North Carolina
Chapel Hill, North Carolina

**Laurie McNamara McClatchey, DDS, MS**
Adjunct Clinical Assistant Professor of Dentistry
Orthodontics and Pediatric Dentistry, School of Dentistry
University of Michigan
Ann Arbor, Michigan

**James A. McNamara, Jr., DDS, MS, Phd**
Thomas M and Doris Graber Professor Emeritus
Orthodontics and Pediatric Dentistry, School of Dentistry
The University of Michigan
Ann Arbor, Michigan
Professor Emeritus
Cell and Developmental Biology, School of Medicine
The University of Michigan
Ann Arbor, Michigan
Research Professor Emeritus
Center for Human Growth and Development
University of Michigan
Ann Arbor, Michigan

**Ann M. Mercado, DMD, MS, PhD**
Clinical Assistant Professor
Orthodontics
Ohio State University
Columbus, Ohio
Member of Medical Staff
Dentistry
Nationwide Children's Hospital
Columbus, Ohio

**Lorri Ann Morford, PhD**
Research Assistant Professor; Supervisor, Genetics/Genomics Core of the University of Kentucky Center for the Biologic Basis of Oral/Systemic Diseases
Oral Health Science
University of Kentucky College of Dentistry
Lexington, Kentucky

**David Musich, DDS, MS**
Clinical Professor
Orthodontics
University of Pennsylvania School of Dental Medicine
Philadelphia, Pennsylvania

**Tung Nguyen, DMD, MS**
Associate Professor
Orthodontics
University of North Carolina
Chapel Hill, North Carolina

**Jeffrey P. Okeson, DMD**
Professor and Chief, Division of Orofacial Pain
Oral Health Science
University of Kentucky College of Dentistry
Lexington, Kentucky

**Juan Martin Palomo, DDS, MSD**
Professor, Director of Orthodontic Residency, Director of Craniofacial Imaging Center
Orthodontics
Case Western Reserve University
Cleveland, Ohio

**Leena Bahl Palomo, DDS, MSD**
Associate Professor, Director of DMD Periodontics
Periodontics
Case Western Reserve University
Cleveland, Ohio

**David E. Paquette, DDS MS MSD**
Faculty, Clinical Orthodontics
St. Louis University
St. Louis, Missouri
Clinical Advisory Board
Invisalign
Santa Clara, California

**Young - Chel Park, DDS, PhD**
Professor Emeritus
Department of Orthodontics
College of Dentistry, Yonsei University
Seoul, Korea
Director, Private Clinic
Orthodontics
Yonsei Beautiful Friend Orthodontic Center
Seoul, Korea

**Dubravko Pavlin, DMD, MSD, PhD**
Professor and Program Director
Orthodontics
University of Texas Health Science Center San Antonio
San Antonio, Texas

**William R. Proffit, DDS, PhD**
Professor Emeritus and formerly Kenan Distinguished Professor
Department of Orthodontics
University of North Carolina
School of Dentistry
Chapel Hill, North Carolina

**Jorge A. Ayala Puente, DDS**
FACE
Cirujano Dentista
Specialist in Orthodontics
Santiago, Chile

**W. Eugene Roberts, DDS, PhD, DHC (Med)**
Professor Emeritus of Orthodontics, and Adjunct Professor of Mechanical Engineering
Orthodontics and Mechanical Engineering
Indiana University and Purdue University at Indianapolis
Indianapolis, Indiana
Visiting Professor of Orthodontics
Orthodontics
Loma Linda University, School of Dentistry
Loma Linda, California

**Antonio Carlos de Oliveira Ruellas, DDS, PhD**
Associate Professor
Orthodontics
Federal University of Rio de Janeiro
Rio de Janeiro, Brazil
Visiting Researcher
Orthodontics and Pediatric Dentistry
University of Michigan
Ann Arbor, Michigan

**Rohit ChamanLal Sachdeva, BDS, M Dent Sc**
Co-Founder and Former Chief Clinical Officer
Orametrix, Inc.
Richardson, Texas

**Glenn T. Sameshima, DDS PhD**
Associate Professor and Chair
Orthodontics
Herman Ostrow School of Dentistry
University of Southern California
Los Angeles, California

**David M. Sarver, DMD, MS**
Adjunct Professor
Orthodontics
University of North Carolina
Chapel Hill, North Carolina
Adjunct Clinical Professor
Orthodontics
UAB School of Dentistry
Birmingham, Alabama

**Antonino G. Secchi, DMD, MS**
Diplomate, American Board of Orthodontics
Former Clinical Assistant Professor of Orthodontics
University of Pennsylvania
Private Practice
Devon, Pennsylvania

**Iosif B. Sifakakis, DDS, MS, Dr Dent**
Lecturer
Orthodontics
School of Dentistry, National and Kapodistrian University of Athens
Athens, Greece

**Raffaele Spena**
Adjunct Associate Professor
Orthodontics
Università di Ferrara
Ferrara, Italy

**Kingman P. Strohl, MD**
Professor of Medicine, Physiology & Biophysics, and Oncology
Case Western Reserve University School of Medicine
Cleveland, Ohio
Sleep Center Director
University Hospitals Case Medical Center
Cleveland, Ohio
Director Sleep Disorders Program
Louis Stokes Cleveland VA Medical Center
Cleveland, Ohio

**Zongyang Sun, DDS, MS, PhD**
Associate Professor
Orthodontics
The Ohio State University College of Dentistry
Columbus, Ohio

**Birgit Thilander, Odont Dr (PhD), Med Dr (hc), Dr Odont (hc)**
Professor Emeritus
Orthodontics
Institute of Odontology, Sahlgrenska Academy
University of Gothenburg

**Patrick K. Turley, DDS, MSD Med**
Professor Emeritus and former Chair
Orthodontics and Pediatric Dentistry
School of Dentistry
University of California at Los Angeles
Los Angeles, California
Private practice Manhattan Beach, CA

**Patricia Turley, DDS**
Private practice, pediatric dentistry
Manhatten Beach, California

**David L. Turpin, DDS, MSD**
Moore/Riedel Professor
Orthodontics
School of Dentistry
University of Washington
Seattle, Washington

**Serdar Üşümez, DDS, PhD**
Professor
Orthodontics
Bezmialem Vakif University, Faculty of Dentistry
Istanbul, Turkey

**James L. Vaden, BA, DDS, MS**
Professor
Orthodontics
University of Tennessee
Memphis, Tennessee

**Timothy T. Wheeler, DMD, PhD**
Professor, Former Academy 100 Eminent Scholar, Former Chair & Program Director
Orthodontics
University of Florida
Gainesville, Florida

**Dirk Wiechmann, DDS, PhD**
Professor
Orthodontics
Hannover Medical School
Hannover, Germany
Private Practice
Bad Essen, Germany

**Leslie A. Will, DMD, MSD**
Chair and Anthony A. Gianelly Professor in Orthodontics
Orthodontics and Dentofacial Orthopedics
Boston University Henry M. Goldman School of Dental Medicine
Boston, Massachusetts
Adjunct Professor
Orthodontics
University of Pennsylvania School of Dental Medicine
Philadelphia, Pennsylvania

**Bjorn U. Zachrisson, DDS, MSD, PhD**
Orthodontics
University of Oslo
Oslo, Norway

# PREFACE

This is the eighth re-writing of a textbook that has remained the most widely used graduate orthodontic textbook in the world and has now been translated in to multiple languages. Tom Graber was the initial editor in the late 1960s. He was encouraged by colleagues within the orthodontic educational community to fill what they saw as a void within orthodontic specialty programs. They perceived that although there were many excellent graduate programs, there was significant variance in the educational assets these programs provided for their residents. In bringing together the thoughts of excellent clinicians and related scientists in a text specifically meant for the advanced study of orthodontics, concepts and techniques could be shared with all benefitting.

An additional thought, shared at the time in both academic and professional association circles, was the need for a means to provide better continuing education to those already in practice. Today we take for granted that technologies and concepts change very quickly, and we must keep ourselves current. Forty-five plus years ago, the need was not as self-evident. Thus, in developing a textbook with recognized and vetted authorities on a wide array of subjects impacting clinical practice, the editors could provide a critical resource to those who had completed their formal education and were subsequently in primarily solo practices offices. The concept was that the text would be a basis for continued learning—a foundation on which these clinicians could better judge new material seen in their journals and professional lectures. By the very nature of this concept, there was an inherent demand that the text itself be updated to reflect the current basis on which the orthodontic specialty was being practiced. This demanded that it be updated on a regular basis, reducing emphasis in some areas, adding in others as both basic science concepts and clinical techniques further matured.

The task of "keeping current" is not an easy one and has become more difficult with the explosion of orthodontic-related research and technical development. Additionally, in the early years of the text, chapters were developed primarily by North American-educated authors. Today's world of orthodontics is significantly expanded with great work being done globally, as is seen in the variety of locations listed by authors in our most prestigious journals. Tom Graber was often heard saying, "Science has no borders!" and as the initial editor of the text sought the best and the brightest to contribute, a tradition we are proud to uphold to this day. Tom was the solo editor for the first two editions published by Saunders and was joined by Brainard Swain when C.V. Mosby became the publisher of what was then the first edition of the current Mosby (now Elsevier) series. Subsequently Tom, seeking a broader expertise to aid in the development of the text, was joined in the editorial role by Robert Vanarsdall in the second edition and then Katherine Vig in the third edition followed by Lee Graber and now Greg Huang in this sixth edition. As the scope of the orthodontic specialty has grown, so has the need for added editorial background and expertise.

We write this text with the presumption that those using it will have had a basic exposure to orthodontic principles provided in dental school education both within their undergraduate dental courses and from basic orthodontic texts used in the DDS/DMD curricula. The purpose of this graduate orthodontic textbook remains the same—to provide a compendium of information from authors who are experts in specific topics that are considered important to the education of orthodontic specialists. This was the vision of Tom Graber when he wrote the first edition which met with much acclaim from educators who used it as the assigned readings for their residents. It is to these educators and the orthodontic residents of the past, present and future that we have dedicated the sixth edition.

In the writing of this text, we are acutely aware of an added need within orthodontic education. That call is to encourage current residents as well as clinicians to become part of the orthodontic specialty teaching and/or research corps for the future. This text demonstrates the broad scope of orthodontics, from basic science concepts to intricate clinical techniques as well as patient management considerations. With such breadth, the specialty provides opportunities for motivated individuals to consider becoming part- or full-time educators or research scientists (or both). We can all remember the teachers we have had who made special impact on our lives. They shared their passion for their subject, the excitement over their research and their interest in mentoring a following generation. There is much within the chapters of this text about which to have excitement and passion—as well as provide motivation for answering still vexing problems through clinical and basic science research.

What is new in the presentation of this sixth edition? The most notable changes are in how the textbook may be used. The advent of computers and advances in technology for transmitting information have resulted in transforming the methods with which we share information and teach students. These technology changes have been matched by research in education that demonstrates that there is broad variability on how individuals learn. By the fifth edition we had started to put part of the text online. This sixth edition expands that effort and the ease with which the electronic version of the text may be used by way of the Expert Consult, a feature rich eBook format for medical and dental education. The ability to have added material online also increases the opportunity for more content as discussed below. Downloading sections and chapters on to your computer, laptop or tablet—or even your phone—is now possible and widely used. Using Expert Consult, readers can access and work with the text on any platform and even communicate on material with colleagues through social media. Indeed, with the inherent convenience of an electronic format, and the opportunities for editors and authors to update material without waiting for a "new edition", the investment one makes in the purchase of the text has the potential to last long after the printed publication date. These considerations coupled with the high cost of physically printing a textbook, could result in the sixth edition being the last one offered in a printed format.

What has changed in terms of content? A lot! Fully one third of the material in this edition is completely new. In addition, chapter authors from prior editions have been joined with co-authors to further update their own material. Improvements range from the organization of the chapters and the subject material to the new chapter authors who have joined us to provide the best background for orthodontists possible within the confines of a broad-based textbook. Additional

information on the science that supports orthodontics, diagnostics and therapeutic interventions has been developed. New chapters on adjunctive treatments as well as management of the potential adverse sequelae from orthodontics have been added. We also have selected several chapters from prior editions and placed them online as "classic chapters". These represent clinical topics that had to be incorporated into other chapters to maintain the already "heavy" book in a manageable size. The material in these online-only chapters further expands the scope of the textbook, better matching the increased scope of material with which a practicing orthodontist must be knowledgeable.

Finally, the chapters within the text have been reorganized to better match the progression of subjects addressed in an orthodontic specialty residency program. Section heads provide a means by which educators and residents can better identify subject material as they move through the material. Equally important, the re-organization provides the practicing clinician with a logical grouping of subjects that can be efficiently referenced. As editors, we hope that the challenge of presenting added material to residents and practitioners is made easier by way of the improved organization of material within the text.

## PART ONE

### Foundations of Orthodontics

Chapter 1: Craniofacial Growth and Development: Developing a Perspective. In the opening chapter of the text, authors David Carlson and Peter Buschang provide an up-to-date discussion of craniofacial growth and development. They review the basic anatomical and functional structures within the craniofacial complex, and starting with pre-natal development, describe the complex interrelationships influencing form and function. In describing the importance of the subject material, they aptly state, "…knowledge of how the craniofacial complex develops and grows provides the foundation for understanding the etiology of the various dental and skeletal malocclusions, the best of all possible treatment approaches, and how patients might be expected to respond after treatment."

Chapter 2: Genetics and Orthodontics. James Hartsfield, joined in this edition by Lori Ann Morford, has further developed basic principles of genetics while focusing on aspects that directly affect orthodontic clinicians. Clinical concerns including aberrant facial growth and development, tooth agenesis and size variability, dental eruption problems and tissue response to orthodontic forces all are impacted by genetic factors. The interaction between environmental factors and genetic expression determine an individual's response to treatment interventions. The authors complete their chapter with a look to the future and the general movement toward "personalized" medical and dental treatment.

Chapter 3: The Biologic Basis of Orthodontics: Tissue Reactions in Orthodontics. Birgit Thilander builds on the contributions of prior authors of this chapter, Kaare Reitan and Per Rygh. There is a review of the tissue components involved in tooth movement followed by a detailed discussion of the response of those tissues to various forces. The local tissue consequence of various types of tooth movement are discussed and illustrated as well as the long-term tissue changes that take place during "retention." A review of the temporomandibular joint underscores the importance of considering tissue reactions in locations distant from orthodontic force application.

In Tooth Movement at the Cellular and Molecular Level, Zongyang Sun and Nan Hatch provide a new chapter segment that focuses on the most current understanding of the control of tooth movement, that is, cellular and molecular changes in response to physiologic as well as orthodontic forces. The means by which external forces are "seen" by cells in order to stimulate tooth movement are discussed in terms of the biologic signaling mechanisms involved. The tissue changes outlined in the first section of this chapter are further described here in terms of components of mechanobiology. There is also a discussion on how biomedicine is opening doors to future patient-specific treatment alternatives.

Chapter 4: Bone Physiology, Metabolism, and Biomechanics in Orthodontic Practice. Eugene Roberts has now been joined by Sarandeep Huja to rewrite this chapter focusing on craniofacial osteology, the dynamics of bone physiology and the impact on orthodontic treatment. In addition, there is detailed discussion on osteoblast histogenesis (bone formation), osteoclast recruitment (bone resorption), and how this interplay affects tissue response to tooth-moving forces. Bone adaptations to temporary anchorage devices are reviewed as well as those aspects that play in favor of retention of mini- screws versus early loss. Finally, the authors address how it is possible to increase the rates of tooth movement by altering the local environment.

Chapter 5: Application of Bioengineering to Clinical Orthodontics. The late Charles Burstone completed the rewrite of this chapter shortly before he died. The recognized preeminent author on orthodontic biomechanics, Dr. Burstone brings together physics, mathematics and engineering to provide the theoretical background for orthodontic appliance construction and manipulation. Specific topics include discussions of the biomechanics of tooth movement (centers of rotation, force magnitude, optimal force and stress), orthodontic appliance components, mechanical properties of wires, selection of proper wires, influence of wire size-length-cross-section, archwire design and the role of friction. No matter what appliance the orthodontic clinician decides to use, it is these shared physical principles that affect the biomechanical success and efficiency of treatment.

Chapter 6: Clinically Relevant Aspects of Dental Materials Science in Orthodontics. Theodore Eliades is joined in this edition by Iosif Sifakakis to discuss the important considerations for the everyday materials in use by the clinical orthodontist. What are the characteristics of different brackets and wire materials, and how do they influence orthodontic mechanotherapy? What are the important clinical concerns with bracket bonding materials, and what might prove adverse to the patient if not properly managed by the orthodontist? What are the considerations in longterm fixed retainer wear, and what wire should a clinician use? These questions and other practical issues are answered within this chapter.

Chapter 7: The Role of Evidence in Orthodontics. One cannot attend a dental or medical meeting without some reference to "evidence-based" practice. The early years of orthodontics were characterized by "gurus" espousing one concept or another without much call for support. "Expert opinion" determined what clinicians in private practice would use for patient care. Today's clinicians are faced with the imperative to use a balanced approach to clinical decision making. Matching findings from respected research with the one's experience and patient goals is a challenge to all practitioners. We all have hopes of providing "the best of care" and also need to respect

potential medicolegal issues as we treat patients. David Turpin and Greg Huang discuss how today's clinicians can evaluate the broad range of relevant information from multiple sources and be biased to make better decisions by way of the best evidence available.

## PART TWO

### Diagnosis and Treatment Planning

Chapter 8: The Decision Making Process in Orthodontics. William Proffit and Tung Nguyen have restructured this chapter to better fit with the background of entering orthodontic residents and seasoned clinicians in orthodontic specialty practice. The focus is on the process of diagnosis and treatment planning, providing a method to systematically evaluate patient information and organize it in a way that helps to avoid errors of omission. Using a problem oriented approach, the authors demonstrate how (1) excellent diagnostic records, (2) a thorough case evaluation and (3) a priority-based listing of findings form the basis of an appropriate therapeutic plan.

Chapter 9: Special Considerations in Diagnosis and Treatment Planning. We are all aware of parent and patient expectations for improved cosmetics after orthodontics. Indeed, very few patients have an appreciation for functional considerations, but they are able to point to a specific tooth out of alignment or an uneven smile. David Sarver dissects the esthetic evaluation of the face and provides a broader context for patient evaluation than what has historically been considered "orthodontic diagnosis". His protocols for the evaluation of facial proportions (macroesthetics), evaluation of the smile (miniesthetics), and evaluation of the teeth and surrounding gingiva (microesthetics) are detailed within this chapter. Societal pressures create the desire for optimal dentofacial esthetics and it falls to the orthodontist to make a thorough evaluation of these characteristics on behalf of each patient.

Chapter 10: Psychological Aspects of Diagnosis and Treatment. This chapter by Leslie Will provides information on the psychological assessment of patients and how it can be accomplished within the context of an orthodontic evaluation. It describes psychological disorders and how clinicians can best manage affected patients. Patients with craniofacial anomalies present a subset of those seen in most clinical practices, but these "special needs" patients require more than an understanding of their physical challenges. The chapter has been expanded to include important psychological considerations for orthognathic surgery patients and the effect of abrupt facial change.

Chapter 11: Orthodontic Diagnosis and Treatment Planning with Cone Beam Computed Tomography (CBCT) Imaging. This is a new chapter and reflects the increasing use of CBCT in orthodontics. CBCT has been available for quite a while, with increased utilization in routine orthodontics over the past 10 years related to improved availability and reduced patient radiation dosages. Our patients see and all of us work in a three dimensional world. One can readily understand the appeal of 3D imaging to patients and clinicians alike. Authors Lucia Cevidanes, Erika Benavides, John Ludlow and Antonia Ruellas have internationally recognized craniofacial imaging expertise. They have joined to provide an outstanding discussion on how CBCT may be used to enhance orthodontic diagnosis and treatment.

Chapter 12: Upper Airway, Cranial Morphology, and Sleep Apnea. As an additional new chapter we have added information in regards to evaluating patients for morphologic and functional traits that may predispose to disturbed sleep syndromes. Juan Martin Palomo, Hakan El, Leena Palomo, and Kingman P. Strohl provide an in-depth discussion on identifying airway problems, and a thorough review of sleep disordered breathing and the classification of associated clinical problems. They discuss how an orthodontist might influence airway patency through various treatment modalities. The authors underscore how the orthodontist fits in to a multi-disciplinary team to best manage these multifactored patients.

Chapter 13: Orthodontic Therapy and the Patient with Temporomandibular Disorder. Jeffrey Okeson is the internationally recognized authority on TMD disorders and especially how these disorders potentially impact orthodontic patients before, during and after treatment. In this updated chapter he reviews the basic concepts of orthopedic stability, how to perform a complete TMD evaluation, and how to develop a treatment plan. His discussion of a stepwise approach for TMD problems that may arise during treatment is a must read for residents and practitioners.

Chapter 14: The Orthodontist's Role in a Cleft Palate–Craniofacial Team. Katherine Vig and Ana Mercado review the important considerations for orthodontists who are treating craniofacial anomalies as part of craniofacial teams. The emphasis is on an orthodontist as a component of "the team" and the appropriate timing for various interventions for the cleft patient. New to this edition is an excellent discussion of the clinically vexing issue of how to approach the missing maxillary lateral incisor in patients with cleft palate. The authors do an excellent job of emphasizing the long term relationship with craniofacial patients and how the clinician must recognize the multi-stage needs of these patients.

## PART THREE

### Mixed Dentition Diagnosis and Treatment

Chapter 15: Patient Management and Motivation for the Child and Adolescent Patient. How does one create an office environment that has patients who are happy and appreciate the services provided? Patrick and Patricia Turley bring information from the pediatric dental literature as well as patient management sphere to develop this new chapter for the sixth edition. The theme of the chapter is how to best guide young patients to comply with instructions both in the office setting and at home. The Achilles heel for orthodontic treatment is most often patient cooperation. These authors present guidance on how best to communicate to patients at different ages and how to encourage compliance with home care responsibilities for hygiene as well as appliance wear. They point out that clinicians need to have a systematic approach for monitoring patient cooperation as well as routine measures to intervene when compliance is lacking.

Chapter 16: Optimizing Orthodontics and Dentofacial Orthopedics: Treatment Timing and Mixed Dentition Therapy. For an orthodontist, the opportunity to intervene and reduce the severity of a developing malocclusion needs to be recognized. Additionally, guidance that can improve the maxilla–mandibular relationships and space for erupting permanent teeth can provide significant benefit to growing patients. The questions for the clinician revolve around when and how one should intervene in a growing child. In this chapter, authors James McNamara, Laurie McNamara McClatchey, and Lee Graber provide an organized approach to mixed

dentition diagnosis and treatment. With the broad spectrum of malocclusions that present to the practitioner, there are an equally varied considerations for treatment timing and approach. There is a brief discussion of serial extraction technique within this chapter, but readers are encouraged to see Chapter 34, Interceptive Guidance of Occlusion with Emphasis on Diagnosis (online only) for further information. Chapter 16 provides information on the proper age for dentofacial orthopedic–orthodontic intervention, appliance construction and management. The appliance types and treatment protocols presented in the chapter are evidence based, but it is understood that there are many types of orthodontic appliances that can be selected as long as the underlying principles of diagnosis, appropriate timing and orthopedic–orthodontic therapy are maintained.

## PART FOUR

### Orthodontic Treatment

Chapter 17: Contemporary Straightwire Biomechanics. Since the straightwire appliance was introduced in the 1970s its use has grown to where it is now the most popular fixed orthodontic appliance design available today. In this chapter, Antonino Secchi and Jorge Ayala provide (1) the historical basis of the appliance, (2) the principles of precise bracket placement and (3) the three separate phases of straightwire mechanics. With excellent clinical cases and explanations, they detail the specific wire sequences, anchorage considerations, and finishing mechanics designed to optimize the benefits of the straightwire bracket system.

Chapter 18: Nonextraction Treatment. Orthodontists are faced everyday with decisions of whether or not they need to remove permanent teeth as part of a comprehensive treatment program. Our journals have documented the trends to more extraction or fewer extractions with a reduced rate of extractions currently in vogue. Realistically, these extraction decisions should be made on the basis of a solid diagnosis and evidence-based treatment planning. With this as a given, what techniques can be used to maximize the success of a non-extraction approach in a borderline patient? This chapter authored by Robert Vanarsdall and Raffaele Spena details an approach that can provide needed dental arch space in a predictable fashion and provides case examples.

Chapter 19: Standard Edgewise: Tweed-Merrifield Philosophy, Diagnosis, Treatment Planning and Force Systems. For many years, orthodontic residents and clinicians have traveled to Tuscon, Arizona to take the "Tweed Course," the oldest dental continuing education program in the world. This chapter is written by James Vaden and Herbert Klontz, co-directors of the Tweed Foundation, along with the late Jack Dale. It provides an historical perspective on the development of the Tweed technique, presents diagnostic and treatment concepts, and describes the Tweed-Merrifield edgewise appliance. The authors review the steps of the Tweed technique as currently practiced and present excellent illustrative case material.

Chapter 20: Biomechanical Considerations with Temporary Anchorage Devices (TADs). The use of temporary anchorage devices has greatly increased the ability of the clinical orthodontist to move teeth efficiently without the side effects of reciprocal undesired moments of force. "Absolute anchorage" as provided by these adjuncts provides a platform from which the clinician can better move teeth in all three planes of space. They have literally increased the range of orthodontic mechanotherapy. Authors Jong Suk Lee, Jung Kook Kim and Young-Chel Park have combined their internationally recognized expertise to provide a discussion of the biomechanical considerations when using TADs.

Chapter 21: Adult Interdisciplinary Therapy: Diagnosis and Treatment. Adult orthodontic treatment has continued to increase as a percentage of the patients seen by orthodontic specialists. There are many reasons including the ability to use "esthetic" treatment appliances, the increased interest in adults in their long term dental health, and the improved understanding within the general dental community that orthodontics can be an integral part of an overall restorative plan. Robert Vanarsdall and David Musich discuss the added considerations when treating adult patients. Treatment criteria differ, and there is concern for adverse tissue response especially where compromised tissue relationships are present before the start of orthodontics. This chapter reviews adult orthodontic diagnostic and treatment regimens, limitations in adult care, and compromises that must be made as well as the special demands for long term retention. Case reports provide excellent reference material for the subject.

Chapter 22: Periodontal-Orthodontic Interrelationships. As we see more adults entering comprehensive orthodontic treatment, we must be more attuned to the implications of periodontal issues. In this updated chapter, Robert Vanarsdall, Ignacio Blasi and Antonino Secchi review periodontal issues that impact orthodontic tooth movement. They describe periodontal "high risk" factors, mucogingival considerations, and problems with ectopic as well as ankylosed teeth. A new section on alveolar decortication and augmentation grafting has been added to address the increased use of these procedures designed to develop the alveolar housing and potentially increase the speed of tooth movement. Excellent clinical examples are pictured throughout the chapter.

Chapter 23: Orthodontic Aspects of Orthognathic Surgery. David Musich and Peter Chemello discuss the added considerations for patients who present with treatment needs that exceed the potential for orthodontic mechanotherapy alone. Diagnostic considerations and a systematic protocol are presented as a guide for orthodontists and oral and maxillofacial surgeons teaming up to provide coordinated surgical care. What are the potentials of surgical orthodontics? What are the problems and pitfalls that must be addressed? What are the timing issues when considering jaw surgery? What are the risks of treatment, and of course, how can the clinician help to stabilize results with long term retention? These questions and more are addressed within this chapter.

Chapter 24: Self-Ligating Bracket Biomechanics. The increased use of self-ligating brackets has brought forth many discussions at orthodontic meetings, articles both for and against their use, and direct-to-consumer marketing that has resulted in more questions from patients as they interact with their orthodontists. This chapter authored by Nigel Harradine provides an historical perspective on self-ligating techniques and proceeds to review the advantages and disadvantages of these appliances. Although some of the advertised claims for reduced treatment times may not have been demonstrated in systematic reviews of the technique, there do appear to be positive indications for clinicians. This chapter provides an unbiased view of current findings and makes specific recommendations for the use of these brackets.

Chapter 25: Lingual Appliance Treatment. Lingual appliance treatment has had more popularity in Europe and Asia than in North America. That may change as increasingly more clinicians adopt partial or full fixed lingual appliance treatment in their offices. This trend has been greatly aided by the integration of three dimensional modeling, the development of custom braces and/or robotically bent archwires, and increased call of "invisible" treatment by adult and adolescent patients. In addition, there is an added benefit of minimal risk of labial surface decalcification—scars seen from labial therapy— with lingual bracket treatment. This chapter has been completely re-written and is co-authored by Dirk Weichmann and Dan Grauer. Although the authors focus on their own lingual appliance type, the principles they discuss can be generalized to a number of lingual treatment systems.

Chapter 26: Clear Aligner Treatment. This chapter has been re-written by three of the most knowledgeable clinicians in the use of clear aligners, David Paquette, Clark Colville and Timothy Wheeler. The chapter focuses on the Invisalign system, the most researched and used clear aligner system in the world. The authors discuss the unique aspects of diagnosis and treatment planning for clear aligners. The continuing development of adjuncts within the aligner system has increased the type and range of tooth movement that can be accomplished. Significant research has been reported and provides a basis for discussion of what movements can be accomplished more easily—and what becomes more difficult with aligners. This comprehensive chapter provides critical considerations that distinguish treatment provided by an orthodontic specialist from the clinician who has less of a background.

Chapter 27: Bonding in Orthodontics. The premier authority on orthodontic bonding, Bjorn Zachrisson is joined in this updated chapter by Serdar Usumez and Tamer Büyükyilmaz. Adhesive dentistry is the norm for restorative clinicians, but direct and indirect bonding of brackets to enamel and restorative materials for orthodontics is equally important. This detailed chapter reviews patient preparation for bonding, techniques for the application of brackets to teeth and artificial surfaces, indirect bonding protocols, re-bonding considerations and the use of bonded lingual retainers. Additionally there is a discussion of the use of microabrasion and resin infiltration to repair decalcified enamel areas. The technical procedures are well documented with clinical pictures.

## PART FIVE

### Specialized Treatment Considerations

Chapter 28: Management of Impactions. This is a totally new chapter designed to aid clinicians in developing a diagnostic and therapeutic protocol for impacted teeth. Adrian Becker and Stella Chaushu are the internationally respected leaders in this important area of orthodontic diagnosis and treatment. The chapter reviews the etiology of impactions, the prevalence of impactions of specific teeth, the assessment of impactions and finally the therapeutic interventions that are required of the clinician. The authors discuss areas for potential failure in management of impactions and provide clinical suggestions to improve success. The chapter is well illustrated in support of the recommended clinical procedures.

Chapter 29: Management of Dental Luxation and Avulsion Injuries in the Permanent Dentition. Patrick Turley has provided a new chapter to cover an aspect of practice that gets little attention in orthodontics, the management of dental trauma. An orthodontists is often the first to see a youngster who has had teeth displaced by way of accident—often because this is the dental office the family has seen most often during the adolescent years. The addition of this chapter fills a prior void by addressing the sequelae of trauma to the teeth, acute management of injuries to the teeth and alveolar structures, and treatment of avulsed teeth. The author also provides information on the importance of treatment of overly procumbent teeth to reduce the risk of incisal fractures. This is information that parents in addition to clinicians need to know!

Chapter 30: Iatrogenic Effects of Orthodontic Treatment: Prevention and Management of Demineralized White Lesions. This is another new subject area addressed in an added chapter for the sixth edition. Well known clinical researchers and authors Philip Benson and Norah Flannigan review the potential for adverse effects of orthodontic appliance wear on labial surfaces that have bonded attachments. The most common adverse effect is the development of white spot lesions. The authors review the prevalence of the problem, means by which it may be diagnosed and most importantly, how these lesions can often be prevented.

In Root Resorption, Glenn Sameshima and M. Ali Darendeliler look at the problem of reduced root length during tooth movement. What are patient and mechanotherapeutic predisposing factors for root resorption? What should the clinician do when root resorption is expected or detected? What is the long term prognosis for teeth with foreshortened roots? All clinicians see these problems in daily practice, and this chapter provides an excellent summary of clinical considerations.

Chapter 31: Minimally and Noninvasive Approaches to Accelerate Tooth Movement: Micro-osteoperforations. Patients are always attracted to decreasing the time it takes to complete orthodontic treatment. Recent advances in the understating of bone biology have been applied to a number of adjunctive techniques that in certain situations may reduce the time for orthodontics. In this new chapter, Ignacio Blasi looks at the use of micro-osteoperforations and the ability of these perforations to increase bone turnover rates, providing for increased speed of tooth movement. Studies have been done that demonstrate a localized positive effect on the speed of tooth movement.

In Low-Level Mechanical Vibrations, Dubravko Pavlin presents information on the influence of low level mechanical vibration on orthodontic treatment, a technique borrowed from orthopedic colleagues. Some of the animal and human studies have reported increased rates of tooth movement and an ability to reduce pain perception when low level vibration therapy is used. Still other studies report no clinical effectiveness. Although the jury is still out on this technique, clinical and basic science research into adjuncts that can influence biologic factors, are likely to bear fruit in the future.

Chapter 32: Biodigital Orthodontics: Integrating Technology with Diagnosis, Treatment Planning and Targeted Therapeutics. Rohit Sachdeva presents a discussion of how clinical decision making should be accomplished, with enhanced integration of digital technologies. Although this chapter focuses on just one of the technology systems available to orthodontists, the thought process that underlies the use of these technologies is shared. These technologies are tools and only serve to enhance the principles of sound diagnosis and treatment planning. They can make good clinicians better, but their sophistication precludes the ability for poorly educated dental

practitioners to use them properly. Benefits to dental specialists can be significant with improved abilities at both diagnostic evaluation and treatment planning as well as, in some instances, the fabrication of appliances. These technologies gain their benefit in reducing the "error of the method" of conventional orthodontics.

## PART SIX

### Orthodontic Retention and Post-Treatment Changes

Chapter 33: Stability, Retention, and Relapse. Don Joondeph is joined in this updated chapter by colleagues Greg Huang and Bob Little, all respected clinicians with a wealth of research material on post-orthodontic treatment changes, developed over many years at the University of Washington. The authors outline a series of problems routinely addressed by orthodontic treatment. With evidenced-based suggestions, they provide important clinical recommendations to reduce adverse post-active treatment changes that take place over time. "Maturational change" to varying degrees is the norm, but patients often have an unrealistic expectation that their teeth will "stay perfect" after orthodontics. Perfection remains a goal, but the structural and functional environment within which the dentition exists over time makes excellent retention planning a "must" to preserve treatment accomplishments and long term patient satisfaction. The authors provide information gleaned from the UW retention studies as a basis for their clinical recommendations.

## PART SEVEN

### Classic Chapters (online only)

Chapter 34: Interceptive Guidance of Occlusion with Emphasis on Diagnosis. Although the general topic has been reviewed within Chapter 16, this classic chapter from Jack and Hali Dale provides more in depth background on the diagnosis of space problems in the mixed dentition and associated interceptive treatment modalities. Diagrams representing the stages of tooth eruption are coordinated with photographic case documentation of a variety of malocclusions secondary to space problems. Interception of crowding through a series of staged clinical decisions is demonstrated. Guided tooth removal is presented as an option for interceptive orthodontics, with goals for decreased time in fixed orthodontic mechanotherapy.

Chapter 35: Functional Appliances. The use of functional appliances remains high world-wide and the material herein provides background important to orthodontic specialist clinicians. This chapter was authored by the late Tom Graber, the original author and editor of the textbook. The goal of the chapter (originally published in the 4th edition) is to provide a basic understanding of how functional appliances work as well as a discuss the attributes of the most widely used designs. Although the topic is briefly addressed in Chapter 16, this specific chapter focuses more in detail on functional appliance construction and clinical management. The author reviews the mechanism of Class II correction with functional jaw orthopedics, compares fixed with removable functional appliance designs and relates how clinicians may concurrently use functional jaw orthopedics with fixed bracket treatment. The chapter is well illustrated with clinical case material and diagrammatic representations of expected treatment results. Orthodontic residents and experienced clinicians alike will gain much from this thorough review of functional jaw orthopedics.

Chapter 36: Treatment of the Face with Biocompatible Orthodontics. This "classic chapter" by Dwight Damon reviews diagnosis and treatment planning protocols used with one of the most popular fixed appliance clinical techniques in use today. Chapter 24 appropriately discusses the general topic of self-ligation brackets, but this chapter on the specific use of the Damon technique has been one of the most requested since its original publication in the fourth edition. The author uses a series of case studies to demonstrate diagnostic considerations and treatment of a variety of malocclusion types. Although the bracket design has improved since the original publication of this chapter, the principles behind the treatment remain the same and are applicable to the self-ligating bracket systems currently available.

In re-writing and presenting this sixth edition of *Orthodontics: Current Principles and Techniques* we are well aware that an undertaking of this sort requires help from many sources. We are thankful for the great work of our authors, those who have been with us before and the outstanding colleagues who have joined them. Our authors have been pressed by us as well as our publisher to succinctly provide their best material. They have done so admirably with the result that we have succeeded in giving our educators and residents a broad based textbook that provides the foundational knowledge for an orthodontic specialist. We have dedicated this sixth edition of the text to them and to the degree that we have made their teaching and learning efforts easier, we are very happy!

This text revision would never have been completed without an outstanding editorial team at Elsevier. Thanks go to Kathy Falk, Laura Klein, Anne Schook, Srividhya Vidhyashankar and all of their supporting staff. As in any large project of this type, problems arise. It is these folks who went above and beyond their normal work hours and assignments to overcome challenging issues and keep us on track. The quality of production was enhanced over prior editions in part because of improved editing and printing technologies, but most of all because of the diligence of the Elsevier personnel.

In this edition of the text, we added a new editor, Greg Huang, chair of the orthodontic department at the University of Washington. His strong contributions were important in many seen and unseen ways. All of us as editors have shared an excitement for the educational mission of the text, one that carries over from the first volume edited by Tom Graber more than 45 years ago. We are thrilled that we can share the expertise of our authors with our colleagues. We remain personally positive and passionate about the orthodontic specialty. Our hope is that the enthusiasm that we share for orthodontics comes through the pages of the text and helps to motivate a new generation of educators, residents and practitioners.

**Lee W. Graber, DDS, MS, MS, PhD**
**Robert L. Vanarsdall, DDS**
**Katherine W.L. Vig, BDS, MS, D Orth, FDS, RCS**
**Greg J. Huang, DMD, MSD, MPH**

# CONTENTS

## PART SIX Orthodontic Retention and Posttreatment Changes



## PART SEVEN Classic Chapters (Online Only)

This page intentionally left blank

1

# 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: 2 tables.*

## INTRODUCTION

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, i.e., 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. 1-1). In what has become known as "Scammon's curve," for example, maturation of the central nervous system 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. 1-2). 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 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.

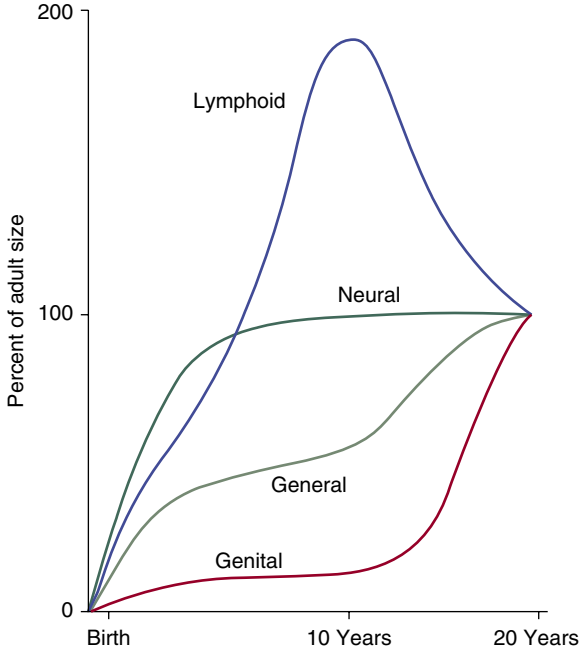



**FIGURE 1-1** *Scammon's curve* illustrating the fact that different systems of the body have different rates of development and come to maturity at different ages.

## Variation in Rates of Growth during Maturation

Two episodes of relatively rapid growth, or growth spurts, have been documented for both general somatic and craniofacial growth. The lesser of these, 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. 1-3). 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 prior to 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 as well as in 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, while the maximum rate of mandibular growth occurs just after PHV.[8,9]

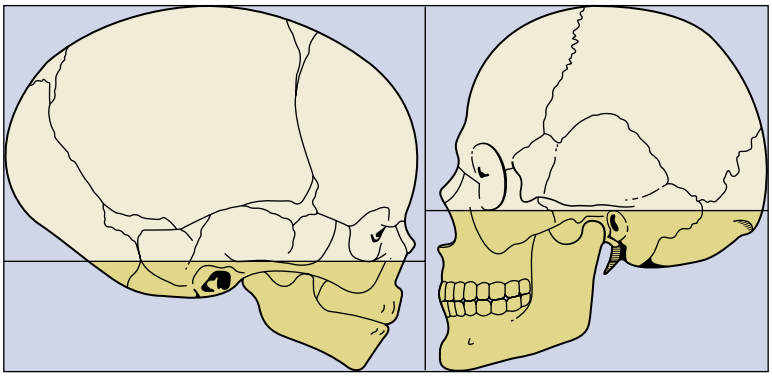


**FIGURE 1-2** Disproportions of the head and face in infant and adult. The neurocranium, which houses the brain and eyes is precocious in its development and growth and therefore is proportionately larger than the face during infancy and early childhood. (Adapted from Lowry GH. *Growth and Development of Children.* 6th ed. Chicago: Year Book Medical Publishers; 1973.)

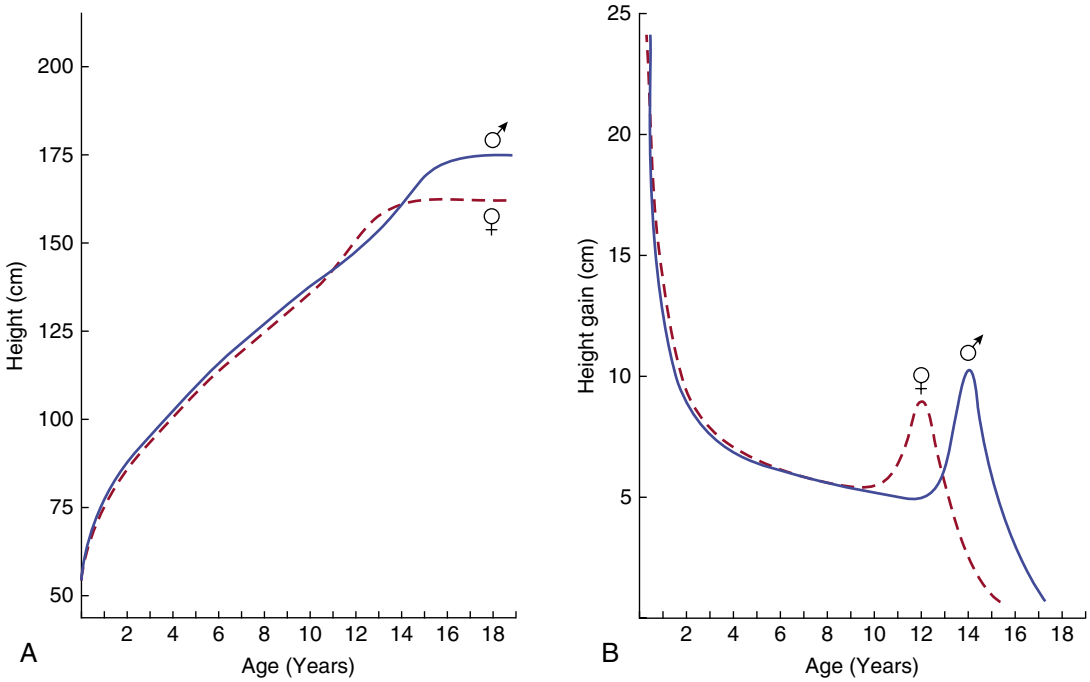



**FIGURE 1-3** Growth velocity curve (growth per unit of time) for skeletal growth as general measure of human ontogeny. Velocity of growth is characterized by decrease in growth rate beginning in the last trimester of prenatal development through maturation in the adult. During adolescence, hormonally mediated growth typically occurs to bring about a spurt in skeletal growth (PHV, peak height velocity). Pubertal growth spurt is characterized by considerable variability in onset and duration among individuals and according to gender. 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, and 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.)

The timing, rate, and amount of somatic growth are best determined by changes in overall height. As such, 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. 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 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]

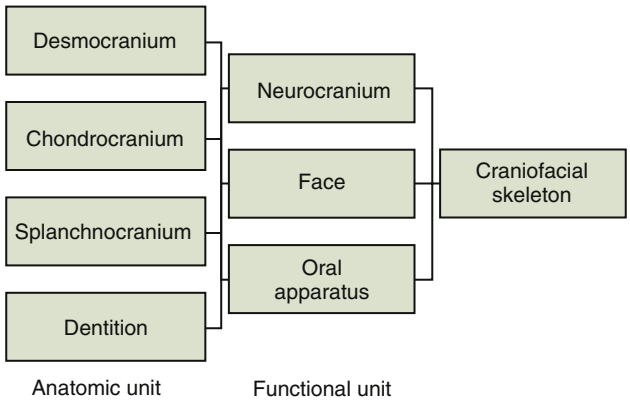



**FIGURE 1-4** Schematic of organization of the craniofacial skeleton into anatomic regions and overlapping functional regions.

## CRANIOFACIAL COMPLEX

The craniofacial complex is comprised of 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. 1-4).

### 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 morphogenesis and subsequent bone growth take place completely via 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.

### Viscerocranium

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 via 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 comprising the craniofacial complex (Fig. 1-5).

### Neurocranium

The *neurocranium* houses the brain and other elements of the central nervous system, 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, comprised 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, comprised of the mandible, develops entirely from the first branchial arch and thus is derived entirely as part of the viscerocranium. The mandible develops and grows via 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 as well as 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.

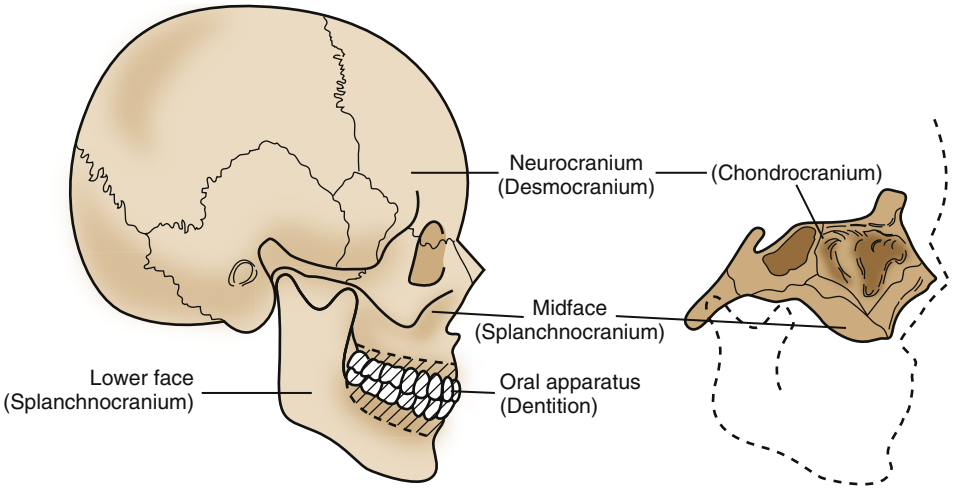



**FIGURE 1-5** Major components of the craniofacial skeletal complex.

## 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 2) 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 1-1.

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 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 is comprised of 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. While 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 as well as 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 comprised 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. 1-6).

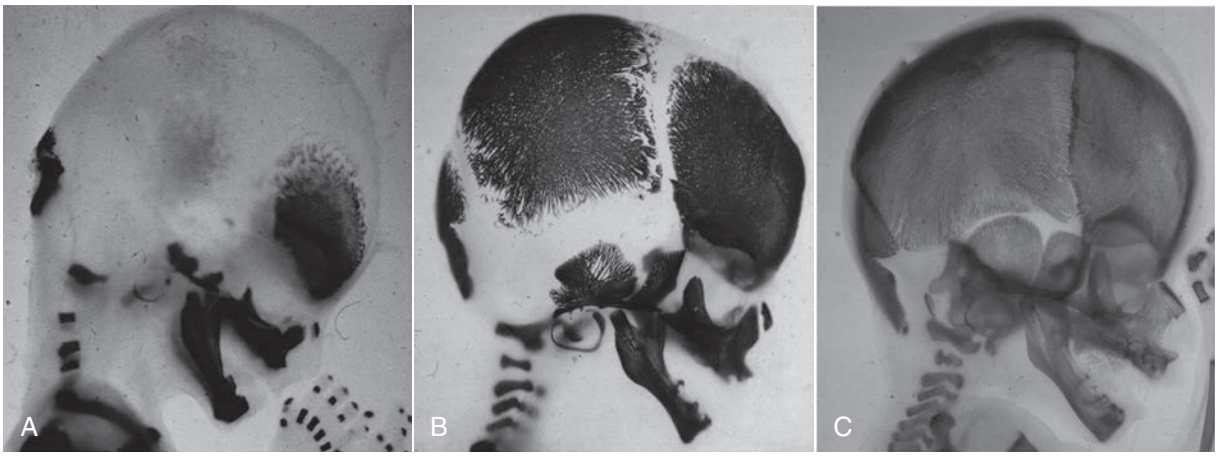



**FIGURE 1-6** Cleared and stained human fetuses indicating craniofacial skeletal structures at approximately 8 weeks' gestation (A), 15 weeks' gestation (B), and 18 weeks' gestation (C).

## TABLE 1-1 Summary of Key Genes Associated with the Development and Growth of the Tissues and Structures 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: S*keletal 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, 16, 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 |
| 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 |

*Continued*

**TABLE 1-1 Summary of Key Genes Associated with the Development and Growth of the Tissues and Structures Comprising the Craniofacial Complex—cont'd**

| Gene/Protein | | General Role and Function | Significance for Craniofacial Development and Growth | References |
|---|---|---|---|---|
| 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-ß1 to Tgf-ß3 | 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*, non-syndromal cleft lip and palate; *sCL/P*, syndromal cleft lip and palate; *TMJ*, temporomandibular joint.

**References**


1. Rice DPC. Craniofacial anomalies: from development to molecular pathogenesis. *Curr Mol Med*. 2005;5:699–722.
2. Zheng L, Yamashiro T, Fukunaga T, Balam TA, Takano-Yamamoto T. Bone morphogenetic protein 3 expression pattern in rat condylar cartilage, femoral cartilage and mandibular fracture callus. *Eur J Oral Sci*. 2005;113:318–325.
3. Opperman LA, Gakunga PT, Carlson DS. Genetic factors influencing morphogenesis and growth of sutures and synchondroses in the craniofacial complex. In: Carlson DS, ed. *Control mechanisms of craniofacial development and growth. Semin Orthod*. 2005;11(4):199–208.
4. Chai Y, Maxson RE Jr. Recent advances in craniofacial morphogenesis. *Dev Dyn*. 2006;235:2353–2375.
5. Nie X, Luukko K, Kettunen P. BMP signaling in craniofacial development. *Int J Dev Biol*. 2006;50:511–521.
6. Greene RM, Pisano MM. Palate morphogenesis: current understanding and future directions. *Birth Defects Res (Part C)*. 2010;90:133–154.
7. Robledo RE, Rajan L, Li X, Lufkin T. The *Dlx5* and *Dlx6* homeobox genes are essential for craniofacial, axial, and appendicular skeletal development. *Genes Develop*. 2002;16:1089–1101.
8. Doshi RR, Patil AS. A role of genes in craniofacial growth. IIOBA. 2012;3(2):19–36.
9. Hinton RJ. Genes that regulate morphogenesis and growth of the temporomandibular joint: a review. *Devel Dyn*. 2014;243:864–874.
10. Melville H, Wang Y, Taub PJ, Jabs EW. Genetic basis of potential therapeutic strategies for craniosynostosis. *Am J Med Genet Part A*. 2010;152A:3007–3015.
11. Xue F, Wong RWK, Rabie ABM. Genes, genetics, and Class III malocclusion. *Orthod Craniofac Res*. 2010;13:69–74.
12. Xue F, Wong RWK, Rabie ABM. Identification of SNP markers on 1p36 and association analysis of *EPB41* with mandibular prognathism in a Chinese population. *Arch Oral Biol*. 2010;55:867–872.
13. Hinton RJ, Carlson DS. Regulation of growth in the mandibular condylar cartilage. In: Carlson DS, ed. *Control mechanisms of craniofacial development and growth. Semin Orthod*. 2005;11(4):209–218.
14. Hatch NE. FGF signaling in craniofacial biological control and pathological craniofacial development. *Crit Rev Eukaryot Gene Expr*. 2010;20(4):295–311.
15. Martinez-Abadias N, Heuze Y, Wang Y, Jabs EW, Aldridge K, Richtmeier J. FGF/FGFR signaling coordinates skull development by modulating magnitude of morphological integration: evidence from Apert syndrome mouse models. *PLoS One*. 2011;6(10).
16. Rice DPC, Rice R, Thesleff I. *Fgfr* mRNA isoforms in craniofacial bone development. *Bone*. 2003;33(1):14–27.
17. Heuze Y, Martinez-Abadias N, Stella JM, et al. Quantification of facial skeletal shape variation in fibroblast growth factor receptor-related craniosynostosis syndromes. *Birth Def Res (A)*. 2014;100:250–259.
18. Buschang PH, Hinton RJ. A Gradient of Potential for Modifying Craniofacial Growth. In: Carlson DS, ed. *Control mechanisms of craniofacial development and growth. Semin Orthod*. 2005;11(4):219–226.
19. Zhou J, Lu Y, Gai XH, et al. The growth hormone receptor gene is associated with mandibular height in a Chinese population. *J Dent Res*. 2005;84:1052–1056.
20. Kang EH, Yamaguchi T, Tajima A, et al. Association of the growth of the growth hormone receptor gene polymorphisms with mandibular height in a Korean population. *Arch Oral Biol*. 2009;45:556–562.
21. Sasaki Y, Satoh K, Hayasaki H, Fukumoto S, Fujiwara T, Nonaka K. The P561T polymorphism of the growth hormone receptor gene has an inhibitory effect on mandibular growth in young children. *Europ J Orthod*. 2009;31:536–541.
22. Veistinen L, Takatolo M, Tanimoto Y, Kesper D, Vortkamp A, Rice DPC. Loss-of-function of *Gli3* in mice causes abnormal frontal bone morphology and premature synostosis of the interfrontal suture. *Front Physiol*. 2012;3:1–6.
23. Sharpe PT. Homeobox genes and orofacial development. *Conn Tiss Res*. 1995;32:17–25.
24. Spears, Svoboda In: Carlson DS, ed. Growth factors and signaling proteins in craniofacial development. *Control mechanisms of craniofacial development and growth. Semin Orthod*. 2005;11(4):184–199.
25. Carlson B. *Human Embryology and Developmental Biology*. Philadelphia: Elsevier; 2014.
26. Trainor PA, Krumlauf R. Patterning the neural crest: hindbrain segmentation and *hox* gene plasticity. *Nat Rev Neuro*. 2000;1:116–124.
27. Hajjar D, Santos MF, Kimura ET. Mandibular repositioning modulates IGFBP-3, -4, -5, and -6 expression in the mandibular condyle of young rats. *Biorheology*. 2006;43(3–4):311–321.
28. Marques MR, Hajjar D, Franchini KG, Moriscot AS, Santos MF. Mandibular appliance modulates condylar growth through integrins. *J Dent Res*. 2008;87(2):153–158.
29. Patil AS, Sable RB, Kothari RM. Role of insulin-like growth factors (IGFs), their receptors and genetic regulation in the chondrogenesis and growth of the mandibular condylar cartilage. *J Cell Physiol*. 2011;227:1796–1804.
30. Frazier-Bowers S, Rincon-Rodriguez R, Zhou J, Alexander K, Lange E. Evidence of linkage in a Hispanic cohort with a class III dentofacial phenotype. *J Dent Res*. 2009;88:56–60.
31. Tang GH, Rabie ABM. Runx2 regulates endochondral ossification in condyle during mandibular advancement. *J Dent Res*. 2005;84(2):166–171.
32. Carreira AC, Lojudice FH, Halcsik E, Navarro RD, Sogayar MC, Granjeiro JM. Bone morphogenetic proteins: facts, challenges, and future perspectives. *J Dent Res*. 2014;93(4):335–345.
33. Balczerski B, Zakaria S, Tucker AS, et al. Distinct spatiotemporal roles of hedgehog signaling during chick and mouse cranial base and axial skeletal development. *Dev Biol*. 2012;371:203–214.
34. Chu FT, Tang GH, Hu Z, Qian YF, Shen G. Mandibular functional positioning only in vertical dimension contributes to condylar adaptation evidenced by concomitant expressions of L-Sox5 and type II collagen. *Arch Oral Biol*. 2008;53:567–574.
35. Bonaventure J, El-Ghouzzi V. Molecular and cellular basis of syndromic craniosynostosis. *Exp Rev Mol Med*. 2003;5(29):1–17.
36. Tassopoulou-Fishell M, Deeley K, Harvey EM, Sciote JJ, Viera AR. Genetic variation in *Myosin 1H* contributes to mandibular prognathism. *Am J Orthod Dentofac Orthoped*. 2012;141(1):51–59.
37. Desh H, Gray SL, Horton MJ, et al. Molecular motor *MYO1C*, acetyltransferase *KAT6B* and osteogenetic transcription factor *RUNX2* expression in human masseter muscle contributes to development of malocclusion. *Arch Oral Biol*. 2014;59:601–607.
38. Hinton RJ, Serrano M, So S. Differential gene expression in the perichondrium and cartilage of the neonatal mouse temporomandibular joint. *Orthod Craniofac Res*. 2009;12:168–177.

## TABLE 1-1 Summary of Key Genes Associated with the Development and Growth of the Tissues and Structures Comprising the Craniofacial Complex—cont'd


39. Jing J, Hinton RJ, Jing Y, Liu Y, Zhou X, Feng JQ. Osterix couples chondrogenesis and osteogenesis in post-natal condylar growth. *J Dent Res.* 2014;93(10):1014–1021.
40. ten Berge D, Brouwer A, Korving J, et al. Prx1 and Prx2 are upstream regulators of sonic hedgehog and control cell proliferation during mandibular arch morphogenesis. *Devel.* 2001.
41. Martin JF, Bradley A, Olsen EN. The *paired*-like homeobox gene *Mhox* is required for early events of skeletogenesis in multiple lineages. *Genes Develop.* 1995;9:1237–1249.
42. Kyrkanides S, Kambylafkas P, Miller JH, Tallents RH, Puzas JE. The cranial base in craniofacial development: a gene therapy study. *J Dent Res.* 2007;86(10):956–961.
43. Hinton RJ. Genes that regulate morphogenesis and growth of the temporomandibular joint: a review. *Devel Dyn.* 2014;243:864–874.
44. Rabie ABM, Tang GH, Hägg U. Cbfa1 couples chondrocytes maturation and endochondral ossification in rat mandibular condylar cartilage. *Arch Oral Biol.* 2004;49(2):109–118.
45. Lei WY, Wong RWK, Rabie ABM. Factors regulating endochondral ossification in the spheno-occipital synchondrosis. *Angle Orthod.* 2008;78(2):215–220.
46. Nie X, Luukko K, Kvinnsland IH, Kettunen P. Developmentally regulated expression of Shh and Ihh in the developing mouse cranial base: comparison the Sox9 expression. *Anat Rec A Discov Mol Cell Evol Biol.* 2005;286(2):891–898.
47. Cendekiawan T, Wong RWK, Rabie ABM. Temporal expression of SOX9 and type II collagen in spheno-occipital synchondrosis of mice after mechanical tension stimuli. *Angle Orthod.* 2008;78(1):83–88.
48. Rabie ABM, She TT, Hägg U. Functional appliance therapy accelerates and enhances condylar growth. *Am J Orthod Dentofacial Orthop.* 2003;123(1).
49. Su P-H, Liu Y-F, Chen J-Y, Lai Y-J, Facial asymmetry and clinical manifestations in patients with novel insertion of the *TCOF1* gene. *Clin Genet.* 2012;82:460–465.
50. Coussens AK, Wilkinson CR, Hughes IP, et al. Unravelling the molecular control of calvarial suture fusion in children with craniosynostosis. *BMC Genomics.* 2007;8:458.
51. Melville H, Wang Y, Taub PJ, Jabs EW. Genetic basis of potential therapeutic strategies for craniosynostosis. *Am J Med Genet Part A.* 2010;152A:3007–3015.
52. Rabie ABM, Hägg U. Factors regulating mandibular condylar growth. *Am J Orthod Dentofacial Orthop.* 2002;122:401–409.
53. Enomoto A, Watahiki J, Nampo T, et al. Mastication markedly affects mandibular condylar growth, gene expression, and morphology. *Am J Orthod Dentfac Orthop.* 2014;146(3):365–363.

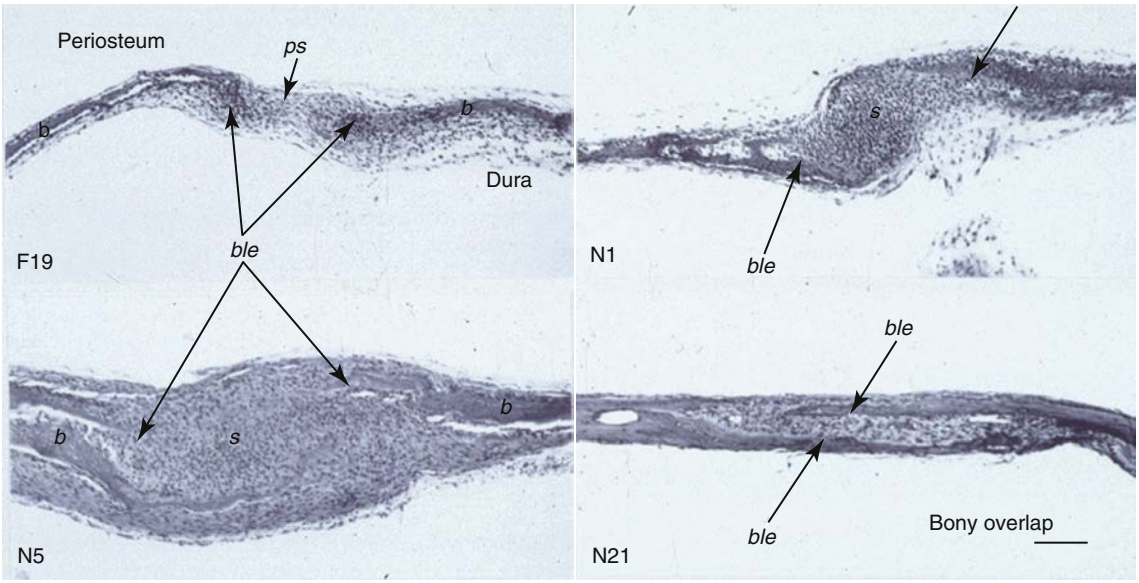



**FIGURE 1-7** Photomicrographs of hematoxylin and eosin–stained histologic sections through the coronal suture of normal rats at embryonic day 19 and postnatal days 1, 5, and 21. Bone (*b*), bone leading edge (*ble*), presumptive suture mesenchyme (*ps*), and suture (*s*). (From Opperman LA, Gakunga PT, Carlson DS. Genetic factors influencing morphogenesis and growth of sutures and synchondroses in the craniofacial complex. *Semin Orthod*. 2005;11(4):199–208.)

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. 1-7).

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 layers of

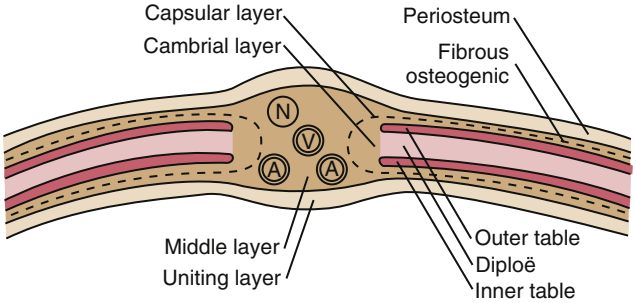



**FIGURE 1-8** Schematic representation indicating the relationship between the periosteum and dura mater as a mechanism for a specialized of intramembranous growth within the sutures of cranial vault bones. (Adapted from Pritchard JJ, Scott JH, Girgis FG. The structure and development of cranial and facial sutures. *J Anat*. 1956;90:73–86.)

the periosteum and the dura reflect into the space between the two cranial vault bones and provide a source of new osteogenic cells (Fig. 1-8). 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 as well as the intracranial dura mater. Secretion of soluble factors by the


**FIGURE 1-9** 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)

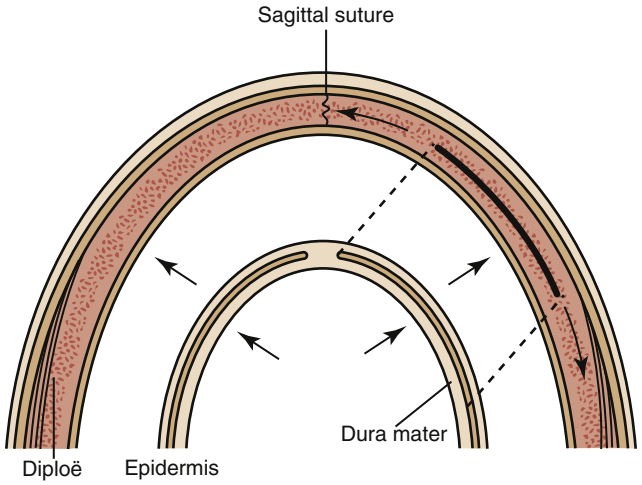



**FIGURE 1-10** Schematic diagram indicating the relationship between expansile growth of the brain as a stimulus for compensatory growth of sutures of the cranial vault. (Adapted from Moss ML. The functional matrix. In: Kraus B, Reidel R, eds. *Vistas Orthod.* Philadelphia: Lea & Febiger; 1962;85–98.)

dura mater in response to growth signals from the expanding, underlying brain is essential for normal cranial suture morphogenesis as well as for the 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 (TGF-β1, TGF-β2, TGF-β3), bone morphogenetic protein (BMP2, BMP7), fibroblast growth factor 4 (FGF-4), insulin-like growth factor 1 (IGF-1), and sonic hedgehog (SHH) (Fig. 1-9).[26,27] Overexpression of transcription factors Runx2 and Msx2 and haploinsufficiency of Twist[28] and Noggin[29] are also associated with suture obliteration, while 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 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. 1-10). 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

Due to 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. 1-11).

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

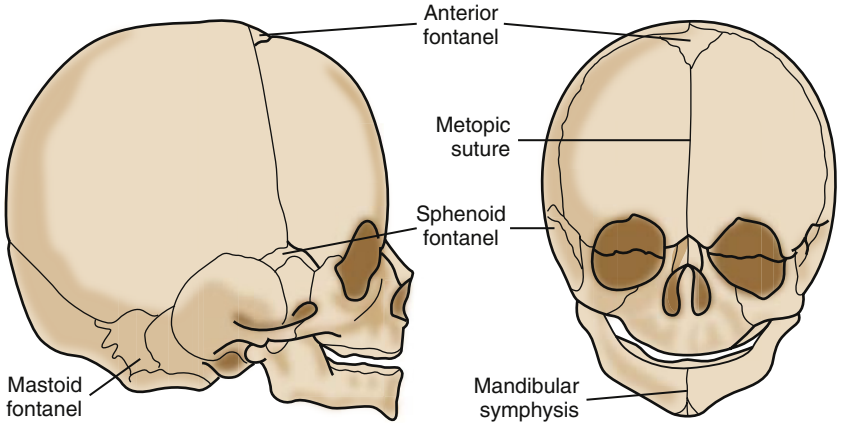



**FIGURE 1-11** Lateral and frontal views of the neonate skull indicating the location of sutures and fontanels. (Adapted from Sicher H, DuBrul EL. *Oral Anatomy*. 5th ed. St. Louis: Mosby; 1970.)

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 life span. 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 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. 1-12).

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

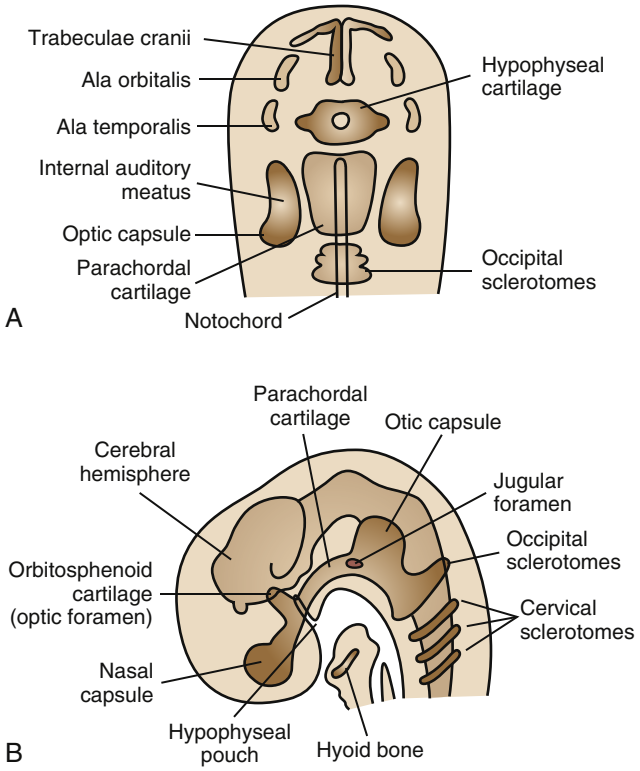



**FIGURE 1-12** Schematic representation of the cartilaginous basal plate comprising the embryonic chondrocranium. A, Dorsoventral view; B, Lateral view.

these centers of ossification arise within the chondrocranium, segments of intervening cartilage form *synchondroses* (Fig. 1-13). 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 via intramembranous ossification.

### Mechanism of Synchondrosal Growth

Cranial base synchondroses are temporary cartilaginous joints located between bones of endochondral origin and growth.

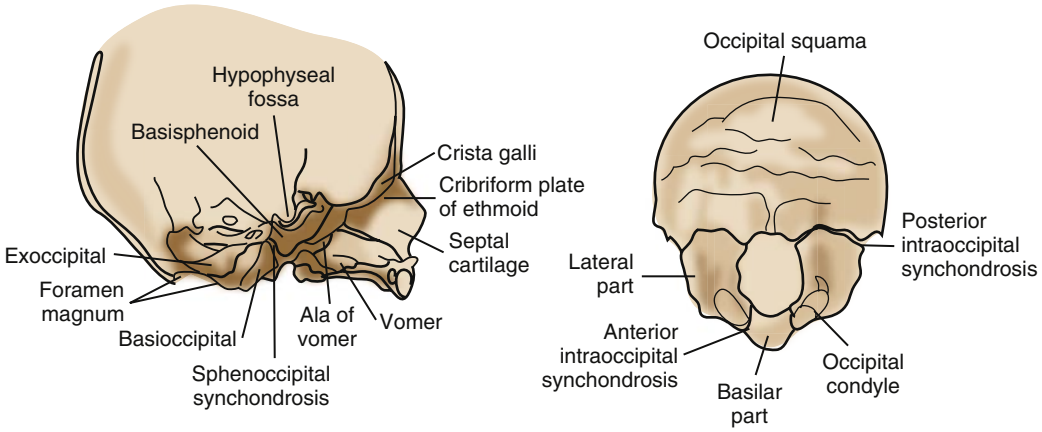



**FIGURE 1-13** Drawing of sagittal and basal views of the neonatal skull indicating spheno-occipital synchondrosis and intraoccipital synchondroses. The sphenoethmoidal synchondrosis will arise between the sphenoid and ethmoid bones. (Adapted from Bosma JF. Introduction to the symposium. In: Bosma JF, ed. *Development of the Basicranium*. Bethesda, MD: US Department of Health, Education, and Welfare; 1976:3–28.)

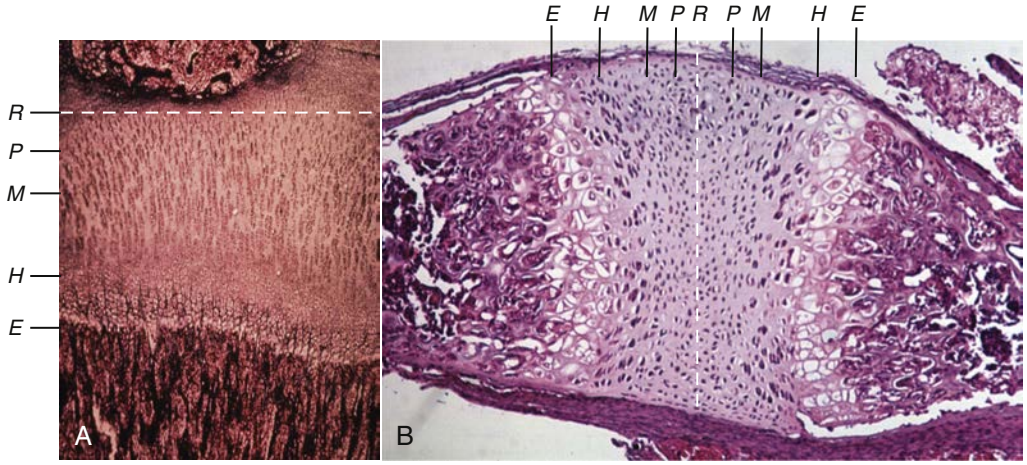



**FIGURE 1-14** Histologic comparison between the cartilages within a growing epiphyseal plate (**A**) and cranial base synchondrosis (**B**) (hematoxylin and eosin–stained). *R*, Resting zone (*dashed line*); *P*, proliferating zone; *M*, maturational zone; *H*, hypertrophic zone; *E*, zone of endochondral ossification.

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 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. 1-14). 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 to be 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 three 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 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 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 (Fig. 1-15). 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. 1-16). 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 due to 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 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 approximately nearly 90% of its adult size by 4.5 years of age, while the posterior cranial base has attained only about 80% of its adult size (Fig. 1-17). 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]

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 due to 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

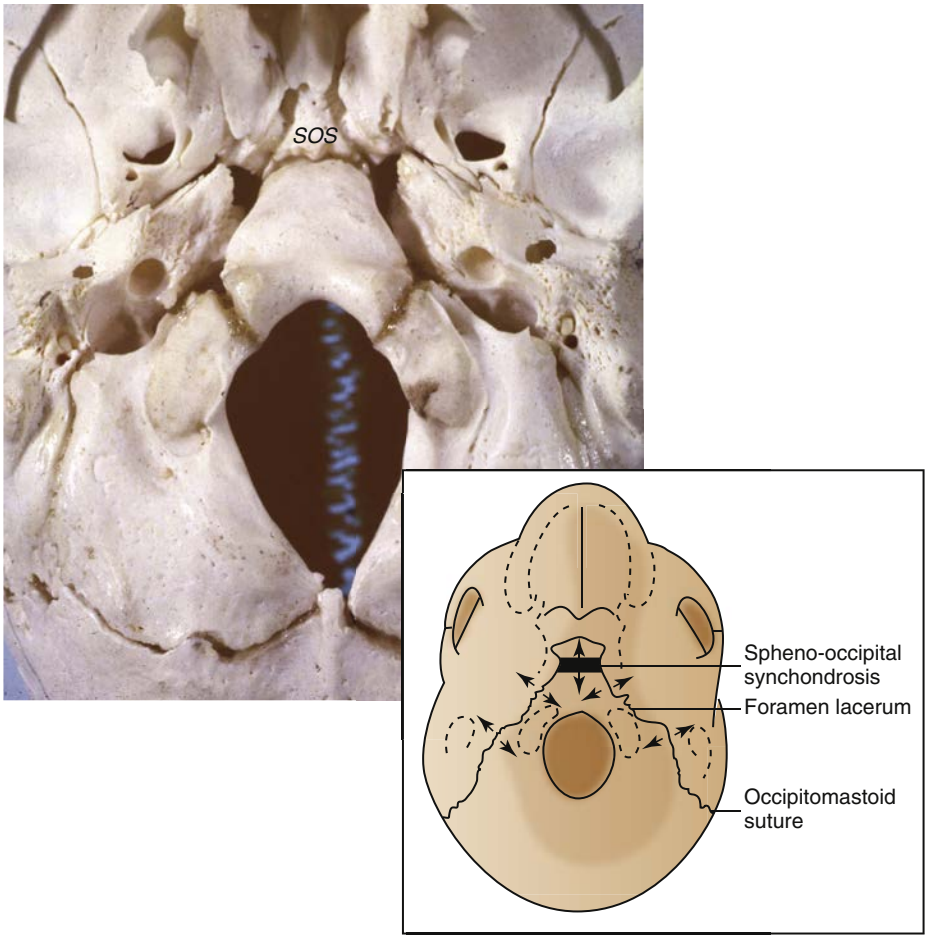



**FIGURE 1-15** Basal view of a juvenile human indicating the spheno-occipital synchondrosis (*SOS*).

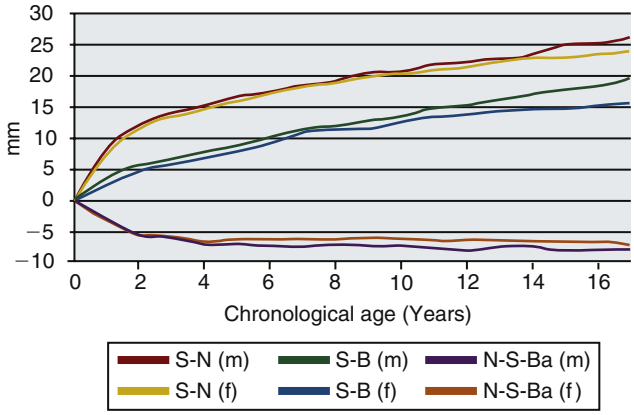



**FIGURE 1-16** Male (m) and female (f) cranial base growth changes from birth through 17 years of age. (Data from Ohtsuki F, Mukherjee D, Lewis AB, etc.: A factor analysis of cranial base and vault dimensions in children, *Am J Phys Anthropol* 58(3):271-9, 1982.)

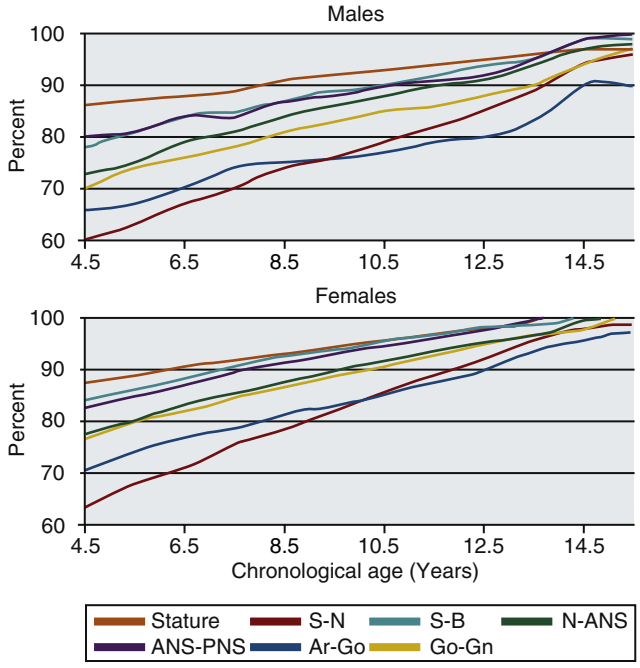



**FIGURE 1-17** Craniofacial growth maturity gradient of males and females. (Adapted from Buschang PH, Baume RM, Nass GG. A craniofacial growth maturity gradient for males and females between 4 and 16 years of age. *Am J Phys Anthrop*. 1983;61:373–382.)

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. 1-18).

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. 1-19). 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 is comprised principally of parasagittal extensions of the cartilaginous anterior cranial base as the nasal septum and cartilaginous nasal capsule into the nasal region. The viscerocranial 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.

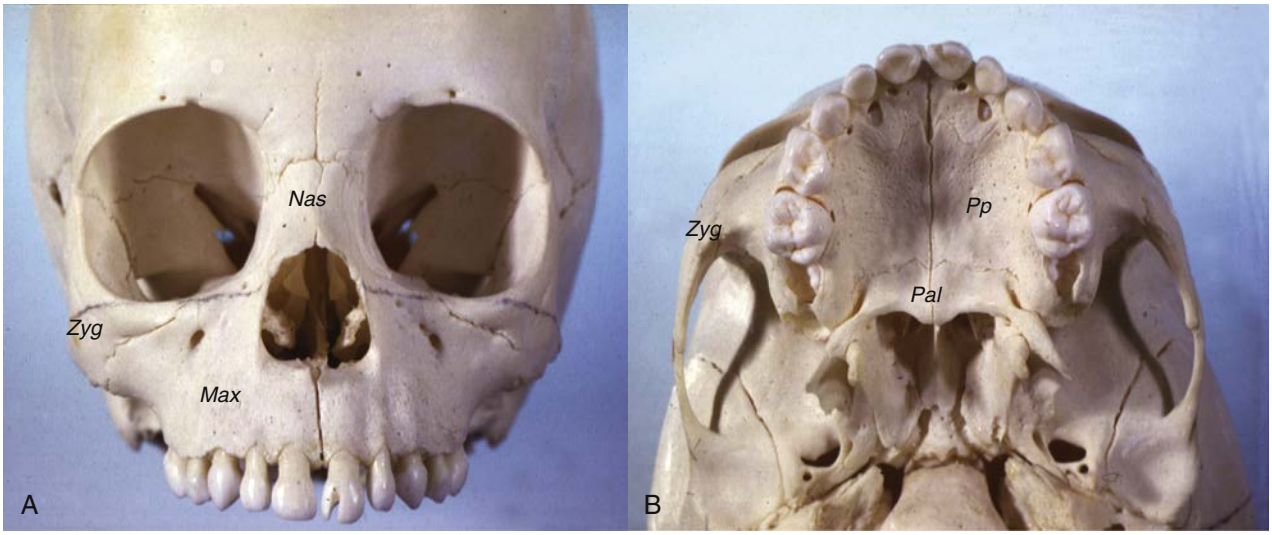



**FIGURE 1-18** (**A**) Frontal and (**B**) basal views of a juvenile human indicating the bones comprising the midface. *Max*, maxilla; *Nas*, nasal bones; *Zyg*, zygomatic bones; *Pal*, palatine bones; *Pp*, palatal processes of the maxillary bones.

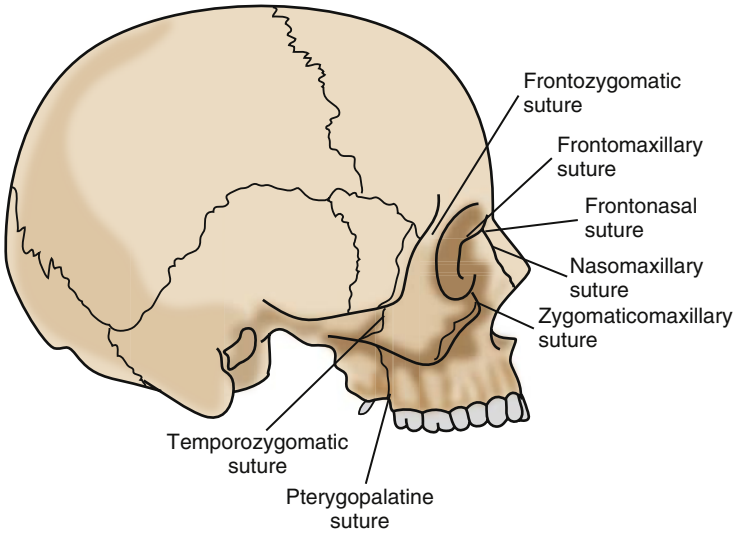



**FIGURE 1-19** Location of the circummaxillary suture system articulating the midface with the neurocranium.

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, since the bones comprising 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. While 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 (approximately 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 due to cigarette smoking and alcohol, 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. 1-20). 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

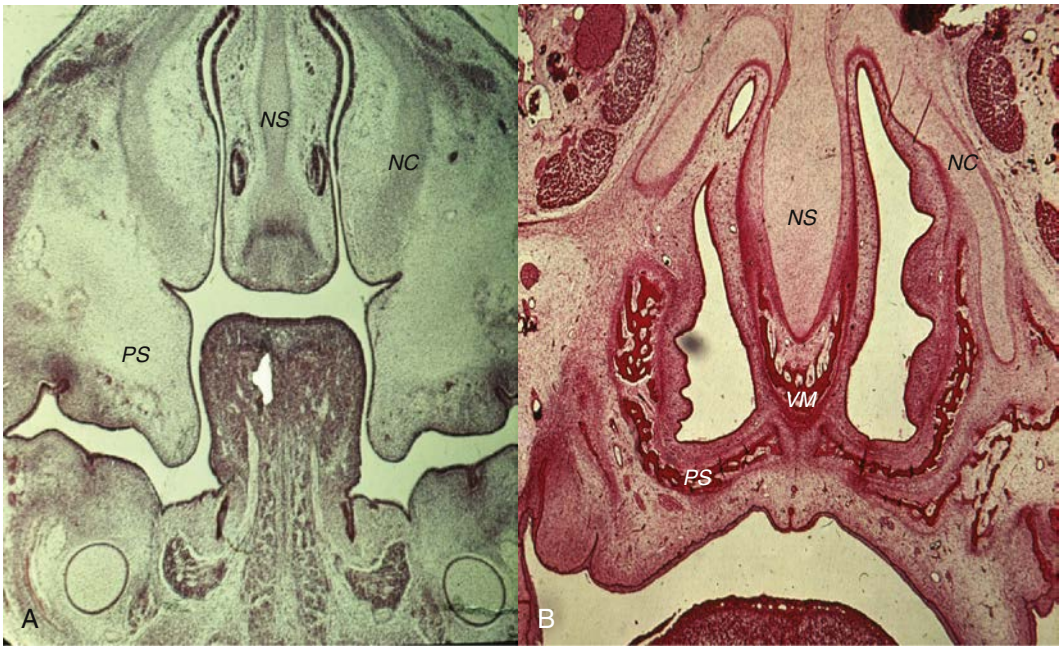



**FIGURE 1-20** Frontal histologic sections of human fetuses at approximate ages of 5 weeks' gestation (**A**) and 11 weeks' gestation (**B**) (hematoxylin and eosin–stained). *NS*, Nasal septal cartilage; *NC*, nasal capsular cartilage; *V*, vomer; *PS*, palatal shelves.

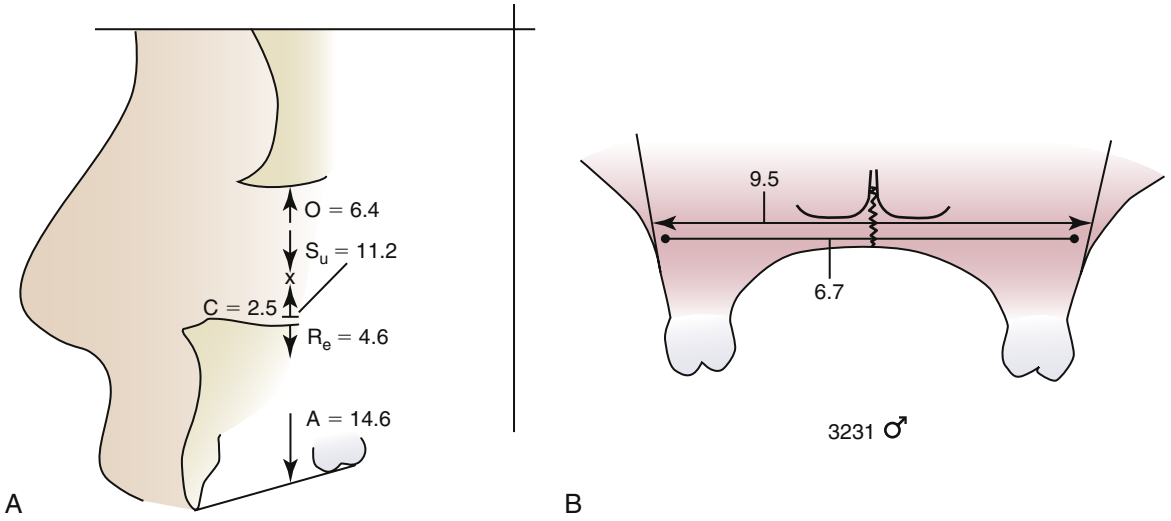



**FIGURE 1-21** (A) Sutural displacement ($S_u$), apposition of the orbital floor (O), resorption of the nasal floor ($R_e$), apposition at the infrazygomatic crest (C), and dentoalveolar development (A) from 4 years of age through adulthood in nine boys. (B) Width changes (mm) of the maxilla and lateral 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.)

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 via intramembranous ossification. Growth at the circummaxillary and intermaxillary sutures occurs in response to midfacial displacements due principally to 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 adolescence (Fig. 1-21). 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] 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, 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.

The midface undergoes a complex modeling pattern throughout childhood and adolescence (Fig. 1-22).[58] As the midface is displaced anteriorly, compensatory bony deposition occurs

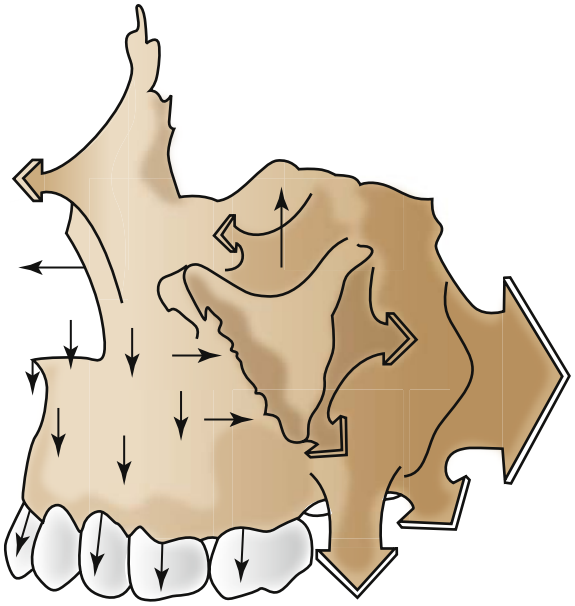


**FIGURE 1-22** Maxillary remodeling, with the sizes of the arrows indicating relative amounts of change and with *dark* and *light arrows* indicating resorption and apposition, respectively. (Redrawn from Enlow DH, Bang S. Growth and remodeling of the human maxilla. *Am J Orthod.* 1965;51:446–464.)

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 due to the combined effects of inferior cortical drift and inferior displacement (see Fig. 1-19). 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 due to 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 mm 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 central nervous system—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

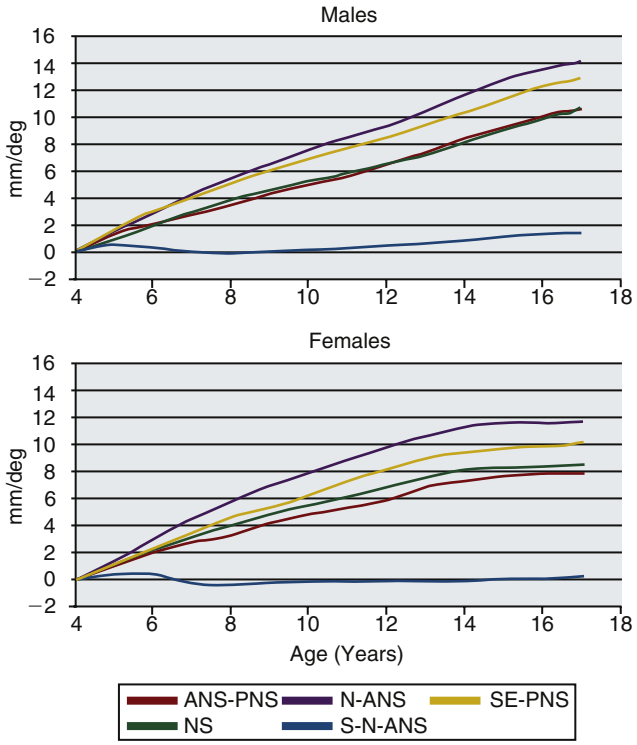
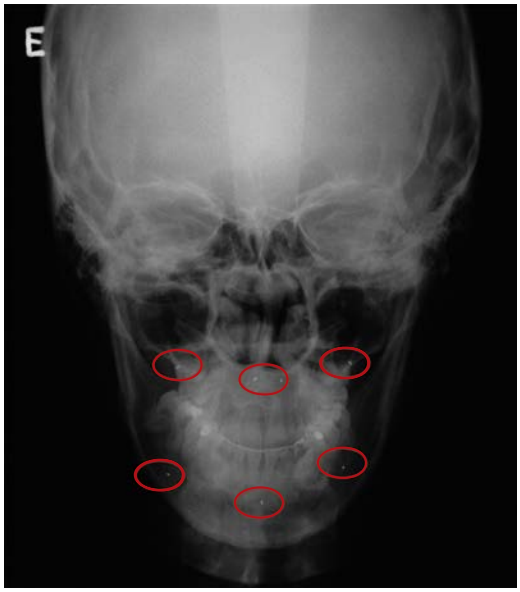



**FIGURE 1-23** Maxillary growth changes between 4 and 17 years of age of males and females. (Adapted from data provided by Bhatia SN, Leighton BC. *A Manual of Facial Growth: a Computer Analysis of Longitudinal Cephalometric Growth Data.* New York: Oxford University Press; 1993.)

than anteroposterior growth potential (Fig. 1-23). By 4.5 years of age, palatal length (anterior nasal spine–posterior nasal spine) and anterior facial height (nasion–anterior nasal spine) have attained approximately 80% and 73% of their adult size, respectively (see Fig. 1-18). 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 time 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. Due to greater transverse displacements



| 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 |

**FIGURE 1-24** Transverse expansion (mm/yr) of metallic bone markers inserted into the maxillary (*Mx*) and mandibular (*Md*) basal structures.

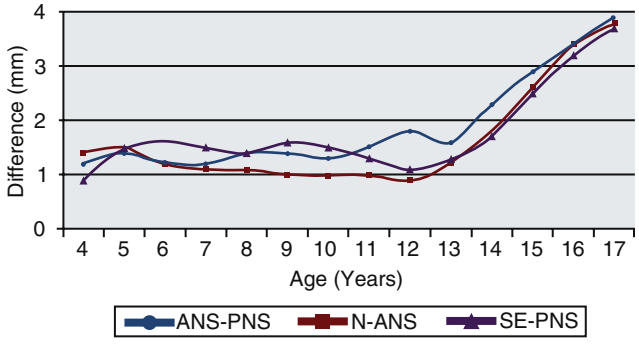



**FIGURE 1-25** Sex differences (male minus female) in maxillary size. (Adapted from data provided by Bhatia SN, Leighton BC. *A Manual of Facial Growth: a Computer Analysis of Longitudinal Cephalometric Growth Data.* New York: Oxford University Press; 1993.)

posteriorly than anteriorly, the midfacial complex also exhibits transverse rotation around the midpalatal suture (Fig. 1-24). 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]

There are definite sex differences in maxillary postnatal growth (Fig. 1-25), with males being larger and growing more than females. Size differences, averaging between 1 mm 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 2 extra years of childhood growth that males have; males enter the adolescence phase of growth at approximately 12 years of age, while 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 rod-like 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 (CN 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. 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. 1-26). 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 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 upon 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

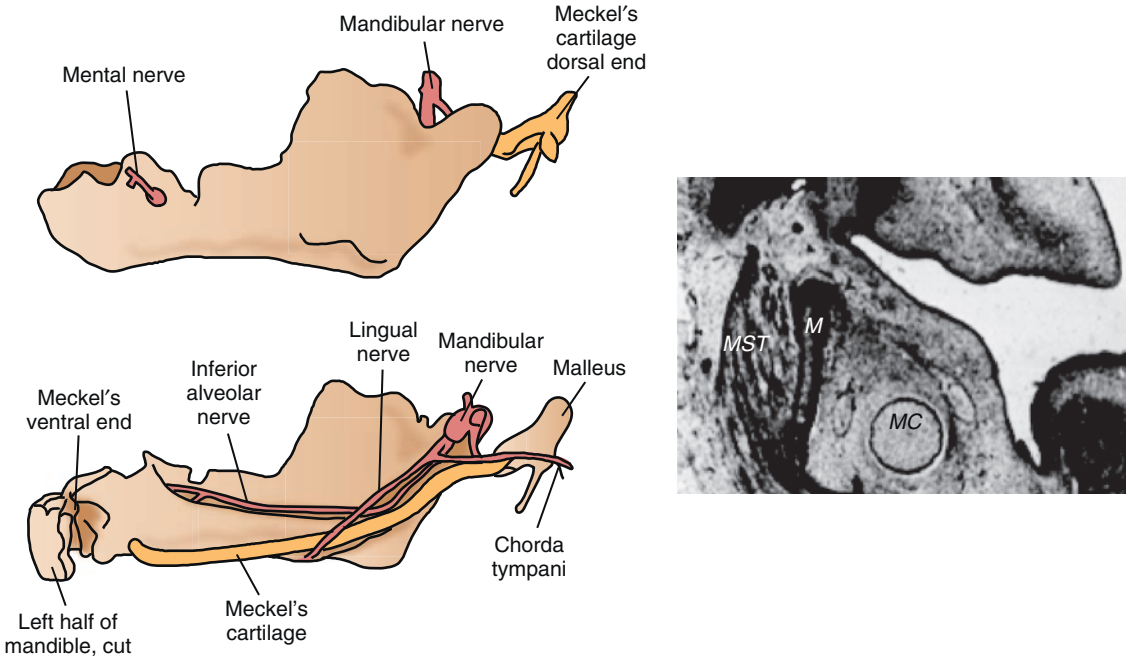



**FIGURE 1-26** Drawings of a fetal mandible with lateral (*top left*) and medial (*bottom left*) views. *Right*, Photomicrograph of coronal view of human fetus indicating Meckel's cartilage medial to the mandible (*M*). *MST*, Masseter muscle. (Drawings adapted from Warwick R, Williams PL, eds. *Gray's Anatomy*. 35th ed. Philadelphia: WB Saunders; 1973.)

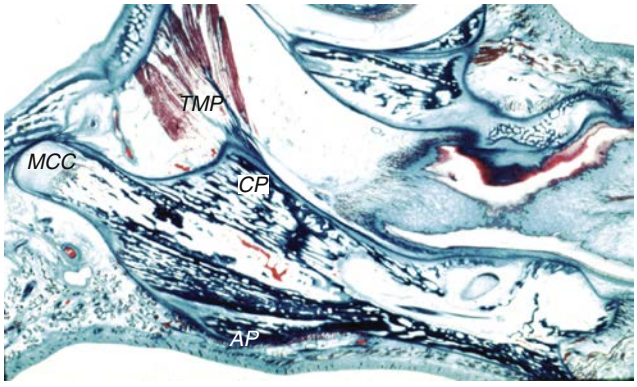



**FIGURE 1-27** Parasagittal histologic section of human fetus (approximately 12 weeks' gestation) (hematoxylin and eosin–stained). *MCC*, Mandibular condylar cartilage; *CP*, coronoid process; *AP*, angular process; *TMP*, temporalis muscle.

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. 1-27).

As the cartilage comprising 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. 1-28). 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

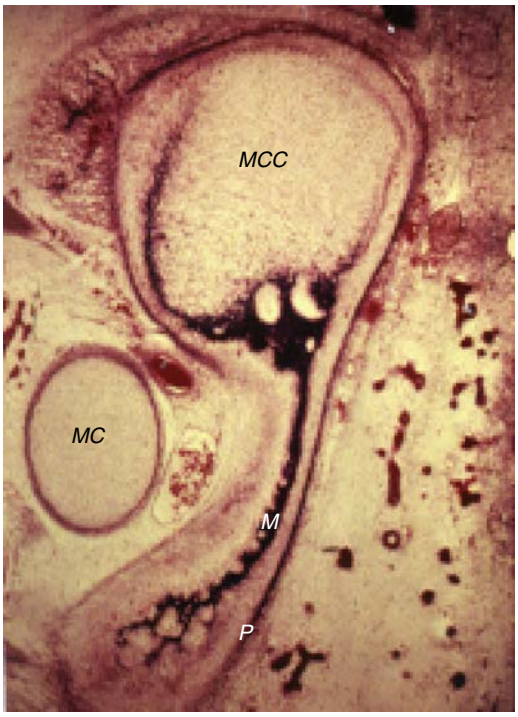



**FIGURE 1-28** Frontal histologic section of a human fetus (approximately 8 weeks' gestation) (hematoxylin and eosin–stained). The bone comprising the body and ramus of the mandible (*M*) originates in the membrane lateral to Meckel's cartilage (*MC*). The periosteal membrane enveloping the mandible gives rise secondarily to the mandibular condylar cartilage (*MCC*).