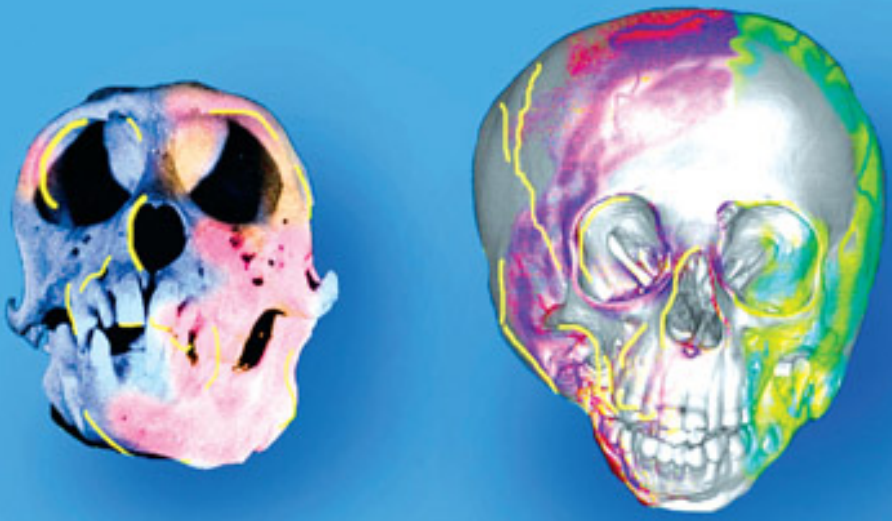
Craniofacial Biology and Craniofacial Surgery



Bernard G Sarnat & James P Bradley

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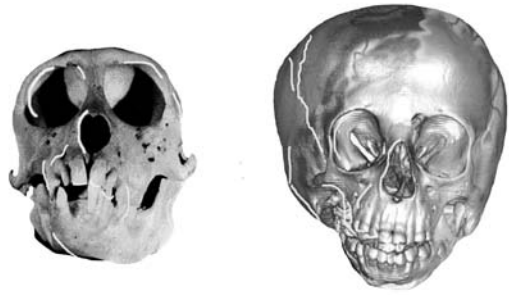

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Recognition

To the mentors of Bernard G. Sarnat, M.D., D.D.S.
To the mentors of James P. Bradley, M.D.

Recognition

To the mentors of Bernard G. Sarnat, M.D., D.D.S., to whom I owe so much:
For research: Isaac Schour, D.D.S, Ph.D.
For general surgery: Marshall Davison, M.D.
For plastic and reconstructive surgery: Vilray P. Blair, M.D., and
Louis T. Byars, M.D.

To the mentors of James P. Bradley, M.D., to whom I owe so much:
For plastic and reconstructive surgery: Joseph G. McCarthy, M.D.
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For research: Michael T. Longaker, M.D.
For craniofacial biology: Bernard G. Sarnat, M.D., D.D.S.

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Foreword

> "Learning doth make the minds of men gentle, whereas ignorance makes them churlish."
>
> Sir Francis Bacon, 1605

The diverse compilation of pre-molecular biological surgical experimentation with advanced stem cell regenerative medicine devoted to the craniofacial complex makes this a unique book. This work combines an historical record of the past with current and future aspirations of diagnosis, prognosis, treatment and prevention of disparities of development. Anomalies of craniofacial development are associated with one third of all congenital birth defects. Whereas most parts of the body are generally concealed below the surface, either by skin or modestly by clothing, the craniofacial complex is the most exposed region of the body, making its defects not only functionally significant, but also having a huge sociological and psychological impact.

Molecular biology and stem cell therapy have revolutionized the study of development and the therapeutic potential of regenerative healing of defects. Rapid advances in our understanding of genetic, molecular and cellular mechanisms underlying craniofacial development are now being translated into novel approaches for disease prevention, tissue repair and regeneration.

Bernie Sarnat's pioneering experiments recorded in this book opened up the possibilities of understanding and modifying the developmental

distortions that current genetic and molecular biological expositions are revealing as the root causes. His co-author, James Bradley, has taken advantage of this tremendous biological background to implement therapeutic and surgical procedures to alleviate disabilities and deformations by employing the technologies of diagnostic capabilities rendered by radiology, CAT-scanning, MRI imaging, ultrasonography and ultimately genetically-based prognoses.

The variations of the components of the oro-gnatho-masticatory apparatus, both in their normal and abnormal development, whether of greater or lesser clinical significance, are manifestations of an assuredly genetical underpinning. Furthermore, epigenetic influences on gene expression patterns are being revealed in phenotypic portrayals of genetic inheritance, that, if defective, have been modified by Bernie Sarnat's experiments and James Bradley's surgical skills.

The initially relatively less complex experiments performed in the early mid-20th century by Bernie Sarnat have given way in the 21st century to insights being revealed *by the more sophisticated* experiments by the refinements of genetic microarray analyses, tissue culture technology, regenerative medicine, organ transplantation, laser lysing of tissues and robotically-controlled surgery in the hands of James Bradley. Bernie Sarnat's innovative experiments on bone biology that have been published over an astonishing 70 year period from 1940 to the present book in 2010 have been cited over 117 times in the research engine "Scopus", attesting to his enormous impact on craniofacial biological research. His work has provided the necessary infrastructural background that has allowed James Bradley to undertake the heroic surgical reconstructions described in this book. The combination of the seminal works of a pioneering biologist with those of a practicing plastic surgeon represented in this book provides a phenomenal insight into overcoming the traditional barriers between laboratory science and clinical practice that the two authors of this book have displayed.

To these variegated musings on the combination of basic sciences with surgical expertise exemplified in this book, the reader has a potential Lucullan feast of thought upon which to chew. As Sir Francis Bacon

observed: “Some books are to be tasted, others to be swallowed, and some few to be chewed and digested”. Enjoy the contents of this book.

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Foreword

Bernard G. Sarnat was the John Hunter of 20th century plastic surgery. Like the celebrated 18th century English surgeon, considered the father of surgical research, Sarnat had an unquenchable curiosity based on observations made during his daily clinical activities. Ever logical, he then went to the animal laboratory to seek the answers.

After obtaining medical and dental degrees, he took his surgical training at the St. Louis shrine of plastic surgery led by Dr. Vilray Blair, recognized as the Father of American Plastic Surgery. This educational background, combined with his personal temperament, set the stage or provided the foundation for a lifetime of asking pertinent clinical questions regarding the growth of the craniofacial skeleton: How can one study the growth of the mandible, midface, orbits and cranial vault? Does the normal craniofacial skeleton grow differently than the abnormal? Does an abnormality in one component of the craniofacial skeleton set off a "domino effect" in contiguous structures? Are the individual roles of the bones, cartilage, teeth and soft tissue envelope integrated to achieve final craniofacial skeletal morphology? How does one produce phenocopies of pathologic craniofacial human conditions? Sarnat realized that these questions could be answered only in the laboratory.

It is remarkable how many animal models he developed — turtles, rats, gophers, lagomorphs, pigs, dogs, and primates. To answer these questions, he recognized that experiments must include craniofacially immature as well as mature animals. One then has to ask the question

whether these experimental findings were transferable to the human. For example, the rabbit can be a "bone factory"; the canine is predominantly a snout animal; only the primates have the circumferential orbit of the human.

Yet, Bernard G. Sarnat was not to be deterred. Over a career that spanned the last half of the 20th century, he studied the role of the condyle and the effect of neuromuscular function on mandibular growth; the contribution of the nasal bones, septum and paranasal sinuses and facial sutures in rabbit and primate midface development; the effect of globe enlargement in orbital development; and the role of the cranial and skull base sutures in cranial vault development.

His experimental designs were ever simple and intuitive — local surgical manipulation. It was only natural that, as a surgeon, he used the tools of his trade in an investigative manner — not unlike John Hunter's transplant experiment with combs of cocks.

What resulted was an improved understanding of craniofacial growth and development — the interplay of functional parts determining skeletal growth. An excellent example is the development of the forehead in response to frontal lobe emergence in higher animals. From an evolutionary standpoint, higher animals needed a second story addition. As humans assumed the upright position, olfaction became less important and snout size decreased (and the hands became more complex!). The frontal bone and the enlarged cranial vault represent the skeletal addition for the ever-evolving cerebral cortex.

In many ways, Bernard G. Sarnat's work set the stage for my generation of craniofacial surgeons. The distraction technique could be employed in the young patient with recognition that the severely hypoplastic mandible had little potential for growth and development. As surgeons, we learned that the midface in syndromic craniofacial synostosis, likewise, had little potential for growth. Consequently, the Le Fort III advancement technique could be employed in these patients at a young age to improve occlusion, relieve sleep apnea and restore facial aesthetics and the surgeon would not be interfering with midface growth.

And now this remarkable surgeon, in the ninth decade of his life, is working with an academic surgeon, who is two surgical generations

younger, in bringing this remarkable tale of research to print and to relate it to modern craniofacial surgery and to contemporary research in this area — it is truly a story of our specialty over 60 years. What a contribution to the discipline of craniofacial surgery by two surgeons whose work transcends two centuries of work!

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Preface

This is an unusual one of a kind work. Something old. Something new which is based in part on something old.

It deals primarily with and brings together a wide ranging group of essays many of which are classics of more than half a century of research done by the senior author. Much of this historical review remains significant and germane today. Some material antedates the emergence of the specialties of craniofacial biology, craniofacial surgery and bone biology. Many of the reports preceded the period of molecular biology. This summary represents a fundamental pioneering contribution to a representative portion of the specialties. A diverse group of experiments was done at different times in an irregular sequence over the many years. However, they fit into a logical pattern which could be likened in a way to the periodic table of chemistry (Mendeleev). Because the face offered so many different structures, muscles and bones, it was a rich source of study.

Added to the past the junior author has contributed significantly to the present by including recent works with the presentation of issues dealing with stem cell, tissue regeneration and tissue engineering research. In addition, appropriately selected clinical work is included, a result of the further development and maturity of the specialties. And what does the future hold? No doubt unpredictable gigantic advances.

A logical sequence has been followed with an introduction, Part I. The Lower Face; Part II. The Midface; Part III. The Upper Face; Part IV. Tooth Development and Associated Structures; Part V. Cranial Sutures and Cranial Base; Part VI. Several reports (Chaps. 32–37) dealing with a

synthesis and integrative interpretation of previous research as well as other selected subjects; Part VII. Public Health Aspects; APPENDIX dealing with becoming a Plastic Surgeon.

Full recognition and thanks are due to the important contributions of colleagues, students with their devoted expert secretarial skills (Catherine O'Hara, Misha Heller, Kristy Wasson, Rebekah Ashley, and Hurig Katchikian, untiring and totally dedicated) staff, and devoted families throughout the years. Especial recognition should be given to Michelle Van Vliet for her expert photography skills and cheerful countenance. Without their unfailing support this work would not have been possible.

We made every effort to minimize errors and inaccuracies. If any did occur, we apologize. And lastly, a great big thank you to both the publishers and editors. We owe a great debt of gratitude in particular and significant recognition to Sook-Cheng Lim, Scientific Editor of World Scientific Publishing and her staff for their patience, dedication, devotion, and meticulous attention to detail and guidance throughout the entire process of this work.

This volume is dedicated to the future leaders in the specialties of craniofacial biology and craniofacial surgery.

Thank you all.

Bernard G. Sarnat, M.D., D.D.S.
James P. Bradley, M.D.

Table of Contents

Craniofacial Biology and Craniofacial Surgery

Bernard G. Sarnat, M.D., D.D.S. and James P. Bradley, M.D.

Introduction

" … find out the cause of this effect,
Or rather say, the cause of this defect,
For the effect defective comes by cause."

— *Hamlet,* Act II, Scene II

There is always a need for further knowledge about the growth of bone(s). This is true particularly because an understanding of the normal and abnormal growth of bone(s) forms the basis of early recognition, possible prevention, and appropriate treatment of many deformities. However, it is less well appreciated that findings on the abnormal may be employed to test and extend our knowledge of the normal. The genetic makeup, as well as various types of diseases, and injuries (such as trauma), inflammation, radiation, and chemicals, may affect skeletal growth sites, thereby causing faulty growth of bone(s). The degree of the subsequent deformity will depend not only on the type, intensity, extent, and chronology of the noxious agent but also on the site and its particular susceptibility and growth activity. A growth deformity of bone may be readily produced by interfering with a cartilaginous but not a sutural growth site.[1]

The problem of plastic-surgical treatment for craniofaciodental deformities is a difficult one. The dysplastic pattern of growth continues. In unilateral disturbances, the discrepancy between the two sides becomes greater as the patient becomes older because of limited or no growth of the affected side. Even though the deformity may not be progressive, it is not self-correcting, and there is no totally satisfactory way to compensate for

the lost or retarded growth. The disturbance itself is not fully remedied by orthodontic, prosthetic, or surgical procedures. However, these measures do give functional and cosmetic improvement. Consequently, the craniofacial surgeon is called upon to treat and improve both the function and the appearance of these abnormalities.

Alteration of the position of the craniofacial complex by various types of osteotomies is a common surgical procedure. Other surgical approaches are directed toward contributing bulk and increasing length by means of bone, cartilage, and soft-tissue grafts as well as flaps. Autogenous tissues have been transplanted and alloplastic materials implanted as masking procedures to build up the less developed side in asymmetries or to the mental or other regions where there has been a symmetrical arrest. Distraction osteogenesis is a significant recent addition to the surgical armamentarium. If these corrections are made in a patient who has not attained full growth, a later procedure may be necessary in adult life.

As a plastic surgeon with a basic science background, in my practice I saw patients with a variety of both soft- and hard-tissue deformities, which frequently were distributed over many parts of the body. Invariably there were many unanswered questions. In an attempt to find answers, I returned part-time to the laboratory. Over the years I conceived, designed, initiated, and carried out a series of experiments in regard to bone(s), teeth, and cartilage as well as cartilage implants in both young and adult animals (turtles, rats, gophers, lagomorphs, pigs, dogs, monkeys, and humans). Each procedure had its advantages and disadvantages. Although an attempt was made to limit the number of variables and to obtain a definite "yes" or "no" answer, this was not always possible.

My early research interests were in skeletal problems of a systemic nature. Later, one of my concerns was the possible effects of trauma — accidental and intentional (surgical) — on growth of bone(s). Eventually, I directed my efforts principally toward local surgical experimentation as it related to both normal and abnormal gross postnatal craniofaciodental growth. Because of the wide variety of different structures, their interrelated individualities, and the challenges presented in both its richness of sites of growth and its complexity, the skull and particularly the face, proved to be a most unusual source of study.

Many of these investigations were carried out in collaboration and done principally at the University of Chicago, the University of Illinois, the Cedars-Sinai Medical Center, and the University of California at Los Angeles.

BONE GROWTH AND CHANGE

Growth and development of the skeletal system has an important role in determining body form. The dynamics of growth of bone(s) is a complex process. Although significant articles in regard to bone growth appeared in the literature more than 225 years ago,[2] many basic questions are still unanswered. What are some of the problems in need of study? What are the inherent difficulties? Any determination of bone growth must concern itself with one or more of the following questions: What are the centers? The sites? The amounts? The rates? Do they vary? When? What are the directions? What are the changes in size and in shape (Fig. 1.1)? What are the changes in proportion? What is the pattern? What are the mechanisms? What factors are influential?

Some principles of the biology of bone are central to this presentation. The basic blueprint of a bone is inherent. Postnatal bone growth is but a continuation of prenatal bone growth interrupted by the event of birth. *In utero*, the fetus with its genetic beginnings is subjected to the vicissitudes of the maternal environment. After birth, the individual is subjected to the effects of the general environment. Development of body form is related to the synchronous coordination of three-dimensional, multiple, differential skeletal growth sites and centers and associated structure activities (Fig. 1.2).

The following generalizations may be made about normal skeletal growth. Growth of bone(s) occurs essentially in three ways: cartilaginous (endochondral) and sutural (appositional without resorption), representing bone(s) as organs; and remodeling (appositional and resorptive), representing bone as a tissue (Table 1.1). A definition of growth is change over time. A basic physiologic concept is that throughout life, bone, the tissue, is in a continuous state of apposition and resorption. Consequently, skeletal size and shape are always subject to change. When skeletal mass increases, as in children, apposition is more active than resorption.

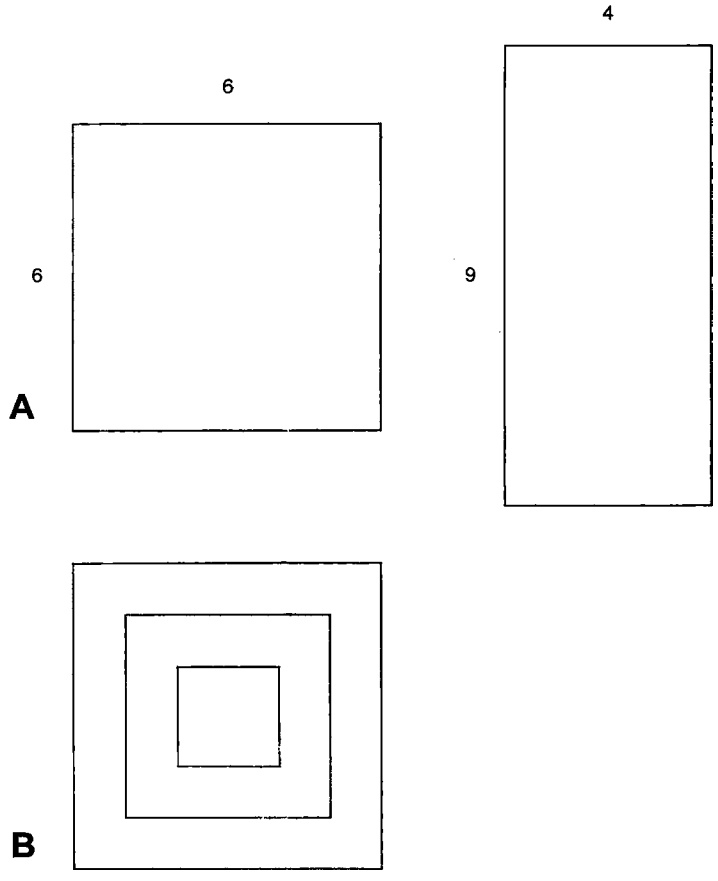

Fig. 1.1 Size plus shape equals form. (**A**) Size is constant but shape is variable; (**B**) shape is constant but size is variable. [From: Sarnat BG (2001). Effect and noneffects of personal environment experimentation on postnatal craniofacial growth. *J Craniofac Surg* **12:** 205–217.]

Cartilaginous and sutural growth are both active (i.e. positive growth). When skeletal mass is constant, as in the adult, apposition and resorption, although active, are in equilibrium (i.e. neutral growth). Cartilaginous and sutural growth have ceased. When skeletal mass decreases, as in old age, resorption is more active than apposition (i.e. negative growth). This concept of growth change is not new[3] and is also evidenced by the following passage from *Alice in Wonderland,* by Lewis Carroll: " … said Alice, 'and if

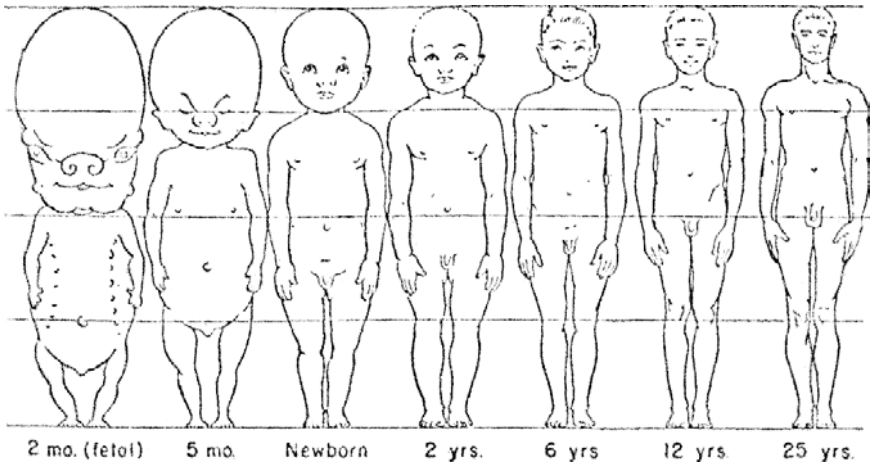

Fig. 1.2 Development of the total human body from *in utero* to adulthood. (From: Scammon, in *Morris Human Anatomy*, 9th ed., edited by C.M. Dodson, 1933.)

it makes me grow *larger,* I can reach the key; and if it makes me grow *smaller* [italics added], I can creep under the door.'"

Various methods have been used in the study and measurement of growth of bone(s) (see Chap. 36). Each, however, has its limitations.[4] One may yield information about the sites of growth, another about the rate, and still another about the direction. However, a combination of methods will potentially yield more information and, in certain instances, more accurately than one method alone. Although some of these methods often lend themselves primarily to experimental work on animals, they nevertheless contribute to our fundamental knowledge of the subject.

The physiologic stability of the bony components is the result of many interrelated factors, normal functional use being a prominent one. Well recognized are the effects of either excessive use, with hypertrophy (i.e. an increase in the mass of bone), or disuse, with atrophy (i.e. a decrease in the mass of bone). Thus modifications in the functions of a part are reflected in alterations in the form of the part.

Despite its hard, semirigid, supporting, mineralized nature, bony tissue, by virtue of the highly sensitive periosteal and endosteal membranes, is

Table 1.1 Bone: Growth, Remodeling and Repair*

	Growth				Repair	Clinical Considerations
	Cartilaginous	Sutural	Remodeling	Skeletal mass		
Infancy and childhood	Active	Active (apposition, no resorption)	Apposition greather than resorption	Increasing (positive growth)	Active	Giantism and other growth deformities Acromegaly
Adulthood	Long or tubular bone, skull base, etc. (epiphysis) Inactive Mandibular condyle (epiphysis-like) Latent (potentially active)	Inactive	Apposition equal to resorption	In equilibrium (neutral growth)	Active	
Old age	Long or tubular bone, skull tissue, etc. (epiphysis) Inactive Mandibular condyle (epiphysis-like) Latent (potentially active)	Inactive	Apposition less than resorption	Decreasing (negative growth)	Active	Senile osteoporosis
Clinical consideration	Conditions affecting cartilage: achondroplasia, rickets, etc.	Conditions affecting sutural growth: synostosis, etc.	Skeletal adjustments to various conditions	Change in size and shape	Fracture, osteotomy, ostectomy, distraction osteogenesis, bone graft	

* Modified, with permission, from: Sarnat BG (1971). *JADA* **82**: 876–889. Copyright 1971 by ADA Publishing, division of ADA Business Enterprises, Inc.

dynamic and ever-changing, adaptable to every nuance of tension and pressure. The basic and dual response of resorption and apposition is evident in the reaction of bone to growth, healing of fractures, alteration in muscular balance, orthopedic therapy, change in position of bone(s) after osteotomy and/or ostectomy, distraction osteogenesis, and other intrinsic and extrinsic factors.

NORMAL CRANIOFACIAL GROWTH

The craniofacial skeleton changes in size and shape in all three planes: height, width, and depth. However, it grows in these three dimensions of space differentially in both time and rate (Figs. 1.3–1.5). Many sites contribute to the multidirectional growth. The dynamics and details of normal postnatal growth, simultaneity, coordination, and change and nonchange of the craniofaciodental skeletal system in both the young and the adult are fascinating, complex, and incompletely understood problems in the field of biology.

Fig. 1.3 The aging face: child, adult, old age. (From UCLA–Center on Aging.)

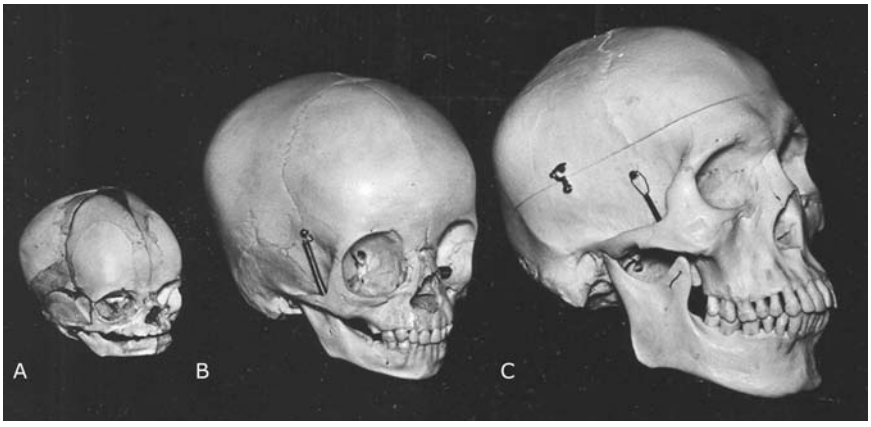

Fig. 1.4 Normal growth of the human skull. (A) clinically edentulous skull at about birth; (B) skull of a child with completely erupted deciduous primary dentition; (C) skull of an adult with completely erupted secondary dentition. Note that in the infant the cranium is prominent, and the face is much less so, representing a smaller part of the total skull size. Also note that the orbit makes up a large part of the face. In the adult, the face is prominent and represents a larger part of the skull size. The orbit makes up a considerably smaller part of the total face in the adult than in the infant. Differential growth takes place at different times and rates in various parts of the skull. [Reprinted with permission from Sarnat BG: Normal and abnormal craniofacial growth: some experimental and clinical considerations. *Angle Orthod* **53**: 263, 1983.]

Craniofacial bones, like bones in general, grow in three principal ways (Table 1.1). One is *cartilaginous* — at the nasal septum — and *endochondral* growth (i.e. the replacement of cartilage by bone) — at the base of the skull, at the spheno-occipital and sphenoethmoidal junctions. These bones are joined by cartilage (synchondroses). In addition, endochondral growth of bone occurs at the septopresphenoid joint and at the mandibular condyle. The second way is *sutural* growth, where bones are united by connective tissue (synarthroses). This is found only in the skull. Sutures grow differentially by apposition without resorption. The amount of growth may vary on either side of the suture, the rate varies for different sutures at a particular time, and the same suture grows differentially at different times. These sites, as well as the endochondral, are of limited growth and usually cease activity as an individual reaches adulthood. The third

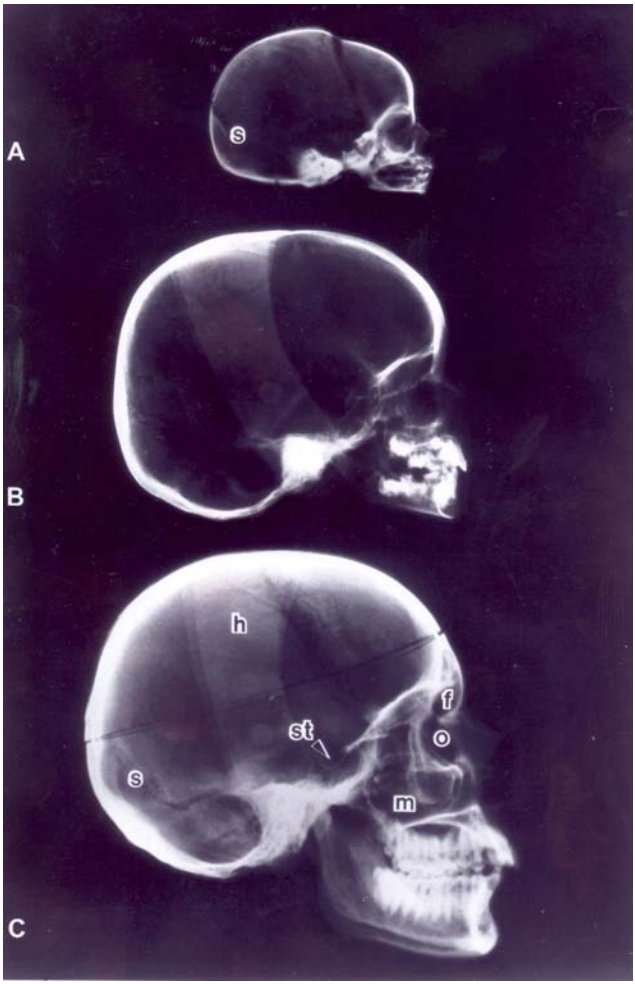

Fig. 1.5 Lateral cephalometric radiographs of skulls shown in Fig. 4. Note in the infant skull the presence of unerupted teeth in the jaws. (**A**) In the child skull, the primary dentition is fully erupted, and the permanent teeth are forming within the jaws. (**B** and **C**) In the adult skull, the permanent teeth are fully erupted. The maxillary (m) and frontal (f) sinuses are not evident in the infant skull, are in early development in the child skull, and are fully developed in the adult skull. Note the open, actively growing suture, S, in the infant cranium, in contrast to the closed inactive suture, S, in the adult cranium. St — sella turcica; o — orbit; h — head holder apparatus. [Reprinted with permission from Sarnat BG: Craniofacial growth, postnatal, in Delbucco R (ed.), *Encyclopedia of Human Biology*, 2nd ed. Academic, San Diego, California, 1997, pp. 71–82.]

Table 1.2 Craniofaciodental Growth

I. bone(s)
   A. Cartilaginous — bone(s) as organs
      1. Endochondral
      2. Nasal septal
   B. Sutural — bone(s) as oggans
   C. Remodeling (appositional and resorptive) — bone as tissue

II. Cavities
   A. Matrix
      1. Brain and cranium
      2. Orbital contents and orbit
   B. Matrix and air
      1. Septum and nasal cavity
      2. Tongue and oral cavity
   C. Air
      1. Maxillary sinus
      2. Frontal sinus
      3. Ethmoid sinus
      4. Sphenoid sinus

III. Teeth

type is *appositional* and *resorptive* growth (i.e. remodeling), which occurs on the outer surfaces (periosteal) and inner surfaces (endosteal) of bone throughout life. The differential responses and interrelationships of these processes are important.

The size and shape of the skull are determined not only by the growth of bones but also by its cavities (Table 1.2). Increases in the size of the contents of the cranial and orbital cavities of the skull influence the growth of adjoining bones and sutures. The air-containing maxillary, frontal, ethmoid, and sphenoid sinuses also increase in size and contribute to growth of the skull. This occurs by a combination of resorption and deposition of bone on the surfaces and adjustments at the sutures. An interesting comparison can be made when the infant, child, and adult skulls are modified to about equal size (Fig. 1.6).

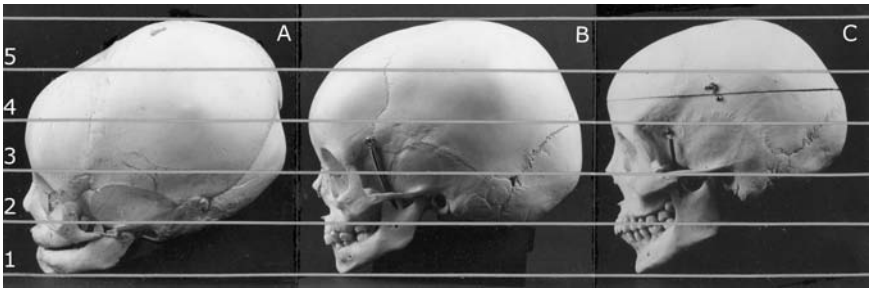

Fig. 1.6 Lateral view photograph of the skulls in Figs. 1–4 enlarged to about the same skull height and oriented in the Frankfurt horizontal plane. Note the differences in form and proportions of the total skull and its components. The distance between the lower border of the mandible and the superior border of the orbit represents about 40% of the skull height in the infant (**A**) and 60% in the adult (**B** and **C**). The orbital height is nearly the same in all three skulls. The cranial height represents about 60% of the skull height in the infant and 40% in the adult. The skull height is divided into fifths.

The cranium and the masticatory facial skeleton are integrated into an anatomic and biologic unit. However, the masticatory skeleton is in part dependent on muscular influences, growth of the tongue, and the dentition. These two parts of the skull follow different paths of development, and the timing of their growth rates is entirely divergent. Nevertheless, the growth of any one part of the skull is coordinated with the growth of the whole.

The more important sites of growth for the maxillary complex are three sutures on each side: the frontomaxillary suture between the frontal bone and the frontal process of the maxilla; the zygomaticomaxillary suture between the maxilla and the zygomatic bone (and, secondarily, the zygomaticotemporal suture in the zygomatic arch); and the pterygopalatine suture between the pterygoid process of the sphenoid bone and the pyramidal process of the palatine bone.[5,6] It is significant that these three sutures are parallel to each other and all are directed from above and anteriorly, downward and posteriorly. Thus growth of these sutures will have the effect of shifting the maxillary complex downward and anteriorly. Transverse growth at the median palatine suture, which is affected by the downward and divergent growth of the pterygoid processes, is both simultaneous and correlated with the widening of the downward-shifting

maxillary complex. There is also anteroposterior growth along the maxillary side of the transverse palatine suture between the horizontal plate of the maxilla and the palatine bone, and along the posterior margin of the palatine bone.

The downward, outward, and lateral growth of the subnasal part of the maxillary body is accompanied by eruption of the teeth and apposition of bone at the free borders of the alveolar process. Thus the apposition in this area contributes to the increase in height and width of the upper facial skeleton. At the same time, the downward growth of the alveolar process accounts for the transition from the flatly curved palate of the infant to the highly arched one of the adult. However, the downward shift of the hard palate by resorption on its nasal surface and apposition on its oral surface tends to obscure the downward growth of the alveolar process. Thus the pathogenesis of the high palate seems to start with a deficiency of the modeling resorption at the nasal floor with a failure of the normal downward shift of the hard palate. However, the vertical growth of the alveolar processes at the free borders continues in correlation with the growth of the mandible and accentuates the discrepancy.

The growth of the upper facial skeleton is closely correlated with that of the mandible. However, the mode of mandibular growth is entirely different from that of the maxillary part of the face. In the latter, the growth is primarily sutural. In the mandible, an important site of growth is the hyaline cartilage in its condyle. These differences explain a certain independence and yet dependence of the growth of these two parts of the facial skeleton.

The growth of the mandible is indispensable for the normal vertical growth of the upper face. (See Chap. 2 for details of mandibular growth.) Upward and backward growth at the condyle, which rests against the articular fossa of the temporal bone at the cranial base, results in movement of the entire mandible downward and forward so that the upper and lower teeth and alveolar processes become more distant from each other. Since the teeth maintain occlusion by continued vertical eruption, the alveolar processes grow at their free borders. Disorders of mandibular growth, therefore, lead secondarily to changes in the upper face. They generally involve only the subnasal part of the maxilla.

Thus the skull, a complex of bone(s), has proven to be both a rich and a challenging source of study, particularly since the combination of different types of bone growth and increase in size of various cavities and growth, calcification, and eruption of teeth is not found elsewhere in the body.

Cranial and orbital growth occur predominantly early in life, while facial growth occurs predominantly somewhat later in life, mostly during the periods of growth and eruption of the primary and secondary dentitions and the development of the paranasal sinuses. A number of excellent references are available that describe the anatomic structures and give the details of craniofaciodental growth and movement.[6,7] Every student of growth will delight in becoming acquainted with the seminal works of Thompson[3] and Brash *et al.*[8]

Environment and Growth

A great deal has been learned about the prenatal and postnatal etiology of craniofacial and other abnormalities in the experimental animal. The material of these reports is only part of a series of experiments in which the relationship of injury to postnatal growth has been studied.

Throughout our lives we are constantly reacting to our environment. Variations in temperature, light, humidity, atmospheric pressure, terrestial and extraterrestial radiation and gravity affect us. In addition, the vast number of toxic agents, intentionally or unintentionally ingested through our food (or essential deficiencies) and water and inhaled form the air, determine our destinies. Consider the effect of our environment upon the skeletal growth sites and the resulting changes in size and shape of the jaws, face, cranium, and body.

There are many mechanisms (nervous, hormonal, metabolic, enzymatic) by which the environment directly induces adaptive changes. Environmental stresses can interact either directly — such as through variations in temperature and oxygen — or indirectly with the genetically controlled enzyme-forming system. There is no evidence that environmental stresses can induce genetic change.[9] Rather, those stresses permit such genetic changes as may occur in natural mutations to be realized and fixed.

Young rats exposed to cold stress had a smaller skull, a longer face in relation to the cranial vault, a narrower nose, a rounder cranium, and a

shorter femur.[10] Natives living at high altitudes and exposed to the environmental stresses of hypoxia and cold have slower postnatal growth and a lesser adolescent growth spurt than other groups.[11] On earth, gravity is considered normal, or 1.0 g. What skeletal and other changes will occur in environments of hypogravity (moon, 0.18 g) or hypergravity (Jupiter, 2.65 g)? These and other factors are of great interest to the new field of cosmic biology and should be of concern to us.

In a 12-session, 2-hour graduate seminar on bone biology at UCLA, I would ask the following take-home open-book final examination question: Earth man and earth woman decide to live on the moon (or Jupiter). Earth woman gives birth to moon (or Jupiter) child. Describe the growth, development, size, shape, and skeletal and muscular systems of moon (or Jupiter) person.

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PART I

THE LOWER FACE

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Growth Pattern of the Pig Mandible*

INTRODUCTION

In this investigation a combined technique of metallic implantation and serial roentgenography was used to study the postnatal growth pattern of the pig mandible. This method of growth study afforded several advantages over those previously used, namely: (1) it was a serial study, (2) there were permanent records, and (3) the implants served as stable reference points from which accurate information could be obtained as to sites, amounts, and relative directions of growth.

REVIEW OF THE LITERATURE

Hunter in 1778,[1] by means of madder feeding and osteometry, observed that the mandible increased in size by apposition at its posterior border while the anterior border of the ramus was remodeled by resorption of bone (Fig. 2.1). He was the first to describe that: (1) resorption was as characteristic of bone growth as was deposition, (2) the body of the mandible gained in height principally by growth of alveolar bone, (3) the shedding of teeth was always accompanied by resorption of alveolar bone whereas eruption of teeth was always accompanied by growth of alveolar bone, and (4) the deciduous second molar and permanent first, second,

*Excerpted from: Robinson IB, Sarnat BG (1955). Growth pattern of the pig mandible: a serial roentgenographic study using metallic implants. *Am J Anat* **96**: 37–63.

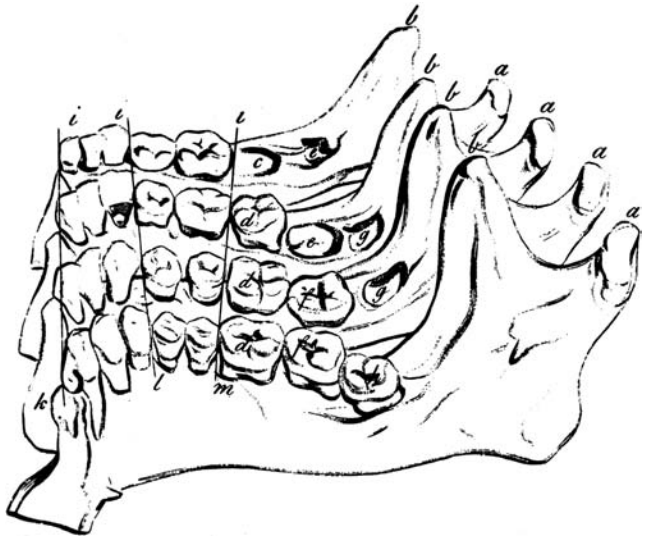

Fig. 2.1 Four lower jaws at different periods of life from the age of five years, when the five shedding teeth are completely formed, to that of the complete set. This figure shows: (1) the lengthening of the mandible posteriorly, which is seen by the oblique line made by the four condyles; (2) the gradual increase of the two processes above the line of the teeth; and (3) the gradual increase of the teeth in proportion as the jaw lengthens. (a) Condyle; (b) coronoid process; (c) alveolus for the permanent second molar is forming; (d) permanent first molar; (e) alveolus for the permanent second molar; (f) permanent second molar; (g) alveolus for the permanent third molar; (h) permanent third molar. The two lines *ik* and *im* mark the distance between the symphysis of the chin and the permanent first molar. The line *il* separates the incisors and cuspids from the deciduous molars in the child's jaw and the permanent bicuspids in the adult jaw. This line is oblique and distances between the two ends of the two lines *ik* and *il* at *ii* are nearly the same as the distance between the ends of the two lines *il* and *im* at *lm*. (From Ref. 1.)

and third molars erupted in the same relation to the mandibular ramus. Since Hunter's classic report, relatively little has been added to the general knowledge about the mode of growth of the mandible (Table 2.1). Humphry in 1864[2] confirmed the findings of Hunter by inserting wire rings into the anterior and posterior borders of the mandibular rami of young pigs. He found that when the pigs were killed after two months the ring fixed to the anterior surface of the ramus was freed as a result of

Table 2.1 Brief Historical Review of Studies on Postnatal Mandibular Growth

Investigator	Method	Type of Study	Animal	No.	Age	Findings
Hunter (1778)	Madder feeding osteometry	Longitudinal Cross-sectional	Pig Human	2 4	?	1. Increase in size by apposition at posterior border of ramus 2. Remodeling of jaw by resorption of anterior border of ramus 3. Increase of condyloid and coronoid processes above line of teeth 4. Increase in height of body due to alveolar growth
Humphry (1864)	Implantation of wires into ramus	Longitudinal	Pig	?	?	Confirmed Hunter's findings
Keith and Campion (1922)	Osteometry	Cross-sectional	Human (skulls)	2	5 and 25 years	Confirmed Hunter's findings
Brash (1924)	Madder feeding	Longitudinal	Pig	?	20–26 weeks	Confirmed Hunter's findings

(*Continued*)

Table 2.1 (*Continued*)

Investigator	Method	Type of Study	Animal	No.	Age	Findings
Brodie (1941)	Serial roentgenographs	Longitudinal	Human	21	3 months to 8 years	1. Condyle contributed to increase in height of ramus and forward growth of mandible; Mandibular angle remained stable; Angular relation between lower border of mandible and cranial base established by third month of life
Hulen (1948)	Metallic implants combined with serial roentgenographs	Longitudinal	Dog	4	?	1. No new findings 2. Primarily description of method
J.H. Scott (1951)	Roentgenograms	Cross-sectional	Pig	3	2 weeks, 3 months, 8 months	1. Little resorption of bone at anterior border of ramus; Little or no growth at inferior border
Baume and Becks (1953)	Histologic	Cross-sectional	Rhesus monkey	20	?	Growth of bone at anterior and inferior borders of mandible
This report (1955)	Metallic implants combined with serial roentgenographs	Longitudinal	Pig	9	8–20 weeks	1. Same as those of Hunter, Keith, and Campion, and Baume and Becks

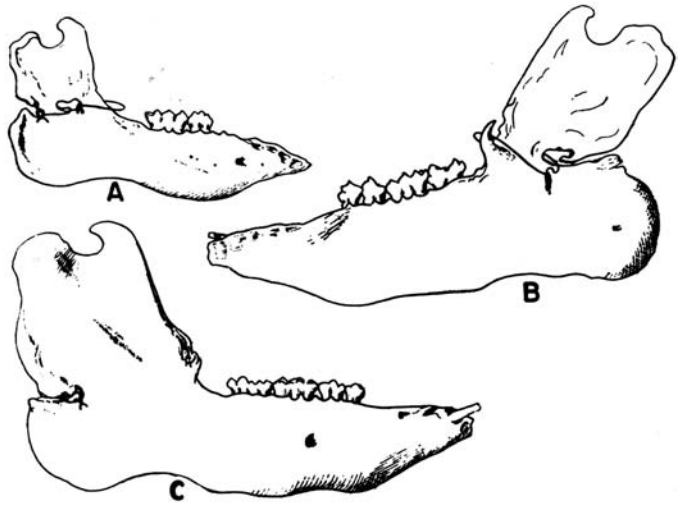

Fig. 2.2 Illustrations of Humphry's experiment, in which he inserted wire rings in the mandibular rami of young pigs to show resorption at the anterior border and apposition of bone at the posterior border. (**A**) Lower jaw of a young pig killed one month after two wires had been passed through a hole in the middle of the ramus and secured, one around the anterior border and the other around the posterior border. The anterior wire projects some distance in front of the ramus, whereas the posterior wire is buried deeply. (**B**) Lower jaw of a young pig killed 11 weeks after a wire was passed around the ramus. The wire projects in front of the anterior border of the ramus, though this is somewhat masked by a horn of new bone having been formed on its anterior and outer side. It is, moreover, buried deeply in the posterior part of the ramus. The ramus looks as if it had been cut more than halfway through by the wire. (**C**) Right side of the lower jaw of the same pig in (**B**). Two months before it was killed, a wire was passed through a hole near the anterior border of the ramus and secured. In addition, a second wire was passed through a hole near the posterior border and secured. The front wire has disappeared. The position which it occupied is marked by a slight thickening at the lower part of the anterior border of the ramus. The posterior wire, still encircling the bone around which it was passed, is at a considerable distance from the posterior border. (From Ref. 2.)

resorption, while the ring fixed to the posterior surface of the ramus was completely embedded, as a result of deposition of bone (Fig. 2.2). Brash[3] repeated Hunter's madder feeding experiments in pigs and arrived at similar conclusions.

MATERIAL AND METHODS

The pig was selected because comparable litter mates of known age could be obtained, and because this animal grows very rapidly in a relatively short period of time. The animals used in this study were 9 female Hampshire pigs from 2 litters obtained from an Illinois farm immediately after weaning at about 8 weeks of age and weighing 22–26 pounds. They were fed on a stock diet of corn supplemented with a mineral and vitamin preparation. The duration of the experimental period was 12 weeks. The pigs' average weight at the completion of the study was 109 pounds.

Surgical Procedures

The animals were anesthetized with a 3% solution of sodium pentobarbital (1/3 cm^3 per pound of body weight) injected into the jugular vein. They were then secured in a supine position on the operating table and the skin overlying the left side of the mandible was shaved. With a sterile surgical technique, the skin and subcutaneous tissues were incised from behind the angle of the mandible forward, following the inferior border for a distance of about 6 cm. The tissues were reflected to expose the masseter muscle, the fibers of which were separated by blunt dissection, thereby exposing the mandibular ramus. A dental bur, mounted in a handpiece, was used to prepare cavities (1–2 mm) in the lateral cortical plate of bone. Dental amalgam was then inserted into these cavities in the following areas: two close to but not at the posterior border of the ramus, one in the center of the ramus, and one in the anterior portion of the body in the region of the mental foramen. The implants were used to ensure accurate superpositioning of the tracings of serial cephalometric roentgenographs. The distances between the three ramus implants were measured with a caliper and recorded for comparison with those made on the roentgenographs. The soft tissues and skin were repositioned and sutured.

Lateral Cephalometric Roentgenographs

Immediately following the surgical operation and at 4-week intervals for a period of 12 weeks, lateral roentgenographs were taken on a specially designed cephalometer,[4] which had been modified for the pig (Fig. 2.3).

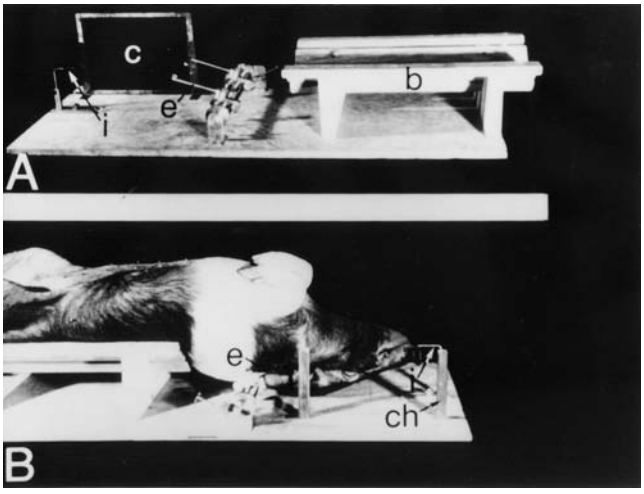

Fig. 2.3 Cephalometer adapted for the pig. (A) Lateral view of apparatus; (B) anesthetized pig lying supine on a back support, with its head positioned for a lateral cephalometric roetgenogram. The film cassette has been removed to show the earposts in position and the incisal pin placed between the upper central incisors at their contact point. b — Back support; c — film cassette in the background; ch — cassette holder in the foreground; e — earpost; i — incisal pin.

The heads of the animals were oriented in the Frankfurt horizontal plane. An ear post was placed in each external auditory meatus and an incisal pin placed between the maxillary central incisors to orient the head in the same position each time the roentgenograph was taken. There was some variation in the vertical positioning of the head. This was of no consequence because, regardless of the vertical orientation of the head, as long as the ear posts were in the external auditory meatuses the lateral roentgenographs were comparable. The exposure time was two-tenths of a second at 100 milliamperes and 55 kilovolt peak (kvp). A target distance of 100.8 cm was used to ensure minimum enlargement.

Tracings of the Roentgenographs

A detailed tracing of the mandible was made from each lateral roentgenograph, with special attention given to the position of the implant images,

the borders of the mandible, the erupted and developing teeth, and the mandibular canal.

Tracings obtained from subsequent roentgenographs were placed over the initial one in a position where the implant images recorded on the tracings exactly superposed. The difference between the two established outlines of the mandible represented the changes in size and shape that had occurred during this period. Areas of apposition and resorption were thus determined. Sites of reference were established for measurement in the mandible.

Preparation of Gross Material

At the end of the experimental period the animals were exsanguinated by severing the jugular vein. Mandibles were dissected from the skulls and the soft tissues removed. Selected mandibles were bleached in a solution of albone C (30% H_2O_2). One mandible was cleared by placing it in 70% alcohol for two days, in 95% alcohol for one week, and in absolute alcohol for one week. It was then placed in a solution of methyl salicylate. Clearing permitted visualization of the implants and allowed final direct measurements of this one animal.

FINDINGS

Gross

At the end of the experiment, 12 weeks later, none of the amalgam implants was visible on the lateral surface of the dissected mandible where they had originally been placed, but some were found exposed on the medial surface of the ramus. The measurements between implants on the cleared mandible were identical with those taken at the time the implants were inserted. Comparison of these measurements with those of the images on the roentgenographs showed variation of less than 1 mm.

Serial Lateral Cephalometric Roentgenographs and Tracings

Inspection of the serial lateral roentgenographs revealed progressive enlargement of the mandible (Fig. 2.4). Because measurements between implant

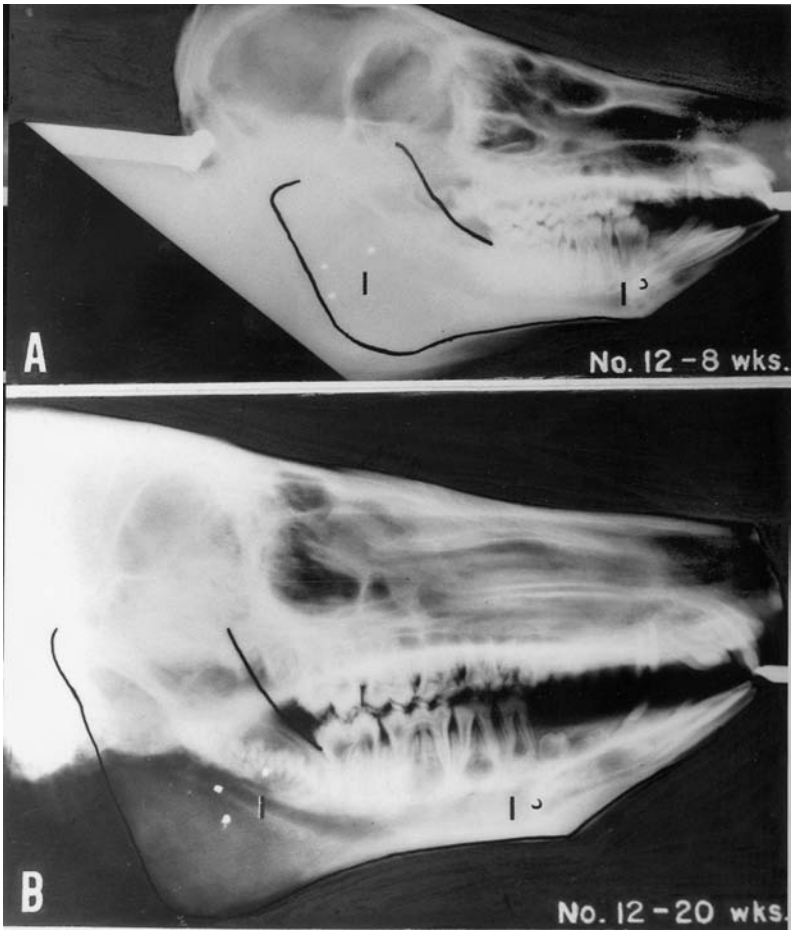

Fig. 2.4 Lateral cephalometric roentgenographs of animal No. 12. The outline of the ramus and body has been drawn in. (**A**) 56 days of age. Note the relation of the four implants (three in the ramus and one in the anterior part of the body) to the various borders at this period. The first permanent molar is still developing and has not yet erupted. (**B**) 140 days of age. The posterior border has grown considerably away from the implants in the ramus. In contrast, the anterior border of the ramus has been progressively resorbed and is now closer to the ramus implants. At this period the permanent first molar has erupted into occlusion while the second molar is undergoing development in the ramus. The crypts of the permanent premolars are now visible as radiolucent areas at the apices of the deciduous premolars. The mandibular canal has widened considerably. The 4 implants in the 56- and 140-day roentgenographs could be superposed.

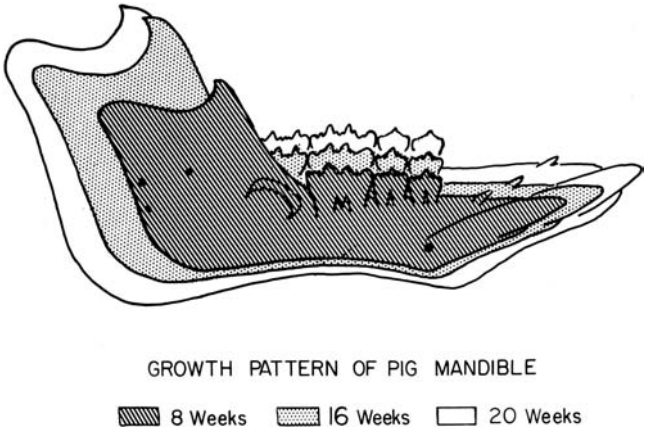

Fig. 2.5 Serial tracings of lateral cephalometric roentgenographs of pig No. 12 superposed on the outlines of the four implants. Note the direction and the amount of growth that has occurred between the various growth periods. Growth has taken place along all the borders with the exception of the anterior border of the ramus which has been resorbed.

images were the same on all the serial roentgenographs for each animal, these implants were used as points of reference for superpositioning the tracings of the roentgenographs. In this way not only sites but also amounts of apposition and resorption that occurred between the times the roentgenographs were taken could be determined. The sites of growth were at the condyle and the posterior, anterior, alveolar, and inferior borders. It was possible to compare the relative amounts of growth. The most prolific growth was noted at the condyle and the posterior border of the ramus (Fig. 2.5).

Increase in Size

Ramus height

The increase in ramus height was primarily a result of growth at the condyle. Some apposition was noted at the inferior border. In some animals growth at the condyle contributed as much as 80% of the total increase in height.

Ramus width

The increase in the width of the ramus was accomplished by apposition of bone along the entire posterior border. Concomitantly, however, resorption occurred at the anterior border (Fig. 2.5). Inasmuch as the amount of apposition was about twice that of resorption, the width of the ramus increased. Resorption of the anterior border of the ramus increased the length of the body of the mandible as measured from the anterior border of the body to the anterior border of the ramus.

Body height

Apposition at the alveolar and inferior borders of the mandible contributed to the total increase in body height. In most animals the alveolar border contributed about 60% of the total body height (Fig. 2.5).

Total mandibular length

Increase in the total length of the mandible, as measured from gonion to gnathion, was accomplished by appositional growth at the posterior border of the ramus and at the anterior border of the body. The posterior border contributed about 80% to the total length (Fig. 2.5).

Eruption of the Permanent Mandibular First and Second Molars Correlated with Mandibular Growth

Calcification and eruption of the permanent first and second molars as well as growth of the mandible were correlated in the serial lateral roentgenographs.

At 56 days of age (Fig. 2.6) the deciduous second, third, and fourth premolars were fully erupted and in contact with their maxillary opponents. The permanent first molar crown was almost fully developed and was situated posterior and inferior to the crown of the fourth deciduous premolar. Four cusps of the permanent first molar were visible. The mesial cusps were embedded in the body and the distal cusps embedded in the ramus, with about 2 mm of bone overlying the four cusps. The axis of the

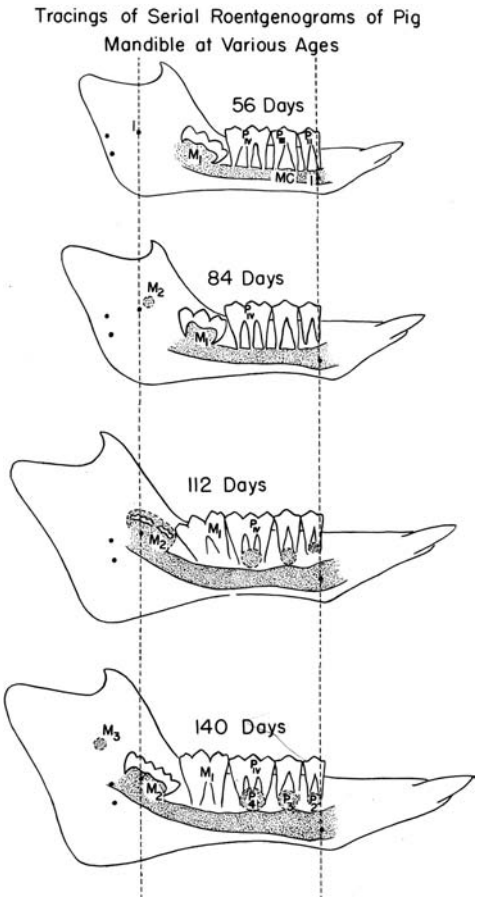

Fig. 2.6 Serial tracings of lateral roentgenographs of a growing pig, illustrating calcification and eruption of the permanent teeth correlated with growth of the mandible. The tracings have been projected in a vertical series on two lines, passing respectively through one implant in the ramus and one in the body of the mandible. M_1, M_2, and M_3 — permanent first, second, and third molars; MC — mandibular canal; P_2, P_3, and P_4 — permanent second, third, and fourth premolars; P_{II}, P_{III}, and P_{IV} — deciduous second, third, and fourth premolars. Since the implants have maintained a stable relationship to each other, the vertical lines remain parallel. Thus, the length of the mandible between the implants remains unchanged. However, this constancy does not apply to the teeth and alveolar bone. Note the progressive resorption of the anterior border of the ramus exposing the permanent molar crown and allowing it to erupt into occlusion. The mandible increased in length due to apposition of bone at both the posterior and the anterior border.

crown was inclined slightly in a forward direction. Root formation was not yet evident. The mandibular canal, visible immediately inferior to the developing permanent first molar, was about 5 mm wide, and was in the lower third of the body of the mandible.

At 84 days of age (Fig. 2.6) the anterior border of the ramus had undergone resorption so that the mesial cusps of the permanent first molar were almost at the surface of the bone. Superiorly and posterior to the distal cusps of the first molar, in the anterior one-third of the ramus and on a level with the plane of occlusion of the teeth, the crypt of the permanent second molar was visible. The body of the mandible had increased in height and the mandibular canal had increased in diameter. With resorption of the anterior border of the ramus, the length of the body had increased.

At 112 days of age (Fig. 2.6) the anterior border of the ramus had undergone further resorption, so that the mesial cusps of the mandibular permanent first molar were fully exposed and almost in contact with the maxillary first molar. The two distal cusps were still embedded in the anterior portion of the ramus, with a slight posterior inclination of the crown. Root formation was evident from the appearance of two well-defined radiolucent zones in the roentgenograph. The relationship of the mandibular canal to the developing tooth was still the same as in the 84-day-old animal, although the canal had increased in diameter. Three cusps were now visible in the permanent second molar crypt, which was enlarged and situated closer to the anterior border of the ramus, at about the junction with the body. Radiolucent areas, crypts of the permanent premolars, were visible between the roots of each of the deciduous premolars above and in close proximity to the mandibular canal.

At 140 days of age (Fig. 2.6) the progressive resorption of the anterior border of the ramus had resulted in the complete exposure of the crown of the permanent first molar, which was now fully erupted and in contact with the maxillary first molar. Root formation was almost completed but the apices were still open. The tooth had a vertical axial inclination relative to the plane of the occlusion of the teeth. The body of the mandible had continued to increase in height. The mandibular canal had increased in diameter but still occupied the lower third of the body. The wide apices

of the permanent first molar roots and the crypts of the permanent premolars were positioned directly above the canal. The cusps of the permanent second molar were enlarged and more of the crown appeared calcified in the roentgenograph. Because of the continued resorption of the anterior border of the ramus, the crown was now situated in the anterior part of the ramus. The axis of the crown was inclined slightly in a forward direction. The crypt of the permanent third molar was visible as a small round radiolucent area in the center of the ramus, superior and posterior to the crown of the permanent second molar.

DISCUSSION

Method of Study

A number of methods have been employed to study the growth pattern of bones (Table 2.1). Gross examination of dried skulls and mandibles has the disadvantage of being a static cross-sectional method of studying bone growth. Vital staining by means of madder feeding and alizarin injections have been used.[3,5,6] This method has both advantages and disadvantages. For example, inclusion of madder creates an abnormal diet for the animals and may affect their growth pattern. The staining intensity varies with the age of the animal and the dosage of the dye used. It cannot yield positive information regarding areas of resorption. Also, since resorption may lead to the removal of stained bone, vital staining will give incomplete data on the pattern of bone formation.

Histologic methods have been employed in bone growth but these studies have primarily been qualitative.[7–10] The growth pattern of bones is difficult to study by histologic methods because of the constant destruction of old layers of bone while new bone is laid down. Bhaskar[10] compared the prenatal and postnatal development and growth of the mandible in normal rats and in a particular group of rats characterized by retardation of bone resorption.

Implants have been used since Hunter's time[1] to study sites of bone formation and resorption as well as to measure the total amount of bone growth. However, this direct method of study will not yield serial data without reoperation or killing of the animal.

Superposing dried bones has been frequently used to study areas of growth. In fact, Hunter[1] was one of the first to superpose dried human mandibles. He used the anterior border of the body as a base, and thus demonstrated growth at the posterior border (Fig. 2.1).

A refinement to the cross-sectional method was made by the use of roentgenography and the superpositioning of roentgenographic tracings over various supposedly stable bony landmarks to obtain the pattern of growth. Scott[11] superposed roentgenographs of pig mandibles of different ages to correlate tooth eruption with mandibular growth. He observed little resorption at the anterior border of the ramus. The disadvantages of this method were: (1) the same living animal was not studied, (2) the base line or points for superpositioning the roentgenographic tracings varied with different animals, and (3) the base changed with growth.

Serial roentgenography eliminates the most serious deficiencies of the other methods previously mentioned because it permits a longitudinal study of the same living individual throughout the growth period. A stable anatomical base, however, must be selected for superposing the roentgenographic tracings. If there is any shift in the anatomical landmark, the findings will be distorted. Broadbent[12] believed that the outline of sella turcia was a stable base and used this as a point of reference for superpositioning roentgenographic tracings of the human skull. In serial studies on the growth of the human mandible, Brodie[13] superposed tangents to the lower border of the mandible as a base line for the serial roentgenographic tracings. The angle formed by this line with a tangent to the posterior border was bisected to locate point gonion, the point of superposition. However, this method was predicated on the fact that there was minimal or no growth at the lower border.

The use of a combination of serial roentgenography and metallic implantation offered a more accurate and reliable method for studying the growth pattern of the mandible. The serial roentgenographs permitted a dynamic study of the mandible, i.e. demonstration of the increase in size and the change in proportion of the same growing bone. In addition, to overcome the problem of finding a stable base for superpositioning the serial roentgenographic tracings, the use of two or more radiopaque implants inserted into the mandible appeared to be a valid method. The ensuing growth could thus be accurately determined and measured by

superpositioning roentgenographic tracings over the images of the metallic implants.

None of the animals in this or other investigations[4,9,14] exhibited interstitial growth of bone. All implant distances remained the same. Growth of hone tissue occurred by the addition of new bone at free surfaces.

Another advantage of the method employed in this study was the ability to measure the amount of new bone formation or resorption that occurred from one period to another without killing or reoperation of the animal. There also was no interference with the normal diet of the animals, such as occurs in madder-fed pigs. This method could also be employed for a quantitative analysis of the absolute rates of growth taking place at the various sites. It would be of interest to extend this type of serial roentgenographic study to younger animals and to investigate simultaneously the growth in width and length of the mandible.

Sites of Growth

Condyle and posterior border of the ramus

In this study the condyle was the most active growth site and it contributed about 80% to the total ramus height. Condylar growth also contributed to the length of the mandible, as measured from condyle to gnathion. The posterior border was the second-most-active growth site and contributed as much as 80% to the total length of the mandible as measured from gonion to gnathion. The amount of apposition at the posterior border was about twice the amount of resorption of the anterior border, thereby increasing ramus width.

Thoma[15] described stunted mandibular development and impactions of permanent molars when condylar growth was arrested early. Sarnat and Engel[16] resected the mandibular condyle in a group of growing rhesus monkeys and noted failure of growth in ramus height, widening of the ramus, and some preangular notching. Eushton[17] observed in estrogen-injected kittens that condylar growth was affected; this in turn caused a decreased rate of remodeling at the junction of the anterior border of the ramus with the body of the mandible. He noticed that when condylar growth was arrested or retarded by local injury or disease at the joint the

remodeling rate was also retarded. The rate and extent of resorption at the junction of the anterior border of the ramus with the body of the mandible determined to a great extent the amount of room available for the eruption of permanent molars.

Anterior border

In this study about one-fifth of the increased total mandibular length was contributed by deposition of bone along the entire anterior (and alveolar) border of the body of the mandible (Fig. 2.5). In the pig the incisors are inclined in a forward direction at an approximate angle of 45° to the inferior border. Due to the long roots and inclination of these teeth, about two-thirds of the anterior border is formed by alveolar bone. Actually, the body of the mandible increased in length by two processes occurring simultaneously — one due to resorption along the anterior border of the ramus, which resulted in an increase in length along the posterior part of the body, and another due to concomitant apposition of bone along the anterior (and alveolar) border of the body.

Hunter's observations on growth of the mandible were based upon the relatively unstable positions of the teeth and alveolar bone, and the assumption that the anterior border of the body of the mandible was stable (Fig. 2.1). However, the findings in this study were derived from implants in mandibular bone proper which in the longitudinal direction remained stable.

Alveolar border

Hunter[1] observed that deposition of alveolar bone accompanied the eruption of teeth. He believed that the alveolar processes of both jaws should be considered as belonging to the teeth rather than to the jaws. Brash[3] maintained that 70–100% of all body height increase took place at the alveolar border with the growth and eruption of the teeth, and that even though the alveolar bone owed its development and continued existence to the presence of teeth it was still subject to the same growth influences as those which govern the supporting parts of the jaws. Respecting growth of the mandible, this study has clearly demonstrated

the contribution of alveolar growth to the increase in body height (about 60%) (Fig. 2.5).

The roles played by the alveolar processes and mandibular bone proper are quite different. The important feature of alveolar bone is its ability to satisfy the ever-changing requirements of the teeth. However, in contrast, the formed mandibular bone remains constant, although there are changes in proportion by surface apposition.

Inferior border

It had been assumed that little or no growth occurs at the inferior border. Consequently, this site had been used as a base for superpositioning serial roentgenographs. The findings of this serial roentgenographic study of the pig mandible revealed that the inferior border in some animals contributed as much as one-half (although much less in others) of the total increase in body height (Fig. 2.5).

In the ramus portion of the mandible, although the condyle was responsible for the major increase in height, the inferior border contributed about one-fourth to the total increase.

Relationship between the ramus and body growth

In Hunter's experiments[1] the ramus increased in width because of appositional growth at the posterior border. Concomitantly, the anterior border of the ramus was resorbed, although to a lesser extent. Resorption of the anterior border of the ramus played an important role in lengthening the body of the mandible. As the anterior border of the ramus continued to be resorbed, it exposed more and more of the body and also the crowns of erupting teeth which formed in what was initially the ramus. Thus, it may be stated that in the growing mandible "the ramus of today will be the body of tomorrow."

Correlation of mandibular growth and development of the permanent molars

The permanent molar initially made its appearance near what at that time was the center of the mandibular ramus. With subsequent growth of the

mandible and the molar it finally erupted from what was then the most posterior part of the body of the mandible (Fig. 2.6). Thus, from this observation there is a harmonious relation between dental development and growth of the mandible. This growth is not dependent upon the developing teeth. However, normal eruption of the permanent molars is entirely dependent upon the normal growth of the mandibular ramus, which in turn may be directed by the activity of the condylar cartilage. In growth of the mandible the only part subservient to erupting teeth is alveolar bone.

This investigation demonstrated that before root formation was completed the erupting crown was being freed by resorption of surrounding bone at the anterior border of the ramus so as to allow it to erupt freely into occlusion with its maxillary opponent (Fig. 2.6). Thus, mandibular body space was being created at the expense of the anterior border of the ramus.

SUMMARY AND CONCLUSIONS

The growth pattern of the mandible was investigated in 9 Hampshire pigs from 8 to 20 weeks of age by means of serial cephalometric roentgenographs in combination with metallic implants.

Tracings of the lateral roentgenographs were superposed on the images of the metallic implants to determine sites, increments, and direction of bone growth.

The findings were:

(1) The longitudinal distance between the metallic implants remained stable and thus revealed no evidence of interstitial growth in the bone.
(2) Appositional growth occurred at the posterior, inferior, anterior, and alveolar borders and at the lateral surfaces of the mandible. The most prolific sites of growth were the condyle and the posterior border. At the anterior border of the ramus there was resorption.
(3) The mandible increased (a) in total length by growth at the posterior and anterior borders, (b) in ramus height by growth at the condyle and inferior border, and (c) in body height by growth at the alveolar and inferior borders.

(4) With changes in proportion of the growing mandible, resorption of the anterior border of the ramus resulted in the creation of a new posterior portion of the body. Thus, in the growing mandible, what was ramus at one time eventually became body.
(5) The growth and calcification of the permanent molars and the growth of the mandibular ramus were independent of each other. However, the eruption of these teeth was dependent in part upon the resorption of the anterior border of the ramus. The molars began their development in the center of the ramus and the crowns finally became exposed and erupted from the body of the mandible due to the progressive resorption of the anterior border of the ramus.
(6) In the growing mandible the body is stable except for changes at its borders. However, the position of the alveolar bone and teeth is subject to continuous change.

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Mandibular Condylectomy in Young Monkeys*

INTRODUCTION

Growth of the condyle is by endochondral ossification (Fig. 3.1). Microscopic examination reveals the presence of three zones: (1) chondrogenic, (2) cartilaginous, and (3) osseous. The condyle is capped by a narrow layer of avascular fibrous tissue which contains connective tissue cells and a few cartilage cells. The inner layer of this covering is chondrogenic, giving rise to hyaline cartilage cells which constitute the second zone. In the third zone, destruction of the cartilage and ossification around the cartilage scaffolding can be seen. However, the cartilage in the head of the mandible is not homologous to an epiphyseal cartilage because it is not interposed between two bony parts. It is not homologous to an articular cartilage because the free surface bounding the articular space is covered by fibrous tissue.

Much has been learned from the clinical studies of patients with either congenitally deficient condyles or those affected by inflammation or trauma.[1,2] The effects that the causes will have upon the growing condyle and subsequent deformity of the mandible are determined not only by the severity and duration of the noxious agent but also by the particular time

*Excerpted from: Sarnat BG. (1951) Facial and neurocranial growth after removal of the mandibular condyle in the Macaca rhesus monkey. *Am J Surg* **94**: 19–30. 1950 Kerbs Award by the Foundation of American Society of Plastic and Reconstructive Surgeons. *Plast Reconstr Surg* **7**: 364–380, 1951.

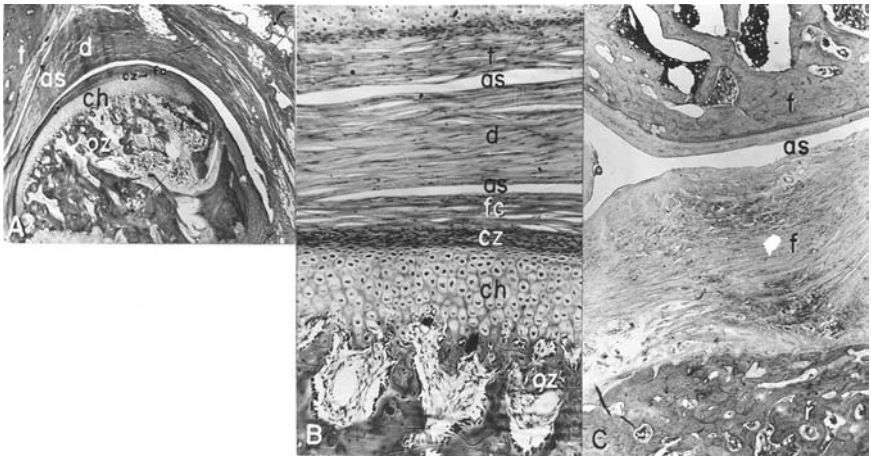

Fig. 3.1 Photomicrographs of hematoxylin and eosin-stained sections of left and right temporomandibular joint areas of monkey No. 5. The right mandibular condyle was resected at eight months of age. The animal was euthanized at 39 months of age. t — temporal bone; as — articular space; d — disk; fc — fibrous covering of condyle; cz — chondrogenic zone; pc — proliferating cartilage; b — bone of condyle; f — fibrous tissue of false joint; r — upper part of the remaining ramus. A (original magnification ×20) and B (original magnification ×120) — left, unoperated-on temporomandibular joint. Histologically, this joint appears to be within normal limits. Active growth of bone is occurring in the epiphysis-like region of the condyle. C — region from which the right mandibular condyle was resected. Note that there is no chondrogenic zone giving rise to bone in this false joint. As a result of removal of the actively growing condyle, there was a functional false joint entirely devoid of a cartilaginous growth site (original magnification ×20). However, there is some apposition of bone at the junction of the fibrous tissue (f) and the bony ramus (r). The wide zone of fibrous tissue serves as a substitute for the removed condyle and neck.

of occurrence. Thus, the effect will be greater early than later in life when condylar growth activity is decreased and the mandible has nearly assumed its adult shape and size.

The purpose of this report is to demonstrate, by gross and roentgenographic studies, the changes 25–35 months, after removal of the condylar growth site of the mandible. What influence will this have not only on growth of the mandible but also on that of the face and cranium? No such report has been found in the literature. Although the anatomic details were not

identical with those of the human being, important information would be obtained in regard to abnormal and normal growth of the skull. We detect disease by observing alterations from the normal. However, it is less well appreciated that, conversely, findings on the abnormal may be employed to test and extend our knowledge of the normal.

MATERIALS AND METHODS

The animals used in these experiments were Macaca rhesus monkeys obtained from Frank Buck in Florida and the Chase Wild Animal Farms, Egypt, Massachusetts. Because the growth activity of the mandibular condyle is greatest during early life, the youngest monkeys obtainable were ordered. The age when the monkeys were received was estimated according to the dentition to be about eight months. They weighed from 2 to 2.5 kg. The monkeys in this experiment included unoperated-on controls, animals in which the right mandibular condyle was resected, and animals in which both mandibular condyles were resected.

The monkeys were anesthetized by means of an intraperitoneal injection of a 3% aqueous solution of sodium pentobarbital (1 cc/kg of body weight) to perform the surgical procedures. The skin surrounding the region of the condyle was shaved. Using a sterile surgical technique, the skin and subcutaneous tissue were incised anterior to the tragus of the ear for a distance of about 1 cm. The parotid fascia and gland were reflected. The capsule of the temporomandibular joint was opened and the mandibular condyle was exposed. Because of the width of the condyle and the short neck, it was found that the condyle, including part of the neck, could be resected more readily by means of a tapered fissure dental bur. The disk was usually not removed. Hemorrhage was controlled. The deep tissues were sutured with No. ooo plain catgut and the skin closed with No. ooo black silk. No attempt was made to fill the space created by removing the condyle. The mandible was not fixed to the maxilla in any way. Thus, the animal was permitted free use of the jaws at all times. The postoperative survival period ranged from 25 to 35 months. An attempt was made to obtain comparable unoperated-on controls. However, this was not entirely feasible, because the exact age of the animals was not known.

Upon the death of the animal, the head was severed and fixed in a 10% solution of formalin. The skulls and mandibles were cleaned by dissection and boiling in a solution of sodium hydroxide. Photographs and roentgenographs of the mandibles and the skulls were taken. The tops of the skulls were sawed off. One animal in which the right condyle had been previously removed was perfused with formalin just prior to death to obtain immediate fixation of the tissues. The head was then sectioned in the midsagittal plane and a roentgenograph was taken of each half. They were then decalcified and sections of the left temporomandibular joint and the right temporomandibular joint area were made for microscopic study.

FINDINGS

Histologic study of the unoperated-on left temporomandibular joint of monkey No. 5 at about 39 months of age revealed essentially the findings on a normal joint and growing condyle (Fig. 3.1). Study of the right side, from which the condyle had been removed 31 months prior to death, revealed the articulating surfaces with no disk interposed. There was no evidence of cartilage being transformed to bone in the condyle-like area, but rather a layer of the dense fibrous tissue which was attached to the ramus inferiorly and articulated with the temporal bone superiorly.

Anterior Aspect of the Skull

Extreme asymmetry was noted in those animals in which one condylar growth site had been removed (Fig. 3.2C). On the operated-on side, total facial height and width were less. This was because of lesser growth of all the bony components, particularly the maxillary and mandibular ones. The face on the operated-on side had a rounder appearance than on the unoperated-on side, which appeared longer and flatter. The maxilla was shorter and narrower, and the plane of occlusion of the teeth was higher than on the unoperated-on side. Thus, the plane of occlusion was considerably closer to the level of the zygomatic arch and the external auditory canal on the operated-on than on the unoperated-on side. Because of the smaller maxilla on the operated-on side, the maxillary sinuses were

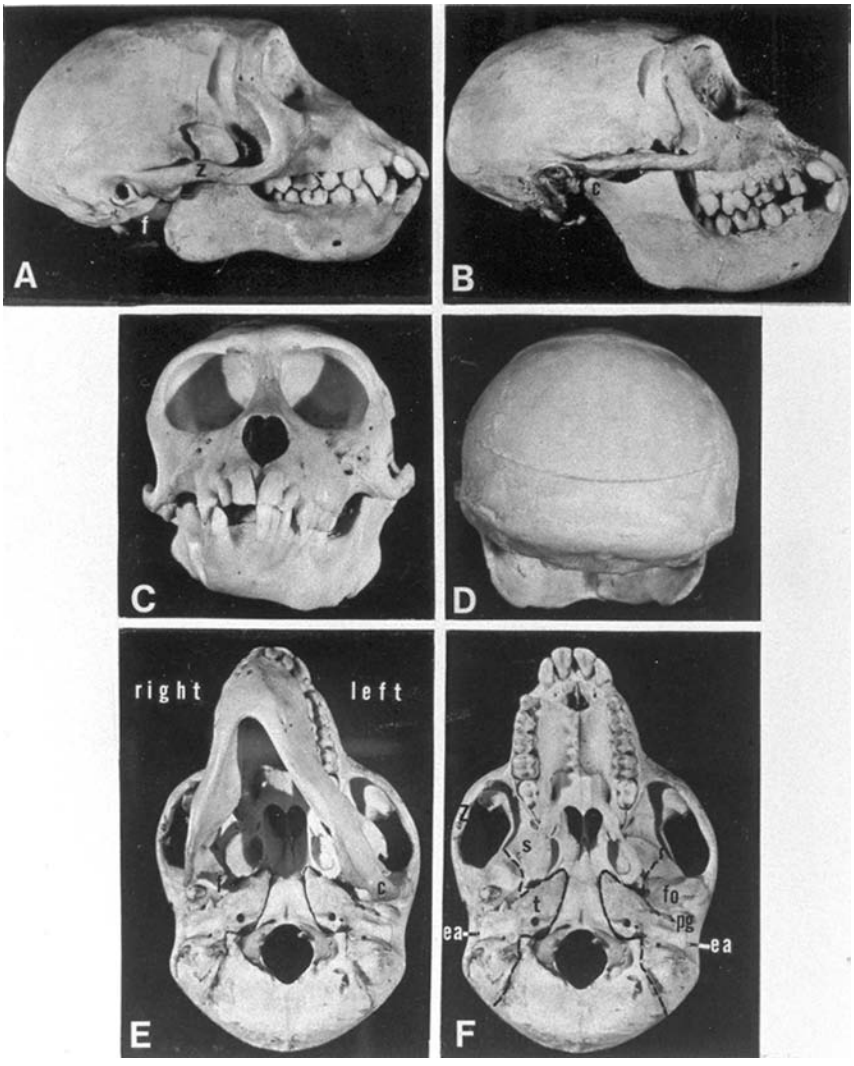

Fig. 3.2. Skulls of young rhesus monkeys. The right mandibular condyle was resected at about 8 months of age (A, C–F) with postoperative survivals of about 29 months. (E, F) Ventral views of skulls, with and without the mandible in occlusion. Note that on the operated-on right side the postglenoid process is less prominent, the mandible articulates with temporal bone anterior to fossa, and the body is less long than on the unoperated-on left side so that the entire mandible is directed toward the operated-on side. C — condyle; ea — external auditory canal; f — false articulation; fo — articular fossa; pg — postglenoid; z — zygomatic arch. (B) Unoperated-on animal.

examined to determine whether or not they also varied in size. However, no definite conclusions could be made because of the small size of the sinuses. The mandible appeared to be swung toward the operated-on side. On the unoperated-on side, the ramus and the mandibular body height and mandibular body length were greater.

Lateral Aspect of the Skull

Comparison of the lateral view of skulls of growing monkeys, in which the mandibular condyle had been excised, with the opposite unoperated-on side of control animals revealed striking differences (Figs. 3.2A,B). Facial height and length were less on the operated-on side. Whereas, on the side with the intact condyle, the zygomatic arch and external auditory canal were in the region of the middle of the skull well above the inferior border of the maxilla, on the operated-on side they were in the region of about the junction of the middle and lower thirds of the skull at about the level of the inferior border of the maxilla or even the occlusal plane of the teeth. Furthermore, on the operated-on side the ramus was shorter and wider, and its upper posterior border, which lacked a condyloid process, was more anterior to the articular eminence than on the unoperated-on side. The sigmoid notch was lacking and the coronoid process was wider, larger, and constituted a much larger part of the ramus. The coronoid process was also directed more posteriorly and above the zygomatic arch, on the side from which the condyle had been removed. Although the distance from the superior surface of the coronoid process to the lower border of the mandible appeared to be somewhat less in the operated-on than the unoperated-on animals, the distance from the articular surface to the lower border of the mandible was considerably less. The mandibular angle was less than 90° on the operated-on side and more than 90° on the unoperated-on side. The antegonial notch was more accentuated, maxillary and mandibular body height were less, and the crowns of the teeth had not erupted as much on the operated-on side.

Basal Aspect of the Skull

Examination was made of the ventral surface of the base of the skulls of growing monkeys in which one mandibular condyle had been

resected, with the mandibles articulated and in occlusion (Fig. 3.2E). This revealed that, on the side from which the condyle was removed, the upper posterior border of the ramus was considerably anterior and in the region of the temporosphenoidal suture. There was a space of about 3–5 mm between the operated surface of the mandible and the skull. It was filled with fibrous tissue at the time of dissection. The unoperated-on side of the mandible appeared longer and the chin was directed to the operated-on side.

Examination of the basal aspect from the ventral surface of the skulls of these monkeys revealed that the anterior and posterior parts deviated toward the operated-on side (Fig. 3.2F). On the operated-on side the following findings were noted: the maxillary teeth were less well erupted and the palate appeared to be somewhat higher; the palatine foramen was more anterior and appeared to be larger; the horizontal plate of the palatine bone was more anterior; the great wing of the sphenoid was smaller; the zygomatic arch was shorter, more curved, did not extend as far posteriorly, and appeared to be heavier; the temporal bone was shorter and not as wide; the articular eminence, the fossa, and the postglenoid process of the temporomandibular joint were either less well developed or absent and in a more anterior and medial position; the external auditory canal was in a more anterior position; the carotid canal and the stylomastoid foramen were also in a more anterior position, as was the posterior part of the temporal bone. Examination of the dorsal aspect of the base of the skull, after removing the top of the skull, revealed no significant differences between the left and right sides.

COMMENTS

Facial Growth

The cranium and the masticatory facial skeleton are integrated into an anatomic and biologic unit. Whereas growth of the cranium is dependent upon that of the brain itself, the masticatory skeleton is, in part, dependent upon muscular influences, growth of the tongue, and the dentition. These two parts of the skull follow different paths of development and the timing of their growth rates is entirely divergent.

Nevertheless, growth of any one part of the skull is coordinated with the growth of the whole.[3]

Growth of the facial skeleton shows, in many ways, independent curves in space and time. An important variation is a result of differences in the essential mechanism of growth of the upper facial skeleton (sutural) and that of the mandible (endochondral). During the growth period the facial skeleton increases in all three dimensions of space, namely height, width, and depth. The detailed way in which the coordination and simultaneity of the enlargement of the face in the three planes are achieved is one of the fascinating chapters of biology.[3]

The more important sites of growth for the maxillary complex are three sutures on each side: the frontomaxillary suture between the frontal bone and the frontal process of the maxilla; the zygomaticomaxillary suture between the maxilla and the zygomatic bone (and, secondarily, the zygomaticotemporal suture in the zygomatic arc), and the pterygopalatine suture between the pterygoid process of the sphenoid bone and the pyramidal process of the palatine bone.[4] It is significant that these three sutures are parallel to each other and all are directed from above and anteriorly, downward and posteriorly. Thus, growth in these sutures will have the effect of shifting the maxillary complex downward and anteriorly.

The downward and forward growth of the subnasal part of the maxillary body is accompanied by eruption of the teeth and apposition of bone at the free borders of the alveolar process. Thus, the apposition in this area contributes to the increase in height of the upper facial skeleton. At the same time, the downward growth of the alveolar process accounts for the transition from the flatly curved palate of the infant to the highly arched one of the adult. However, the downward shift of the hard palate by resorption on its nasal surface and apposition on its oral surface tends to obscure the downward growth of the alveolar process. Thus, the pathogenesis of the high palate seems to start with a deficiency of the modeling resorption at the nasal floor and with a failure of the normal downward shift of the hard palate. However, the vertical growth of the alveolar processes at the free borders continues in correlation with the growth of the mandible and accentuates the discrepancy.

Growth of the upper facial skeleton is closely correlated with that of the mandible. From the findings of this experiment, mandibular growth

can even be considered to be a leading factor of facial growth. However, the mode of mandibular growth is entirely different from that of the maxillary part of the face. In the latter, the growth is primarily sutural. However, in the mandible the main growth site is the hyaline cartilage in its condyle. These differences explain a certain independence of the growth of these two parts of the facial skeleton.

This experiment demonstrated that with inhibition of increase in ramus height, increase in maxillary and mandibular body height were concomitantly inhibited.

The extreme types of the high and narrow face and of the low and broad face are explainable by the leading role which the mandibular condyle plays in the development of the facial proportions. The different rate of cartilaginous growth of the mandibular condyle is responsible for variation in length of the ramus and the different rate of vertical eruption of teeth under varying conditions. The more cartilaginous growth is accentuated, the higher the mandibular ramus will be and, thus, the entire face. The height of the mandibular ramus determines not only the variations of the mandible itself but also those of the upper facial skeleton. While the mandibular ramus gains in height, by proliferation of the condylar cartilage the body of the mandible moves away from the cranial base and the maxillary body. Into the widening vertical space the teeth erupt with more formation of alveolar bone, so that the mandibular and maxillary alveolar processes grow toward each other. Inhibition of this growth, as in loss of activity of the condylar growth site, results in a shorter ramus, causes an undereruption of the teeth, less development of alveolar bone and, therefore, less height of the maxilla and mandibular body. The zygomatic arch is shorter and rounder. The face is rounder on the affected side.

The loss of the condylar site of growth is compensated for by the considerably modified pattern of growth in shape and size of the skull. The changes occurring in the mandible after condylectomy are a result partly of the growth arrest and the new articulation being subjected to forces which differ in direction, and probably strength, from the normal forces. In adaptation to these changes in functional stress, the bone is remodeled in part, so that the direction of spongy trajectories is made to coincide with the new lines of pressure and tension.

Although the growth of the mandible is to a high degree dependent upon that of the condylar cartilage, mandibular growth does not entirely cease if the condylar cartilage has been destroyed. In those cases, for instance, which occur early in life, the mandible and face attain a characteristic shape. Although the mandible grows, it never gains normal size. The distorted growth of the mandible in a condylar arrest of the jaw occurs mainly under the influence of growth and function of the tongue and pharynx. The pattern of growth is now entirely dependent upon the apposition of bone at the outer surfaces and modeling resorption on the inner surfaces. Both of these processes are lessened.

Normally, the coronoid tip is at the level of the zygomatic arch. However, when the condyle is removed, the coronoid tip is above the zygomatic arch. This has to do with the relation between condylar and coronoid growth. In a normal animal condylar growth causes a downward shift of the mandible. Thus, the tip of the upward-growing coronoid process is held at the same level. If, after condylar resection, the downward shift of the mandible ceases, the coronoid process grows visibly upward by apposition. Another factor to consider is the upward pull of the ramus by the muscles of mastication because of lack of condylar support. Thus, the coronoid process becomes relatively prominent. Since the ramus and its processes have failed to maintain posterior growth with the unoperated-on side, the coronoid tip is directed more posteriorly, no doubt as a result of the temporalis muscle pull.

The changes seem to be related not only to the deficiency of the condylar growth site and of ramus growth but also to a lack of direct articulation with the mandibular fossa of the temporal bone. Apparently, the articulation of the growing condyle in the mandibular fossa of the temporal bone exerts an effect on it, as well as the sphenoid and zygomatic bones, which articulate with the temporal bone. The effect of absence of the condyle was demonstrated in the condylectomized animals by less development and posterior progression of the temporal, sphenoid, and zygomatic bones. In addition, the mandibular fossa and its associated processes were either less developed or absent.

Although the findings are striking in these experiments with monkeys of about 8 to 43 months of age, even more striking findings would probably be obtained if an experiment were extended over a longer period of

time, both earlier and later. It would be of interest to determine the changes in the musculature (and how these changes affected bone growth) after removal of the mandibular condyle.

SUMMARY AND CONCLUSIONS

The condyle is an important and active growth site of the mandible.

Removal of the mandibular condyle in a group of growing monkeys with a postoperative survival period as long as 35 months demonstrated that not only was there a severe lack of growth of the mandible on the operated-on side but also the facial and cranial bone complexes were less developed than those on the unoperated-on side. Consequently, there was an extreme asymmetry of the skull in all of its aspects.

The basic science information obtained from this experiment suggests a number of possible clinical applications in this field of craniofacial surgery.

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Mandibular Condylectomy in Adult Monkeys*

INTRODUCTION

Sarnat and Engel[6] and Sarnat[5] reported the effects of condylectomy on mandibular and facial growth in growing Macaca rhesus monkeys. The essential findings on the side operated-on, in contrast to the unoperated-on side, were a lesser total facial height, a shorter ramus, a longer and wider coronoid process which extended above the zygomatic arch, and an occlusal plane which was about level with, instead of being considerably lower than, the zygomatic arch. These changes were ascribed not only to loss of the condylar growth site but also to a lack of direct articulation of the mandible with the mandibular fossa of the temporal bone and the consequent muscle imbalance. Heurlin, Gans, and Stuteville[2] reported similar findings in two young adult and two adult Macaca rhesus monkeys after unilateral or bilateral fracture dislocation of the mandibular condyle and a postoperative survival of one year.

The purpose of this investigation was not only to determine the skeletal changes in the jaws and face of the adult squirrel monkey after unilateral condylectomy but also to compare these findings with those already reported on the growing M. rhesus monkey after condylectomy.

*Excerpted from: Sarnat BG, Muchnic H. (1971) Facial skeletal changes after mandibular condylectomy in the adult monkey. *J Anat* **108**: 323–338.

MATERIALS AND METHODS

Animals

Four female and four male squirrel monkeys (*Saimiri sciureus*) caught wild in South America, and said to be adult, were used. Upon their arrival we judged these animals to be adult by dental criteria, since all teeth of the permanent dentition were erupted and in occlusion. The monkeys were then housed for six months before resection of the mandibular condyle. They were fed a standard diet.

Anesthesia

To obtain photographs, roentgenographs, and dental impressions and to perform surgical procedures, phencyclidine hydrochloride (Sernyl, Parke, Davis & Co.), 1–5 mg/kg, was injected intramuscularly for anesthesia. Excess salivation produced by this drug was controlled by subcutaneous administration of atropine sulphate (0.3 mg/kg). In addition, in the operated-on control and experimental animals, about 1 ml of 1% procaine hydrochloride with 1:100000 epinephrine was injected subcutaneously in the region of the temporomandibular joint.

Surgical Procedure

Two animals served as unoperated-on controls, two other animals were sham operated-on, i.e. the surgical procedure was carried out up to resection of the condyle, and in the remaining four animals the right condyle including part of the neck was resected. The sexes were equally represented in each group.

The skin surrounding the region of the condyle was shaved. With a sterile surgical procedure a vertical incision of about 1 cm was made through the skin and subcutaneous tissue anterior to the tragus of the ear. The parotid fascia and gland were reflected. The capsule of the temporomandibular joint was opened and the mandibular condyle and neck exposed. Resection of the wide condyle in the region of the short neck was done with a tapered fissure burr in a dental handpiece after freeing

it from the lateral pterygoid muscle. The disk was not removed. Hemorrhage was controlled. The deep tissues were sutured with No. 000 plain catgut and the skin closed with No. 000 black silk. No attempt was made to fill the defect created by removing the condyle with other tissue. Since the mandible was not fixed to the maxilla, the monkey was permitted free use of the jaws at all times. The animals were observed periodically during the postoperative period, which was terminated at 24 months.

At death the head was severed from the body and fixed in a 10% solution of formalin. The mandible was disarticulated from the skull. The skulls were cleaned by further dissection and boiling in water with a detergent. They were then bleached in a 3% solution of hydrogen peroxide.

Photographs and Roentgenographs

After the animals were anesthetized, lateral and frontal photographs were taken of the head both prior to the surgical procedure and just before death. These and other views were also obtained of the dissected skulls. Tracings were made of the left and right lateral views of the upper face and teeth.

Lateral cephalometric roentgenographs were made using a specially designed cephalometer when the squirrel monkeys were first obtained, six months later just prior to the surgical procedure, and after death. The heads of the animals were positioned in the Frankfurt plane. An ear post was placed in each external auditory meatus and an incisal pin placed between the maxillary central incisors to orient the head in the same position each time. The roentgenographs were obtained with a standard medical roentgen apparatus at a target film distance of 140 cm operated at 50 IDA, 54 kV and an exposure time of 1/20 s. Tracings of the roentgenographs were made on matte acetate paper. Additional roentgenographs were taken of the left and right hemisected dissected mandibles with a senograph roentgen apparatus at a target film distance of 28 cm operated at 20 mA, 23 kV and an exposure time of 2 s. Tracings of these were made on matte acetate paper and they were superposed on various landmarks.

Histological Sections

After surgical removal, the right condyles were placed in a 10% solution of formalin. In addition, animal No. 3.8 the left the condyle was removed at death, two years after the right condyle had been resected, and was also fixed in a 10% solution of formalin. These were decalcified, embedded in paraffin, sectioned in the midsagittal plane, and stained with hematoxylin and eosin.

RESULTS

Antemortem Observations

Periodic observations during the postoperative period suggested normal ability to eat; gross mandibular movement and gross facial appearance also seemed to be within the normal.

Postmortem Observations

Region of the temporomandibular joint of the operated-on side

On the side from which the condyle had been resected, fibrous tissue was found surrounding the temporomandibular joint region. The posterosuperior border of the ramus was anterior to the glenoid fossa. Dissection revealed in the temporal area dense fibrous tissue which articulated with the fibrous tissue of the superior ramus, thereby creating a false joint. The area of articulation was broader, irregular, and in an anterior position to the corresponding area of the unoperated-on left side.

Lateral aspect of the skull

Comparison of the lateral views of the prepared skulls of monkeys from which the mandibular condyle had been excised with those of the opposite unoperated-on sides or with the control animals revealed gross differences (Figs. 4.1A,B). These were in contrast to the lack of clinical findings. Facial height was less on the operated-on side, with the primary loss between the level of the zygomatic arch and the lower border of the mandible. On the side with the intact condyle, the zygomatic arch and

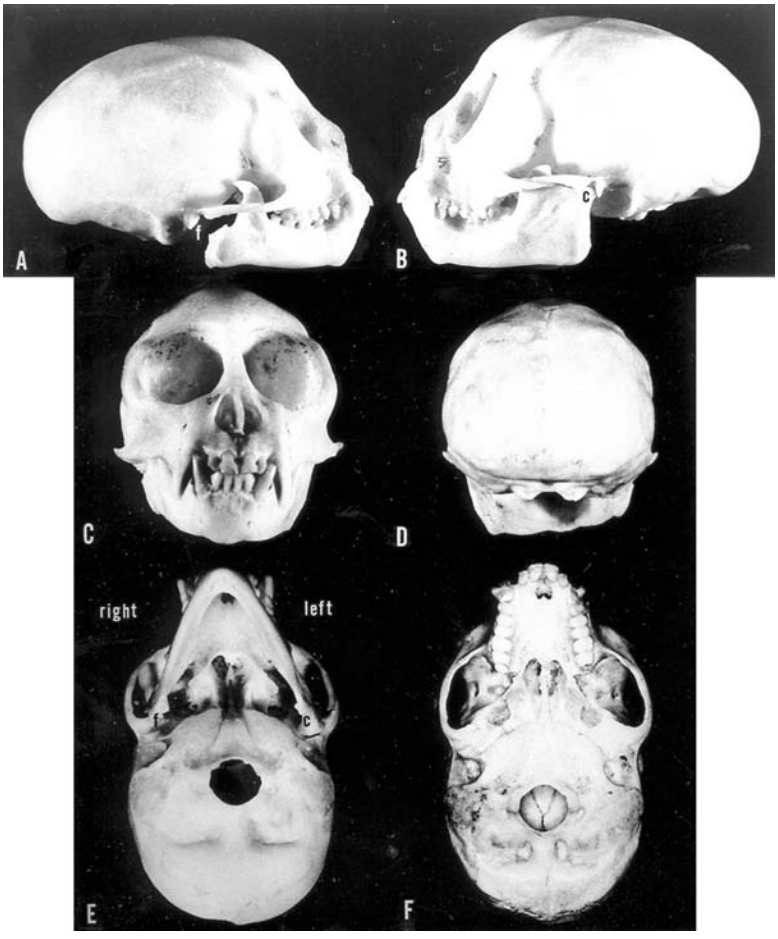


Fig. 4.1 Photographs of the skull of adult squirrel monkey No. 3.4. The right mandibular condyle was resected as an adult two years before death. Lateral views of the operated-on right side (**A**) and unoperated-on left side (**B**). Note on the operated-on right side (**A**) the lesser facial height; the lack of a condyle; the short posterior ramus and lack of articulation with the cranium; the more prominent coronoid process directed more posteriorly and above the zygomatic arch; the greater prominence of the antegonial notch; and the lesser height of the mandibular body. In (**C**) (anterior view) and (**D**) (posterior view), note the higher level of the mandible on the operated-on right side. Figure 4.1 shows ventral views with (**E**) and without (**F**) the mandible in occlusion. Note on the right side of (**E**) the increased distance of the articulating surface of the mandible from the temporal bone and the position of the left condyle in the fossa. The mandible has not shifted toward the operated-on left side (c — condyle; f — false articulation).

external auditory canal were well above the inferior border of the maxilla (Fig. 4.1B). On the operated-on side, however, they were at about the level of the inferior border of the maxilla close to the occlusal plane of the teeth (Fig. 4.1A). Maxillary height, measured from the level of the zygomatic arch to the occlusal surface of the maxillary teeth, was reduced.

Furthermore, on the operated-on side the posterior ramus was shorter and its upper posterior border, which lacked a condyloid process, lay anterior to the glenoid fossa. The sigmoid notch was lacking and the coronoid process constituted a larger part of the ramus. The coronoid process was also directed more posteriorly and above the zygomatic arch on the side from which the condyle had been removed. Although the distance from the superior surface of the coronoid process to the lower border of the mandible was about equal in both the operated-on and the unoperated-on animals, the distance from the articular surface of the false condyle to the lower border of the mandible was considerably less in the former monkeys. The antegonial notch was slightly more accentuated and marraibular body length (gonion to gnathion) was less.

Anterior aspect of the skull

Removal of one condyloid process resulted in facial asymmetry (Fig. 4.1E). On the operated-on right side total facial height was less and the zygomatic arch was lower. The plane of occlusion of the teeth was at about the level of the zygomatic arch and the external auditory canal. The mandible, when viewed alone, had a prominent coronoid process and an absent condyloid process on the operated-on right side. On the unoperated-on left side both processes were visible.

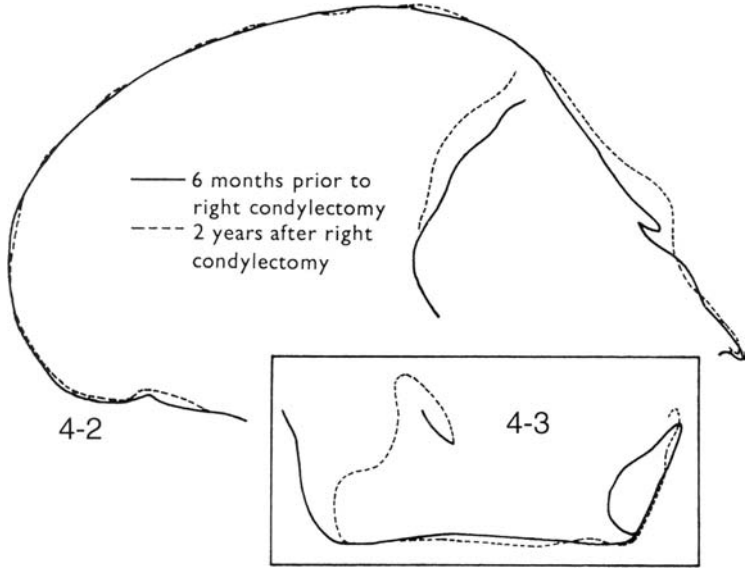
Ventral aspect of the skull

The ventral surface of the skull in which the right mandibular condyle had been resected was examined with the mandible articulated and in occlusion (Fig. 4.1E). On the side from which the condyle had been removed, the upper posterior border of the ramus was in a more anterior position. There was a greater distance between the operated-on posterosuperior ramus of the mandible and the skull than on the unoperated-on side.

This space was occupied by fibrous tissue at the time of dissection. The fossa of the temporomandibular joint was less well developed and in a more anterior position. No swerving of the inferior border of the mandible toward the operated side was noted.

Roentgenographic and Photographic Observations

Superpositioning along the cranial outlines of the tracings of lateral cephalometric roentgenographs taken two years before death and at death revealed no appreciable change in size of the cranium, although in some instances there were minor changes in shape (Fig. 4.2). Superposition of the roentgenographic tracings along the symphysis and lower right mandibular border showed a considerable deficiency of the posterior ramus (Fig. 4.3).



Figs. 4.2 and 4.3 Tracings of lateral cephalometric roentgenographs taken 2½ years before death (solid line) and at death (broken line) of monkey No. 3.4. Note that in Fig. 4.2 the tracings are superposed along the cranial outlines and there is little difference. In Fig. 4.3 the tracings of the right mandible are superposed along the symphysis and lower border of the mandible. The right condyle was resected two years before death. Note the extensive loss of bone which occurred in the posterior ramus area.

Roentgenographs were taken of the disarticulated, dissected, hemisectioned mandibles. The roentgenograph of the unoperated-on side was reversed to facilitate comparison. The side of the mandible from which the condyle had been resected two years before death had a much shorter posterior ramus, no sigmoid notch and a coronoid process larger relative to the ramus than on the unoperated-on side. The distance from the occlusal level of the teeth to the lower border of the mandible also was less, and was most apparent in the posterior part of the mandible. The bone of the alveolar crests was flat on the operated-on side. Tracings were made of the roentgenographs of the unoperated-on left side (Fig. 4.4A) and of the right side (Fig. 4.4B) from which the condyle had been resected two years prior to death. In Fig. 4.4C, the tracings were superposed on the teeth and a difference was noted at the lower borders. In Fig. 4.4D, the coronoid processes were superposed and found to coincide. When the tracings were superposed along the lower border of the mandible, the teeth on the operated-on side were at a lower occlusal level (Fig. 4.4E). The extreme loss of ramus bone was also demonstrated in relation to the small area of resection ("r" indicated in black; Fig. 4.4E).

Tracings were made of the upper face from the photographs of the unoperated-on left side (Fig. 4.5A) and the right side (Fig. 4.5B) from which the mandibular condyle had been resected two years before death. In Fig. 4.5C the tracings were superposed on the teeth and the differences in maxillary alveolar bone heights and the levels of the zygomatic arches were demonstrated. When the tracings were superposed on the external auditory canals and the upper border of the zygomatic arches, the lesser maxillary height of the operated-on left side was again apparent (Fig. 4.5D).

Histological Observations

Examination of the right mandibular condyle, resected at the beginning of the surgical experiment, revealed an outer layer of dense fibrous connective tissue, a middle zone of hyaline cartilage and an inner region of bone and narrow spaces (Fig. 4.6A). Under higher magnification it was noted that the bone had sealed off the cartilage with no endochondral bone formation (Fig. 4.6C). Examination of the left condyle resected at death two years later yielded similar findings (Figs. 4.6B, D).

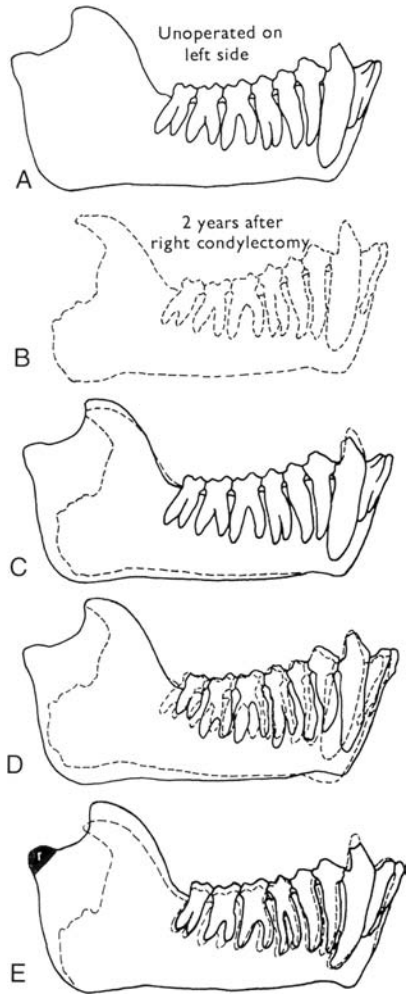


Fig. 4.4 Tracings of postmortem lateral roentgenographs of the disarticulated, dissected, hemisected mandible of adult squirrel monkey No. 3.4. The right mandibular condyle was resected in this adult monkey two years before death. (**A**) Unoperated-on left side (solid line; reversed to facilitate comparison); (**B**) Operated-on right side (broken line); (**C**) Tracing of (**B**), superposed on (**A**) along dental outlines; (**D**) Tracings of (**B**), superposed on (**A**) along outlines of coronoid processes; (**E**) Tracings of (**B**), superposed on (**A**) along outlines of the lower border of mandibles. The dark area, r, represents the approximate extent of condylar resection. Note, in the tracing of the right mandible from which the condyle was resected, the extensive resorption of the posterior ramus, and that in (**D**) and (**E**) the teeth are not as fully erupted as on the unoperated-on side.

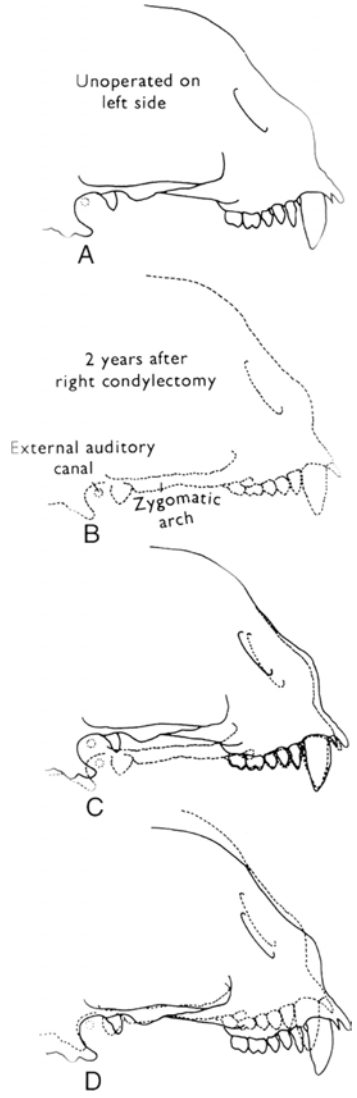


Fig. 4.5 Tracings of the upper face from right and left lateral photographs of the adult monkey skull in Figs. 4.1**A**, **B**. Unoperated-on left side (solid line); operated-on right side (broken line) from which the condyle was resected two years before death. (**A**) Unoperated-on left side (reversed to facilitate comparison); (**B**) Operated-on right side; (**C**) Tracings of (**B**) superposed on that of (**A**) along dental outlines; (**D**) Tracing of (**B**) superposed on tracing of (**A**) at external auditory canals and upper borders of zygomatic arches. Note the extensive resorption of maxillary bone.

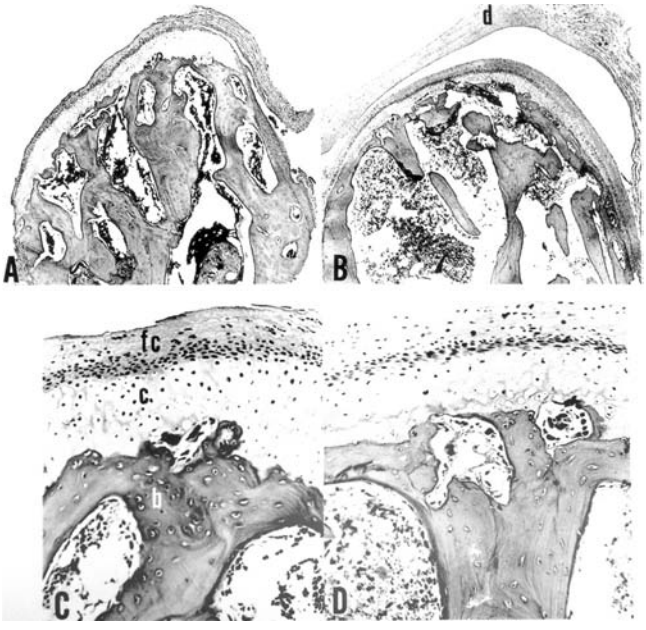


Fig. 4.6 Photomicrographs of hematoxylin- and eosin-stained sections of the right (**A**) and left (**B**) mandibular condyles of adult squirrel monkey No. 3.8. The right mandibular condyle was resected at the beginning of the experiment and the left one two years later, at death. Note the similar histological characteristics of the two condyles. The hyaline cartilage layer is inactive in relation to endochondral osteogenesis, with no evidence of calcification, resorption, or replacement by bone. b — bone; c — cartilage; d — disk; fc — articular fibrous connective tissue. (**A**) and (**B**) ×45; (**C**) and (**D**) ×200.)

DISCUSSION

Comparison of Findings after Condylectomy in Adult and Growing Monkeys

The purpose of this investigation was not only to determine the skeletal changes in the jaws and face of the adult squirrel monkey after unilateral condylectomy but also to compare these findings with those in the growing M. rhesus monkey after condylectomy.[5,6] Because of expense the squirrel monkey was used. Although the species differences must be considered, in the final analysis, general comparisons can be made.

Study of the temporomandibular areas after disarticulation of the mandibles from the crania revealed comparable changes in both the adult and the growing monkeys. In both cases the false articular joints, which consisted of fibrous tissue, were irregular, broader, and more anterior than on the unoperated-on sides. A tenable explanation might be that the space left after removal of the condyle and the neck was filled with blood, which organized into fibrous tissue. This fibrous tissue extended upward from the superior surface of the ramus of the mandible to the temporal bone. The masticatory muscles and scar tissue rotated the mandible upward and forward.

The findings were similar for the skulls of the adult and growing monkeys except for the following differences. In the adult monkeys less extreme changes were noted than in the growing monkeys in facial height, the amount of the coronoid process above the zygomatic arch, and swerving of the body of the mandible toward the operated-on side. In the growing monkeys, a false bony condyloid process was frequently found. This was not true in the adult monkeys. Within the group of growing monkeys, the findings were more extreme, with a longer postoperative survival. Histologic study of the condyles of the adult animals revealed no endochondral bone formation, while this was present in the growing monkeys.

In the report by Heurlin *et al.*,[2] the findings, after fracture dislocation of the mandibular condyle in adult monkeys, were similar to those reported for growing monkeys after condylectomy.[5,6] These authors classified the two monkeys on which a unilateral procedure was performed as young adults and the two monkeys with a bilateral procedure as adults. On the postmortem lateral roentgenographs of the young adults, the last molars were not fully erupted one year after the surgical procedure. Since these animals were not fully adult, one of the goals of the present study was to eliminate this uncertainty. Rosenblum and Cooper[4] found that the last permanent tooth to erupt in *Saimiri sciureus* was the maxillary canine at 21.5 months (mean). At 27 months the head–body length had nearly stabilized. When our monkeys arrived, the teeth were fully erupted and in occlusion. Since the monkeys were operated on 6 months later, they were at least 27.5 months old. More important, comparison of tracings of cephalometric roentgenographs

over a 30-month period revealed no appreciable change in cranial size, and histological examination of the condyles removed initially and 2 years later at death showed no evidence of endochondral bone growth activity.

In previous reports on growing monkeys, it was stated that ramus growth is primarily affected while growth of the body of the mandible appears to be affected to a limited degree.[6] The changes occurring in the mandible after condylectomy are a result of the growth arrest and the new articulation being subjected to forces which differ in direction, and probably strength, from the normal forces. In adaptation to these changes in functional stress, the bone is remodeled in part, so that the direction of spongy trajectories is made to coincide with the new lines of pressure and tension.[5]

Since the facial skeletal changes are similar, but not the same, in both the adult and the growing monkeys after condylectomy, it seems that removal of the growth site is not the principal responsible factor. Rather, the changes are probably secondary to disruption of normal temporomandibular joint function, including elimination of sensory receptors. Loss of the anatomical integrity of the temporomandibular joint, loss of function of the lateral pterygoid muscle, altered function of the medial pterygoid, masseter, temporal, and suprahyoid muscles, and establishment of a false joint all served to modify the direction and amount of muscular pull with altered position and motion of the mandible. These changes in function could influence the remodeling and resorption of the ramus and adjacent bony structures.

Growth of bone occurs at the superoposterior surfaces of the mandible.[3] Whether the mandibular condyle is a primary or secondary site of growth is much discussed. Although this experiment on the adult monkey, as in previous experiments on the growing monkey, demonstrates the extreme loss of bone in the posterosuperior ramus after condylectomy, it does not prove that the condyle is not a growth site. What role does the condyle play in growth of the mandible? An experiment which would contribute important information would be one wherein endochondral bone growth is eliminated but the integrity of the temporomandibular joint is maintained.

Dental Occlusion

After unilateral condylectomy in the adult monkey, the dental occlusion and the body of the mandible appeared to be normal. In contrast, in the growing monkey the inferior part of the body of the mandible in particular showed a shift toward the operated-on side.

The distance between the occlusal surface of the teeth and the lower border of the mandible on the side from which the condyle had been removed was less than on the unoperated-on side of the mandible (Fig. 4.4E). Furthermore, the difference increased from the anterior part of the mandible to the posterior part so that the planes of the occlusal surface and the lower border of the mandible converged posteriorly, whereas on the unoperated-on side they remained about parallel. The distance between the occlusal surface of the maxillary teeth and the lower border of the zygomatic arch of the side from which the condyle had been removed was less than on the unoperated-on side (Fig. 4.5D). This might be explained on the basis that the posterior part of the mandible was rotated superiorly by masticatory muscle and scar tissue pull. This was followed by resorption of ramus, body and alveolar bone with the teeth following the bone. An alternative consideration is that this might be a result of increased pressure on the teeth leading to their depression with loss of bone — alveolar, including interdental, maxillary, and mandibular.

Roentgenographic Changes

There was some variation in the vertical positioning of the head when the cephalometric roentgenographs were taken. This was of no consequence, because positioning of the ear posts in the external auditory meatuses ensured that the lateral roentgenographs were comparable. The standardization permitted superpositioning of the tracings of the films. However, the findings should be interpreted with an appreciation of their limitations. First, the tracings and roentgenographs are two-dimensional representations of three-dimensional structures. Secondly, the left and right sides of the mandible could not always be definitely identified. Insertion of a radiopaque marker on one side prior to the taking of the head plates would facilitate identification.

Tracings of the roentgenographs of the operated-on right side (Fig. 4.4B) and the unoperated-on left side (Fig. 4.4A) of the mandible were superposed in various ways. This brought out several facts. When the tracings were superposed on the teeth, an extensive deficiency of bone was noted in the superoposterior ramus, superoanterior coronoid, and lower border of the mandible regions (Fig. 4.4C). When the tracings were superposed on the coronoid processes, it was surprising to find that they coincided (Fig. 4.4D). The anterior part of the mandible was rotated downward and the posterior part upward. The lower borders of the mandibles intersected in the premolar regions. When the tracings were superposed along the lower borders of the mandibles, the defect of the ramus appeared to be most extensive (Fig. 4.4E). This also illustrated the amount of bone lost in relation to the relatively small amount removed two years previously. The anterior border of the coronoid process and the occlusal level of the teeth were lower on the operated-on side. The borders for superpositioning were selected arbitrarily and probably not one of them reflects the actual relationship.

The roentgenographic changes in the trabecular pattern of the ramus after condylectomy in growing monkeys have been reported previously.[1,5,6] The findings on the adult monkey were similar, with the trabecular pattern oriented to the new false condyle. The differences are a result of the changes in function of the temporomandibular joint with alterations in the direction and amount of muscular pull and the position and motion of the mandible.

Controls

No gross differences were noted between the left and right sides of the mandibles in the unoperated-on and operated-on control animals (sham) and the left unoperated-on sides in the animals which had had a right condylectomy. Since the mandible is a single bone, alterations in the function of one side can influence the other side. Consequently, the unoperated-on left side of the mandible was not a true control for the perated-on right side. Because the mandibles of the different squirrel monkeys did vary in size, comparisons were preferred between the operated and the unoperated-on side of the same mandible.

SUMMARY

The right mandibular condyle was resected in a group of adult squirrel monkeys with a postoperative survival as long as two years. The findings on the operated-on side compared with the unoperated-on side were a lesser total facial height, a shorter ramus with extensive deficiency in the posterosuperior region, less maxillary and mandibular alveolar bone, particularly in the molar region, with a lesser height of the zygomatic arch in relation to the lower border of the mandible. In addition, on the operated-on side the tip of the coronoid process extended well above rather than to the level of the zygomatic arch, and the zygomatic arch and external auditory canal were just above the level of the occlusal plane rather than well above it. The trabecular pattern of bone in the roentgenographs of the ramus was reoriented to the false articular area. Thus, after removal of the condyle with creation of a false temporomandibular joint and with alterations in muscle function and position of the mandible, there was considerable remodeling and resorption of bone.

These gross facial skeletal changes are comparable with those found in growing M. rhesus monkeys after unilateral condylectomy. In the growing monkeys the changes were interpreted to be the result of loss of both a growth site and the anatomical integrity of the temporomandibular joint. However, it is concluded now that since similar skeletal architectural modifications occurred in the adult monkeys, the important factor is loss of physiological integrity of the temporomandibular joint region rather than loss of a growth site.

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Temporalis Muscle and Coronoid Process*

Following resection of the temporalis muscle, a smaller or absent coronoid process has been reported in growing animals (Table 5.1).[1,2] The trauma of resection, altered function, hemorrhage, scar tissue, and changes in vascularity may have influenced the results. The purpose of this experiment was to observe in adult *Macaca mulatta* the fully grown coronoid process after decreasing or eliminating neurofunctional activity of the temporalis muscle unilaterally without the trauma of local resection. In two males and three females the motor root of the trigeminal nerve which innervates the temporalis muscle was resected intracranially. In three control animals of both sexes the same surgical procedure was performed except for resection of the nerve. At postmortem, one year later, the temporalis muscle mass was atrophic on the resected side. There were no significant morphological differences, however, between the right and left sides of the mandible, including the coronoid process, regardless of which motor root of the fifth nerve had been resected, which side had been sham-operated, or sex. An extensive deposit of calculus on the buccal surfaces of the teeth on the operated nerve side was a consistent, conspicuous finding.

*Excerpted from: Sarnat BG, Feigenbaum JA, Krogman WM. (1977) Adult monkey coronoid process after resection of trigeminal nerve motor root. *Am J Anat* **150**: 129–138.

Table 5.1 Relationship of Temporalis Muscle to Coronoid Process: Review of Selected Surgical Studies

Investigator	Year	Temporalis Muscle Surgical Procedure	Animal	No.	Age at Operation	Postoperative Survival	Findings on Operated Side
Anthony	1903	Removal of entire left suprazygomatic portion	Dog	1	1 day	9.5 months	Coronoid process?
Pietkiewicz	1907	Similar to Anthony					Coronoid process (condyle and ramus), some diminution in size
Walkhoff	1910	Removal of part of suprazygomatic portion	Dog	1	4 weeks	11 months	Coronoid process?
Washburn	1947	Unilateral removal of "majority"	Rat	12	1 day	3–5 months	Coronoid process absent
Horowitz and Shapiro	1951	Removal of right and periosteum at origin and insertion	Rat	8	30 days	51–173 days	Coronoid process absent
Rogers	1955	Excision, unilateral intracranial section third division of trigeminal nerve	Monkey	?	?	?	Coronoid process? "neglect of buccal pouch"

(*Continued*)

Table 5.1 (*Continued*)

Avis	1959	Removal of right suprazygomatic portion	Cat	10	6 weeks	16 months	Coronoid process somewhat short and axis straight upward instead of curving upward and backward
Liebman and Kussick	1965	Right myectomy	Dog	1	10-14 weeks, shortly after weaning	maturity	Coronoid process, no shortening of, straightening and vertical alignment of posterior soncave border
Boyd *et al.*	1967	Removal (right) from origin and rolled on itself	Guinea Pig	9	?	80 days	Coronoid process smalled in only two specimens
Moss and Meehan	1970	Removal of left suprazygomatic portion except anterior head	Rat	63	11 days	2–43 days	Coronoid process, decrease in size
Soni and Malloy	1974	Removal (left) from origin and rolled on itself	Guinea Pig	7	14 days	46 days	Coronoid process, reduction in height
This report		Unilateral intracranial resection of right or left motor root, third division of trigeminal nerve	Monkey	5	adult	12 months	Coronoid process, no significant difference

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Fractured Mandible and Incisor*

INTRODUCTION

Although there are a number of references to the clinical aspects of fractures of the jaw,[1–5] relatively few experimental studies have been reported. While fractures of the jaw in dogs or guinea pigs have been studied,[6–8] no report on the effects of fractures of the jaw and teeth in the rat and on the simultaneous reaction of all the calcified structures present at the site of fracture was found in the literature.

This study is based on 38 rats, 29 of which were subjected to unilateral and 9 to bilateral fractures of the mandible (Table 6.1). The animals were killed from six and one-half hours to 158 days after operation. The effects were studied in both the living and the killed animals on gross, roentgenographic, and histologic bases (Fig. 6.1 (1)–(3)). The mandible in the rat contains throughout its length a continuously growing and erupting incisor. Consequently, an opportunity is afforded to study the effects of fractures simultaneously on all of the different calcified structures of the body, namely the growing bone and the growing tooth (Table 6.2).

The roentgenographs, with few exceptions, showed little correlation with the stage of histologic repair.

*Excerpted from: Sarnat BG, Schour I. (1944) Effect of experimental fracture on bone, dentin and enamel: study of the mandible and incisor in the rat. *Arch Surg* **49**: 23–38.

Table 6.1 Data on Thirty-Eight Rats Which were Subjected to Unilateral or Bilateral Fractures of their Mandibles Arranged According to the Progressive Stage of Repair of the Bone*

Stages	No. of Left or Right Mandibles Fractured	Period of Survial	General Histologic Characteristics	Special Comments
Procallus	10	6½ hours to 21 days	Hemorrhage; granulation tissue; young connective tissue	Roentgenographic findings show evidence of fracture
Fibrocartilaginous callus	8	11–102 days	Dense fibrous connective tissue: fibrocartilage beginning of bony callus	Roentgenographic findings show no evidence of healing of fracture
Bony callus	29	33–158 days	Bony union: architectural reconstruction	Roentgenographic findings show variation in regard to evidence of healing of fracture

*Modified from: Sarnat, BG and Schour, I. (1944) Effect of experimental fracture on bone, dentin and enamel: study of the mandible and incisor in the rat. *Arch Surg* **49**: 23–38, 1944.

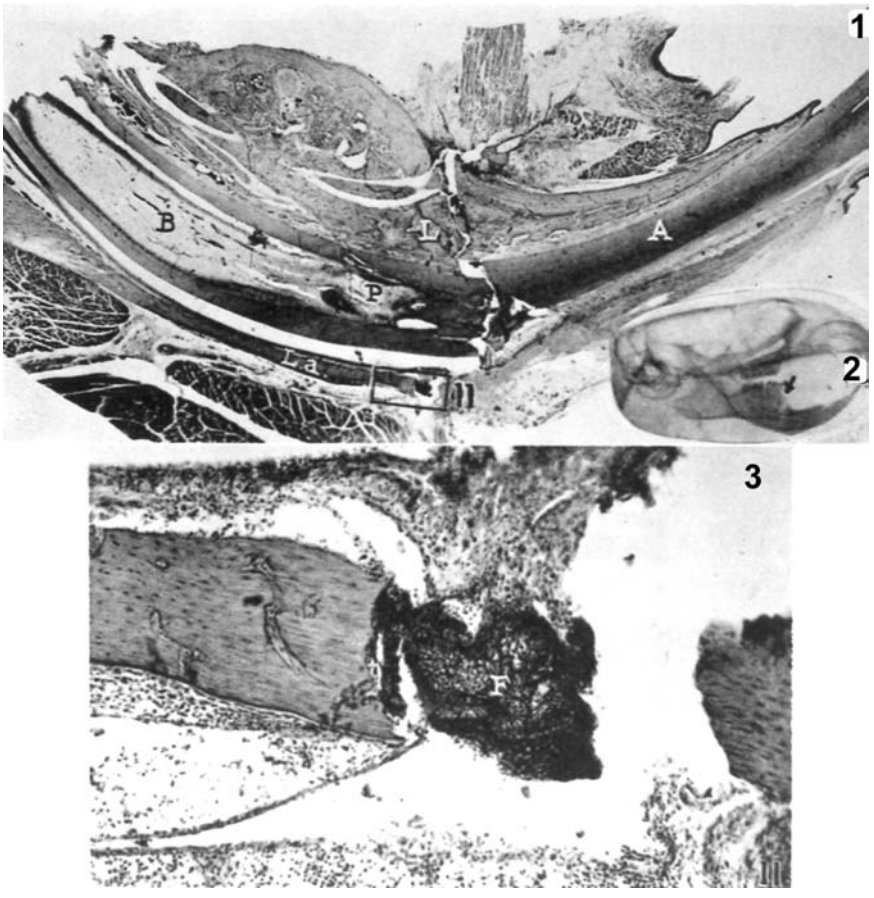

Fig. 6.1 (1) Photomicrograph of a decalcified midsaggital section of the lower right incisor and the mandible of rat No. 2, which was killed six and one-half hours after mandibular fracture. Hematoxylin and eosin stain. Note the fracture which divided the incisor into the anterior (**A**) and posterior (**B**) fragments. The fracture is complete and extends from the lingual bone (L) — which is fragmented across the tooth — to the labial bone (L.a.). The pulp (P) shows hemorrhage and acute inflammation. Hemorrhage and fibrin network are seen at the site of the fracture. Procallus stage (see (3)) ×7. (2) Roentgenograph of the right half of the head of the same animal as in (1). The arrow indicates the site of fracture. Natural size. (3) Photomicrograph of the area indicated in (1). Note the fibrin network (F) at the site of fracture of the labial bone and the surrounding inflammatory reaction. Procallus stage. ×107.

Table 6.2 Differential Reactions of Bone and Teeth to Injury*

Formative Cells	Bone. Osteoblasts	Cementum. Cementoblasts	Denun. Odontoblasts	Enamel. Ameloblasts
Location of formative cells	Periosteum, endosteum, lining of haversian canals	Single layer lining the periodontal ligament adjacent to the cementum	Single layer lining pulp adjacent to most recently formed dentin	On surface of enamel in formative stage, absent in adult enamel
Cellular contents	Osteocytes	Cementocytes	Acellular	Acellular
Channels	Canaliculi, haversian canals, Volkmann's canals	Canaliculi	Dentinal tubules, avascular	None
Contents of channels	Processes of osteoblasts, osteocytes, vessels, and nerves	Processes of cementocytes	Processes of odontoblasts	None
Response to injury in growing and mineralizing stages	Sensitive to metabolic changes leaving semipermanent record	Sensitive to metabolic changes leaving semipermanent record	Very sensitive to metabolic changes leaving permanent record	Very sensitive to metabolic changes leaving permanent record

(*Continued*)

Table 6.2 (*Continued*)

Formative Cells	Bone. Osteoblasts	Cementum. Cementoblasts	Denun. Odontoblasts	Enamel. Ameloblasts
Response to injury in adult stage	Continuous apposition and resorption; rich regenerative power through osteogenic properties of periosteum, and bone marrow	Regenerative capacity through cementoblastic properties of periodontal cells	Can transmit stimuli through its tubles from dentinoenamel junction to pulp and limited response through odontoblasts (secondary dentin)	Entirely physical, passive, incapable of response by inflammation or regeneration nonvital
Response to fracture	Very active through rich cellular activity along internal and external surfaces of bone	Partial through periodontal ligament cellular response	Passive or partial through secondary pulpal or cemental reaction	None
Degree of mineralization	70%±	50%±	70%±	96%±

*Modified from: Sarnat, BG and Schour, I. (1944) *Arch Surg* **49**: 38.

Dental Changes

A fractured tooth differs from a fractured bone by the absence of formation of callus and by its limited reaction. The dental structures, by contrast, are for the most part passive and nonregenerative, as follows:

(1) Adult enamel reacts only mechanically and is not capable of response by inflammation or repair. The enamel matrix calcifying at the time of fracture is arrested in its calcification and shows resorption. Occasionally it loses its epithelial covering, which is then replaced by connective tissue or cementum.
(2) Dentin shows no direct reaction, but the region between the fragments becomes infiltrated by cells of the pulp or the periodontal membrane. The larger fragments are joined by fibrous union.

    The odontoblasts are injured, and an atypical secondary dentin is formed in the pulp.
(3) The pulp shows a rich and varied response, ranging from necrosis to complete recovery and including the formation of bone and hemopoiesis.

Healing of Bone

The stages of histologic repair of the fractured mandible in the rat may be summarized in the following chronologic order:

(1) Procallus:

    (a) Hemorrhage and initial blood clot (first few hours);
    (b) Organization of blood clot and invasion by granulation tissue (first few days);

(2) Fibrous and/or fibrocartilaginous callus (first few weeks);
(3) Bony callus (first to second month) and reorganization of bone (first year).

These events are in complete agreement with those occurring in the healing of other flat bones.

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The Temporomandibular Joint

This is the first and only book to deal with the subject in this particular manner. It is of course not feasible to include the contents of the BOOK* at this time.

The chosen title indicates our philosophy. We have developed and emphasized a basic biological approach to the difficult and, in many instances, unanswered clinical problems involving the temporomandibular joint and, in the broader context, the masticatory apparatus. There are two parts to the book. Part I emphasizes the biology of the temporomandibular joint region, and incorporates clinical correlations. This serves as a foundation for Part II, which is devoted almost entirely to clinical evaluation, accurate diagnosis, and proper treatment, reinforced by reference to the basic science aspects. We are not aware of another book on the temporomandibular joint that takes this approach.

Because no one person can be expert in all aspects of such a broad subject, we have invited contributions from those whom we consider highly knowledgeable in specific areas. Thus, basic scientists and clinicians have pooled their knowledge and experience to provide a unique view of temporomandibular joint disorders.

The main purpose of this book is to distill the enormous accumulation of biological and clinical data into a unified text that will provide an

*Sarnat BG, Laskin DM. (1991) (editors and 30 contributors) *The Temporomandibular Joint: A Biological Basis for Clinical Practice*, 4th edition, WB Saunders, Publisher, Philadelphia, Pennsylvania, 505 pages (Fig. 1).

accurate basis for clinical practice. In any multiauthored book, however, particularly one dealing with such a complex subject, there are bound to be some differences of opinion and interpretation. As editors, we have attempted to encourage such diversity, when controversy still exists. We see this as an advantage because, by presenting more than one expert point of view, readers may reach their own conclusions on the basis of the information provided. Such interpretation is aided by the comprehensive basic biologic background that is included.

Bernard G. Sarnat & Daniel M. Laskin

FOREWORD TO THE FOURTH EDITION

As one with primarily a basic science background, it has been a great pleasure to read the scholarly contributions which this exceptionally well-illustrated book contains. Forty years have passed since the appearance of the first edition of *The Temporomandibular Joint*, in 1951, and this presentation of the biomedical information with the clinical aspects concerning the temporomandibular joint continues to be unique in the world literature.

The contents of this multiauthored book provide the fundamental information necessary for both diagnosing and treating the various conditions that affect the masticatory apparatus. Some of the chapters presenting the biological basis for rational therapy of disorders of the temporomandibular joint include descriptions of comparative functional anatomy, condylar and craniofacial growth, neurophysiology, and pathologic aspects of various diseases and anomalies. The reader also learns that the temporomandibular joint is an extraordinary example illustrating some of the principles of phylogeny, the primary temporomandibular joint of amphibians and reptiles having evolved to a combined gliding and hinge joint in humans. Understanding this enables one to appreciate better the biomechanics of this complex structure.

Considerable attention is also given to the masticatory musculature. Because of their involvement both as primary and secondary causes of mandibular dysfunction and temporomandibular joint disorders, great emphasis is placed on the physiology and pathology of these structures. This serves as an excellent prelude to determining correct etiology, forming an accurate differential diagnosis, and establishing appropriate methods of treatment.

The particular presentation used in this book has an obvious advantage in that it correlates current information from biology with the various clinical aspects, including new perspectives. Without question, the reader will find that this integration will make it less difficult to understand some of the perplexing problems of the temporomandibular joint.

The editors are to be commended on the choice of material, organization, and format. The text is written in a lucid style and extremely well edited. Each of the chapters is contributed by a world authority in the

particular field. Although each chapter is an entity in itself, it is intimately integrated with the rest of the book. Fourteen chapters have been updated and, with the additional 12 new chapters, reflect a great sum of current information on the various subjects. There is something for everyone in this comprehensive book: student, teacher, scientist, and clinician. The editors, as well as the authors and publishers, are to be congratulated on having prepared a volume of this magnitude, with so many excellent qualities.

Gert-Horst Schummacher

FOREWORD TO THE FOURTH EDITION

A benchmark of a publication's success is the credibility of its contents. The fourth edition of this very popular and substantive text on the temporomandibular joint and related structures continues to meet this high standard. In this edition the skills, knowledge, and expertise of major, internationally recognized authorities on the subject are again brilliantly combined. The format is logically divided into two parts: Part I, entitled "Biological Basis," and Part II, entitled "Clinical Practice: Diagnosis and Treatment." This structuring, with related correlations, provides an accurate summation of the most current scientifically accepted theory and concept, and forms the basis for a rational approach to therapy. As a clinician with a basic science background, I find this method of presentation extremely beneficial.

The two editors have a long and enviable record related to the temporomandibular joint. Over the years their dedicated efforts, knowledge, and research have opened up vistas for the thoughtful and credible management of this complex apparatus. Forty years ago, at midcentury, when this book was first published as a monograph, our basic and clinical understanding of this single facet of the stomatognathic system was woefully meager. The dental and medical professions were groping in their diagnostic and treatment protocols. In that early era of discovery, Drs. Sarnat and Laskin were among the very first to develop and present both a scientific and a clinically sound basis for our comprehension of this complex subject. Certainly, as in other scientific endeavors, there were some errors of interpretation, presentation, or omission. These were recognized early and conscientiously altered, corrected, or eliminated by the incorporation, in subsequent editions, of the most current, accurate information from authoritative authors. Thus, we have continued to witness, in these sequential editions, a unique correlation of basic science and clinical information addressing the important needs of practitioners and their patients not found in other textbooks on the subject.

The proper practice of either dentistry or medicine is based on the factual foundations of basic and clinical science. This text offers that valuable data to those desirous of enhancing their knowledge and skills related to the temporomandibular joint and associated structures. The exceptionally

broad coverage of the subject, presented by a wide spectrum of recognized and reputable contributors in a rational progression throughout the text, provides the serious student, interested scientist, and dedicated practitioner with a wealth of integrated, valuable current information. Any individual attempting to gain this material independently from research reports, journals, continuing education courses, or specialty meetings would have to expend months and even years of personal time. The accumulated information so beautifully presented in this edition accomplishes the task for the reader in an organized and authoritative manner. The editors are to be congratulated on providing us with another landmark edition of this classic text.

Harold T. Perry

PREFACE TO THE FOURTH EDITION

In the preface to the first edition of this book (1951), the need was recognized for valid information about the temporomandibular joint and its associated structures. Since then many excellent, well-documented scientific studies have appeared in the literature, and these have strengthened our knowledge base significantly. The dimensions and complexity of problems involving the temporomandibular joint, coupled with the veritable explosion of new knowledge in the past decade, warrant a fourth edition.

The chosen title indicates our philosophy. As in earlier editions, we have developed and emphasized a basic biological approach to the difficult and, in many instances, unanswered clinical problems involving the temporomandibular joint and, in the broader context, the masticatory apparatus. There are two parts to the book. Part I emphasizes the biology of the temporomandibular joint region, and incorporates clinical correlations. This serves as a foundation for Part II, which is devoted almost entirely to clinical evaluation, accurate diagnosis, and proper treatment, reinforced by reference to the basic science aspects. We are not aware of any other book on the temporomandibular joint that takes this approach.

Since the publication of the last edition, much has changed. Thus, in this fourth edition, many former concepts have been modified in the light of recent knowledge. Outdated information has been eliminated and the most recent findings in this rapidly expanding area have been added, making the scope of the book much greater. Although it is indeed a thoroughly revised work, with new contributors and new contents, we have made a concerted effort to maintain our previous standards of excellence. Our hope is that this will be *the authoritative and definitive work* in this field.

Because no one person can be expert in all aspects of such a broad subject, we have invited contributions from those whom we consider highly knowledgeable in specific areas. Thus, basic scientists and clinicians have pooled their knowledge and experience to provide a unique view of temporomandibular joint disorders. We welcome and thank the following new contributors and cocontributors: Stephen Creanor (“Comparative

Functional Anatomy"), Alphonse Burdi ("Morphogenesis"), Arthur Storey ("Neurophysiology"), Barry Sessle ("Neurobiology of Facial and Dental Pain"), Robert Yemrn ("Pathophysiology of the Masticatory Muscles"), Philip Sapp ("Pathologic Aspects"), Tore Hansson ("Pathologic Aspects of Arthritides and Derangements"), Paul Robinson ("Congenital and Developmental Anomalies"), Jeffrey Fujimoto ("Experimental Studies"), Eliot Gale ("Epidemiology"), Per-Lennart Westesson ("Imaging"), Anders Holmlund and Gustav Hellsing ("Arthroscopy"), John Rugh and Suzanne Davis ("Temporomandibular Disorders: Psychological and Behavioral Aspects"), Glenn Clark and Robert Merrill ("Diagnosis and Nonsurgical Treatment of Masticatory Muscle Pain and Dysfunction Syndrome; Diagnosis and Nonsurgical Treatment of Internal Derangements"), and Sigvard Kopp ("Diagnosis and Nonsurgical Treatment of Arthritides"). And, of course, we continue to appreciate those who contributed to the previous edition and now join us once again: Sanford Block, Henry Cherrick, E. Lloyd DuBrul, Donald Enlow, Charles Greene, William Hylander, Murray Meikle, Henry Noble, David Poswillo, and William Ware.

The main purpose of this book is to distill the enormous accumulation of biological and clinical data into a unified text that will provide an accurate basis for clinical practice. However, any multiauthored book, particularly one dealing with such a complex subject, there are bound to be some differences of opinion and interpretation. As editors, we have attempted to encourage such diversity, when controversy still exists. We see this as an advantage because, by presenting more than one expert point of view, readers may reach their own conclusions on the basis of the information provided. Such interpretation is aided by the comprehensive basic biologic background that is included.

In closing, we wish to thank those students, teachers, practitioners, and researchers whose enthusiastic reception of previous editions encouraged us to make this new effort. We acknowledge the staff at the W.B. Saunders Company for their dedicated support, which contributed so much to the value of this book.

Bernard G. Sarnat & Daniel M. Laskin

Sarnat BG, Laskin DM (editors and contributors). (1980) *The Temporomandibular Joint: A Biological Basis for Clinical Practice*, 3rd edition, Charles C Thomas, Springfield, Illinois. 512 pages, 370 figures, 7 tables.

FOREWORD TO THE THIRD EDITION

The temporomandibular joint, a part of the masticatory apparatus, is a highly complex and precisely integrated morphologicofunctional unit. It has a long evolutionary history. Soft parts preceded hard; function preceded form; and need was the arbiter of response, with the changing environment being the decisive trigger. To postulate a logical sequence: environmental need led to functional response, which in turn led to structural adaptation. Thus speaks the phylogenetic record.

Ontogeny joins phylogeny in pointing to the intricate morphofunctional nature of the temporomandibular joint: it has both a hinge and a gliding action; it is a factor in deglutition; it facilitates the soft tissue–mandibular mechanisms involved in speech; it plays an important role as a growth locus in the age-unfolding of the craniofacial complex.

The temporomandibular joint is subject to the same pathologic and pathophysiologic disorders as other joints of the human body. Anatomical and functional differences, however, require a special understanding of the complex relationships between teeth, muscle, and bone that influence the clinical manifestations of these conditions and affect their treatment. Developing such an understanding requires a broad scope of information that is difficult to obtain in one place and in comprehensible form. This authoritative book fills the void in the important subject of the temporomandibular joint and masticatory apparatus.

The first edition served this need remarkably well, as evidenced by the fact that it was used as a reference in *Gray's Anatomy*, was used in undergraduate, graduate and post-graduate courses, and was a source of ready reference for many clinicians. The second edition re-evaluated the conceptual principles and added new vistas of phylogeny and embryology, besides having an increased scope of clinical interpretation and treatment. In the third edition the scope has been increased further, methodology has been amplified, treatment goals have been envisioned and

extended, and a far greater depth of integrative evaluation and interpretation is manifest from chapter to chapter.

A wide variety of difficult, complex clinical problems is associated with the masticatory system. These are brought to the attention of many different disciplines in dentistry, medicine, and psychology. The coeditors, with their extensive research and clinical experience over many years, are admirably equipped to both edit and contribute to this comprehensive work, which stands as a giant by itself.

Wilton Marion Krogman

PREFACE TO THE THIRD EDITION

Time brings change. Since the publication of the second edition of this book, much has changed. Thus, a new edition is justified to modify past concepts in the light of current knowledge, to eliminate information that is outdated or less useful, and to add recent or more useful information. This publication not only reflects such changes, but also provides a depth and scope far greater than in the past. The third edition is indeed a new book with many new contributors and substantial new contents, and with the same high editorial and professional standards. As in the previous editions, the basic science approach to clinical practice is emphasized. Our hope is that this will be the authoritative, definitive work related to the temporomandibular joint and masticatory system.

There are two parts to the book. Part I pertains primarily to the biology of the temporomandibular joint with some clinical correlations. Part II is devoted essentially to concepts of clinical practice, accurate diagnosis, and proper treatment, reinforced by reference to the basic science aspects. In this edition further emphasis is given to complex clinical problems and in particular to the myofascial pain–dysfunction syndrome. Because of the many new correlations between the basic and clinical sciences, the title has been modified to *The Temporomandibular Joint: A Biological Basis for Clinical Practice.*

Unfortunately, in the care of many complex problems of the temporomandibular joint and related structures, iatrogenic disease is not uncommon. A cardinal principle in effective treatment is first to do no harm — *primum non nocere.* In this book the emphasis is on this theme as well as on the use of therapy that does not produce irreversible changes.

In any multiauthored book there may be differences of opinion and interpretation of findings. No editorial privileges were exercised when such situations existed. This is as it should be. Thus, in some chapters varying and differing thoughts are expressed. For example, the role of the condyle as a primary site of growth has been challenged by some of the contributors. Is this position the correct one or is it possible that at different times the growth function of the condyle changes? At present there is neither unanimity nor sufficient evidence for a positive decision. Because

of the many important basic clinical relationships, this problem merits continued study. Hopefully, by the time of publication of the fourth edition there will be further clarification.

Although this is a multiauthored book, the selection of topics and their order of presentation provide a continuity enabling the reader to progress from one section to the next using the previous information as a basis of understanding. At the same time, individual chapters can be reviewed when specific questions arise. The various chapters are extensively referenced, thus offering a source of additional information for those interested in greater detail. Each contributor is an expert in the field, so that the material presented is not only authoritative but also current.

Of the distinguished contributors to the first edition, most have died. Our sincere respects and thanks are given to them for their contributions to our fundamental knowledge of the masticatory apparatus. For this third edition we would like to thank all of the current contributors, as well as the many others involved directly or indirectly in its development, for their excellent cooperation, patience, and understanding. Finally, permit me (B.G.S.) to take this opportunity to welcome with pleasure a colleague and former student, Daniel M. Laskin, as the coeditor of this volume.

Bernard G. Sarnat & Daniel M. Laskin

Sarnat BG (editor). (1964) *The Temporomandibular Joint*, 2nd edition, Charles C Thomas, Springfield, Illinois. 260 pages, 112 figures.

PREFACE TO THE SECOND EDITION

The temporomandibular joint, which is part of a higher unit of structure, the masticatory system, represents a unique functional adaptation to the evolutionary changes in the mammalian skull. It differs from other joints of the body in several ways. First, it is a complex joint with an articular disk and it is capable of an unusual combination of hinging and gliding movements. Second, it is exceptional because the spatial relations of the component parts are influenced not only by muscular balance and structural morphology but also by the occlusion and malocclusion of the teeth. Third, it is unique because the joints cannot operate independently; both act as a single functional unit. Any alteration in the activity of one side will therefore affect the other, an important factor frequently overlooked in the analysis of disturbances in this region. Last, the articular surfaces of this joint are not covered by hyaline cartilage but by avascular fibrous tissue with a few scattered cartilage cells. Just beneath this layer on the condyle is an epiphyseal-like growth center. This serves as both a pacemaker and organizer for growth of the mandible. All these morphological and functional variations contribute to the complex problems in both the diagnosis and the treatment of temporomandibular joint disease.

Along with the contributors, the editor is grateful for the opportunity to acknowledge the cordial reception given to the first edition of this book. It was a source of special pleasure to learn of its acceptance not only by the medical and dental professions, but also by those in the basic sciences.

The same general purpose has been kept in mind in the preparation of this edition as in the previous one, namely to present and correlate the latest authoritative information, both basic and clinical, pertaining to the temporomandibular joint and related structures. The original contributors have had the privilege of revising the text and adding new material. In addition, several new chapters have been included. They are "Evolution of the Temporomandibular Joint," by Dr. E. Lloyd Du Brul; "Embryological Development of the Temporomandibular Joint," by Dr. Barnet M. Levy;

"Roentgenography of the Temporomandibular Joint," by Dr. Robert M. Ricketts; and "Surgery of the Temporomandibular Joint," by Drs. Bernard G. Sarnat and Daniel M. Laskin.

It is with deep regret that a contributor to the first edition has been claimed untimely by death. This opportunity is taken to pay our final respects to our personal friend and longtime colleague, Dr. Joseph P. Weinmann.

Bernard G. Sarnat

Sarnat BG (editor). (1951) *The Temporomandibular Joint*, Charles C Thomas, Springfield, Illinois. 165 pages, 62 illustrations.

PREFACE TO THE FIRST EDITION

There is an increasing need for a critical examination and evaluation of our knowledge pertaining to the temporomandibular articulation and related structures. Although there is a considerable literature on the clinical aspects of the temporomandibular joint, some of it is based upon interpretations which are not entirely valid. Unfortunately, this misinformation has been perpetuated by being "handed down" from one report to another. The need for correct information is evidenced by the number of difficult clinical problems in terms of diagnosis and treatment directly or indirectly associated with this region.

The purpose of this monograph is to bring some of our knowledge up to date and to correct some of the misconceptions by a review and analysis of the temporomandibular articulation from the point of view of both the basic and clinical sciences. Most disturbances of the temporomandibular joint are either congenital, inflammatory, traumatic, or neoplastic in nature. Congenital absence or deficiency of the condyle, which contains the most important growth site of the mandible, is associated with marked deformity of the face. In the past, middle ear infection has been the most common inflammatory lesion which spread to the temporomandibular joint and not only affected the condylar growth site but also caused an ankyiosis. Arthritis of the temporomandibular joint may be on either an inflammatory or a traumatic basis. The latter is usually a result of faulty occlusion. Benign tumors of the condyle are not common and malignant tumors are rare.

The following will be considered in relation to the temporomandibular joint: (1) the masticatory apparatus from a gross anatomical and functional point of view; (2) the growth and development of the jaws and face; (3) histologic, pathologic, and experimental aspects; and (4) treatment by means of corrective dentistry. This monograph, however, is not intended to serve as a complete review and summary of the subject, but rather as a basis for critical evaluation of the literature and for further study.

Articulations are part of a higher functional unit. The temporomandibular joint is part of the masticatory apparatus, comprising not only

this joint but also the teeth and their supporting structures, the jaws and their musculature. Alteration in the functions of any one of these structures will be reflected in all other parts of the masticatory apparatus.

The temporomandibular joint is a delicately balanced structure, and its functional and anatomic integrity is dependent upon the normal relations and functions of the rest of the masticatory apparatus. It is well known, for example, that traumatic arthritis can be caused by an occlusal disharmony. The correct diagnosis and proper treatment of such conditions, however, are dependent upon an understanding of the normal structure and function as well as of the pathologic physiology of the masticatory apparatus.

In order to clarify some of the problems related to the temporomandibular joint, a series of symposia and lectures were organized by the editor. In selecting the faculty and subject matter, the following objectives were set down: (1) to present the latest authoritative basic science information, including correlative material pertaining to the entire masticatory apparatus; and (2) on the basis of this knowledge, to interpret the clinical findings, diagnosis, and treatment of these disorders.

This program was offered through the Postgraduate Division of the University of Illinois College of Dentistry during April and May of 1949 and much of it will be included in the Postgraduate Long Distance Telephone Extension broadcasts of December 10, 1951 and January 14, 1952. The 1949 course was received most enthusiastically by all who attended, namely general dental and medical practitioners, otologists, prosthodontists, orthodontists, and oral, plastic and orthopedic surgeons. Many students who took the course, and others who had heard about it, indicated a desire to have this information made available in permanent form. Because of these requests, the material has been published.

This monograph represents the combined efforts of many individuals. With their willing and splendid cooperation, the organization, development, and realization of this publication has been a source of especial pleasure. I also wish to express my thanks to Miss Claire Stanton for her assistance.

Bernard G. Sarnat

Condylar Tumors

UNILATERAL HYPERPLASIA OF THE MANDIBULAR CONDYLE

This condition is generally characterized by a slowly developing, progressive, unilateral enlargement of the condyle causing facial asymmetry and shifting of the midline of the chin to the unaffected side, resulting in a cross-bite malocclusion (Fig. 8.1). Unilateral overgrowth of the mandible occurs with roentgenographic evidence of enlargement of the condyle (Fig. 8.2). The ramus and the body of the mandible are longer and larger on the affected side, giving a prognathic appearance. There is a compensatory eruption of the maxillary teeth and downward growth of the maxillary alveolar bone in an attempt to maintain occlusion. There is also compensatory eruption of the mandibular teeth resulting in increased alveolar height and a bowing effect on the inferior border of the mandible.

The discrepancy between the two sides of the mandible usually first becomes apparent during the second decade of life. A chondroma or osteochondroma can produce a similar mandibular deformity.

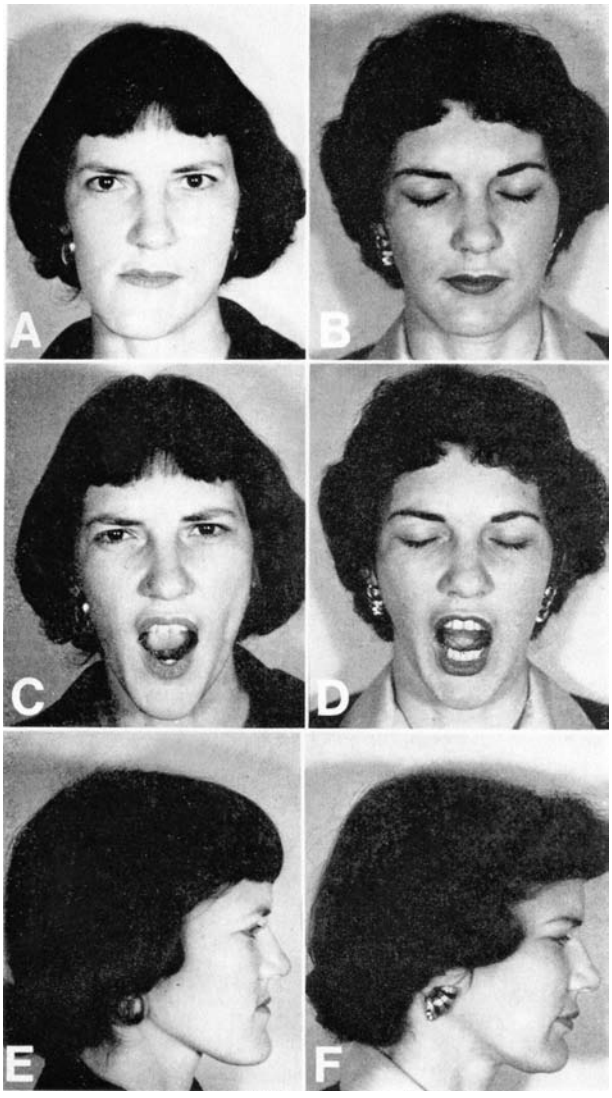

Fig. 8.1 Preoperative (A, C, E) and postoperative (B, D, F) photographs of a patient with left unilateral condylar osteoma resulting in increased length of the left side of the mandible and a cross-bite malocclusion. Note, in the preoperative photograph with the jaws in occlusion (A), that the middle of the chin deviates to the patient's right and, with the mouth open, (C) that the chin is in the midline. [From: Sarnat BG, Laskin DM (eds.) and contributors. (1991) *The Temporomandibular Joint: A Biological Basis for Clinical Practice*, 4th ed. W.B. Saunders, Philadelphia, Pennsylvania. 505 pp.]

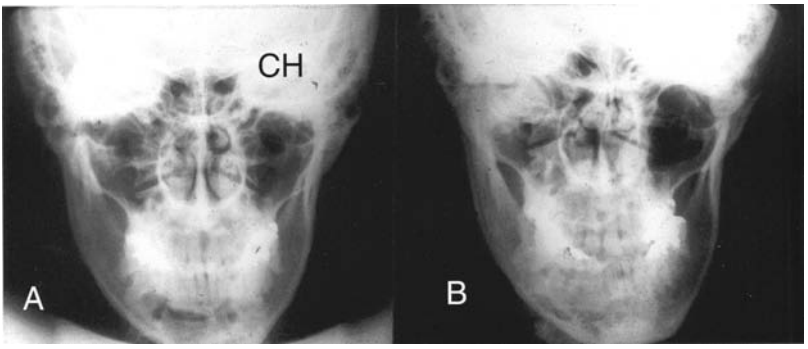

Fig. 8.2 (**A**) Preoperative roentgenograph of a patient (Fig. 8.1) with a left condylar hyperplasia (CH). Note that with the jaws brought together the midline of the chin is shifted. (**B**) Postoperative roentgenograph of the same patient in **A** after resection of the left condylar enlargement and repositioning of the mandible. [From: Sarnat BG. (1964) *The Temporomandibular Joint*, 2nd ed. CC Thomas, Springfield, Illinois.]

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Overgrowth of Coronoid Processes*

INTRODUCTION

In differential diagnosis of ankylosis of the mandible, bilateral generalized enlargement of the mandibular coronoid processes is rarely reported. In one patient laminagrams were helpful in arriving at the proper diagnosis, and movement was restored by surgical removal of the enlarged coronoid processes through an intraoral approach. Over a 14-year period, several physicians and dentists had examined this patient, but the proper diagnosis had been overlooked.

An important and not infrequent diagnostic problem with which the dentist and, less often, the physician may be confronted is restricted opening of the mouth. Limitation of motion in a joint is related to some involvement of the masticatory system and is either intra-articular (true ankylosis) or extra-articular (false ankylosis).

This article is concerned with an unusual and rarely reported condition of bilateral extensive general enlargement of the mandibular coronoid processes causing a definite limitation of mandibular movement because of impingement on the zygomatic bone.

*Excerpted from: Lyon, Leonard Z, Sarnat BG. (1963) Limited opening of the mouth caused by enlarged coronoid processes: report of case. *J Am Dent Assoc* **67**: 644–650.

REPORT OF CASE

A white man, 27 years old, complained of restricted opening of the mouth and inability to protrude his lower jaw since the age of 13 years. It had grown worse until he was about 22 years old. Since that time, there had been no apparent change. Roentgenographic studies, including laminagrams, were made, with a diagnosis of arthritis of the temporomandibular joint. Cortisone had been injected intra-articularly, with no change in the condition. The patient had been seeing a psychiatrist for the previous three years because of a speech defect: there was no history of bruxism. Complete medical studies disclosed no other problems.

Examination

Physical examination revealed that the patient was well developed and well nourished. The face was developed within normal limits and was symmetrical. With maximum effort, there was limited opening of the mouth; the distance between the maxillary and the mandibular incisors was 11 mm (Fig. 9.1A). The patient was unable to protrude the mandible, and lateral motion was limited. On opening and closing the mouth, restricted movement of the condyles in the mandibular fossae was palpated bilaterally, and there was no shifting of the midpoint of the chin. No spasm of the masticatory muscles was found.

A tentative diagnosis of bilateral enlargement of the coronoid processes was made.

Examination of laminagrams confirmed the diagnosis of bilateral enlarged coronoid processes which impinged on the zygomatic bones in opening the mouth and restricted mandibular motion.

Operation

With the patient under local, intravenous (thiopental sodium), and nasoendotracheal (gas) anesthesia, an intraoral incision was made from the distal surface of the mandibular second molar and upward along the anterior border of the ramus. The incision was extended anteriorly and inferiorly along the buccal surfaces of the necks of the molars. The tissues were

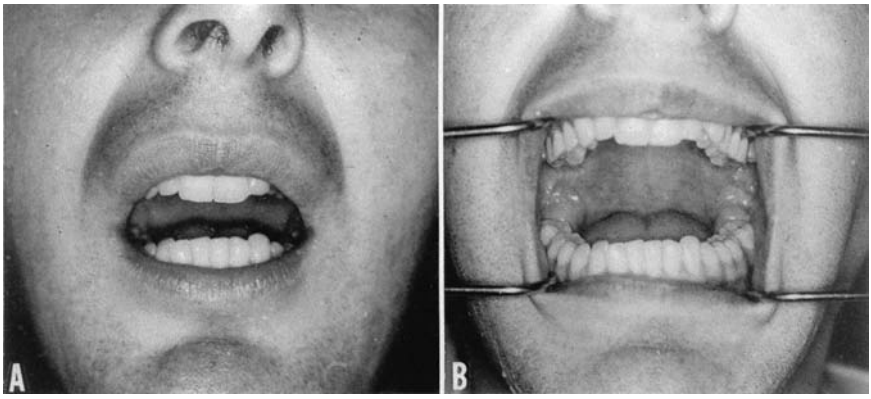

Fig. 9.1 Photographs taken preoperatively (**A**) and two months postoperatively (**B**) of a patient with limitation of opening his mouth because of impingement of enlarged coronoid processes on zygomatic bones.

dissected free, and the anterior border of the ramus was exposed up to the level of the sigmoid notch, thereby revealing the coronoid process. By means of a long surgical crosscut bur, the coronoid process was sectioned partially at its base and then separated completely from the mandibular ramus by means of a chisel and mallet. Additional dissection was required to free the coronoid process from the temporalis muscle and tendon fibers. The coronoid process was then removed. The soft tissues were reapproximated, and the wound was closed with interrupted black sutures.

Postoperative Course

The patient's postoperative course was satisfactory and uncomplicated. He had little pain but considerable edema, which gradually subsided in about 5 days. Within 18 days, he was able to open his mouth to a distance of 19 mm between the maxillary and the mandibular incisors; in three and a half months, to a distance of 35 mm (Fig. 9.1B). He was encouraged during this period to exercise his jaws and to use wooden, spring clip clothespins to increase the vertical opening. The patient was cooperative and elated with his progress. He stated that he was able to eat a complete

diet better, faster, and with less fatigue in chewing than at any time in the previous 14 years.

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Surgery of the Mandible: Some Clinical and Experimental Considerations*

INTRODUCTION

An understanding of normal growth of the mandible forms the basis for early recognition and proper surgical treatment of a number of deformities. Mandibular growth is a result of an integration of activities in a number of regions. Two types of bone growth occur in the following principal areas: (1) appositional, at all of the free borders, with the exception of the anterior border of the ramus; and (2) epiphysis-like growth at the condyle (Fig. 3.1). Concurrently there is continuous surface remodeling. Normal development of the mandible is dependent upon the synchronous coordination of the growth activities of the various sites. By means of both clinical and experimental studies, information has been obtained on the role played by these various sites. Any interference which will affect the growth sites will alter the orderly progression of development and will result in some type of mandibular deformity.

The purposes of this report are (1) to present experimental and clinical material regarding growth of the mandible, (2) to correlate this with the development of pathologic conditions, and (3) to consider in the light of this information the surgical treatment of some mandibular deformities.

*Excerpted from: Sarnat BG, Robinson IB. (1956) Surgery of the mandible: some clinical and experimental considerations. *Plast Reconstr Surg* 17: 27–57.

Growth of the condyle is by endochondral ossification, as in an epiphysis. Microscopic examination reveals the presence of three zones: (1) chondrogenic, (2) cartilaginous, and (3) osseous. The condyle is capped by a narrow layer of vascular fibrous tissue, which contains connective tissue cells and a few cartilage cells. The inner layer of this covering is chondrogenic, giving rise to hyaline cartilage cells, which constitute the second zone. In the third zone destruction of the cartilage and ossification around the cartilage scaffolding can be seen. The condylar cartilage of the mandible is not homologous to an epiphyseal cartilage, because it is not interposed between two bony parts. The condylar growth site appears in the 50 mm stage of the embryo and its activity attains peak levels during the prenatal period. Postnatally, this growth site maintains its activity longer than most other centers in the skull, persisting in the human until at least the 20th year. This provides the forward and downward vector for mandibular growth and contributes as well to increased width of the jaw.

ABNORMAL GROWTH: SOME SURGICAL CONSIDERATIONS

Generally, mandibular growth deformities can be classified into those in which the mandible is larger or smaller than normal. Although the deformity is often bilaterally symmetrical, unilateral disturbances are not uncommon.

The condyle is the most important growth site of the mandible. Any disturbance of this area which will decrease the growth activity will result in an underdeveloped mandible. The effect that injury will have upon the growing condyle and subsequent deformity of the jaw is determined not only by the severity and duration of the noxious agent, but also by the particular time of occurrence. Thus, the effect will be more extreme early in life, when condylar growth activity is greater, than later in life, when condylar growth activity is considerably decreased and the mandible has nearly assumed its adult shape and size.

UNDERDEVELOPMENT OF THE MANDIBLE

The underdeveloped mandible may be caused by a disturbance of the condylar growth site. Unilateral disorders of the condyle may be due to

local conditions although, occasionally, they may result from some type of systemic involvement. Bilateral disturbances of the condyle arise mainly from some general systemic condition although they, too, may result from local causes such as a bilateral condylar fracture.

The characteristic clinical and roentgenographic observations on the human mandible following an arrest of growth of one condyle are: (1) on the side of injury, a short, wide condyle and ramus; a longer, heavier, and posteriorly directed coronoid process; a shallow sigmoid notch; a short body; an antegonial notch; and fullness of the face; (2) on the opposite, uninjured side, elongation of the body and a flat appearance of the face; and (3) malocclusion, with the mandible skewed toward the side of the affected condyle.

With a bilateral condylar growth arrest there is usually a symmetrical lack of growth of the mandible. This is characterized by the *vogelgesicht* or bird face, a short mandible, with the chin retruded to about the level of the hyoid bone. Antegonial notching is present bilaterally. The teeth are malposed, impacted, and unerupted, and some of them may be in the ramus.

Local Causes

Any local interference, such as trauma, inflammation, and radiation, which will affect the condylar growth site will alter the orderly progression of development and will result in some type of mandibular deformity.

Trauma

Growth arrest of the mandibular condyle may result from birth trauma (sometimes sustained during forceps or breech deliveries) directly to the joint area or transmitted from another part of the jaw. Some degree of facial paralysis may be noted at the time of injury but the deformity is usually not discovered until months afterward. Later in life trauma sustained directly to the joint or to the chin (a scar may be noted) with the force transmitted to the condyle may result in an underdeveloped mandible due to arrested growth.

The effects of removal of the mandibular condyle or condyles on the growth of the mandible were demonstrated most dramatically in

experiments on monkeys (see Chaps. 3 and 4). In the animals in which only one condyle was removed, the ramus of that side was considerably shorter and somewhat wider than on the unoperated-on side. The failure of the ramus (and coronoid process) to grow posteriorly and its altered configuration may be explained by the absence of the condylar growth site. The angle at which the ramus met the body approached more nearly a right angle in the operated-on jaws than in the normal, which tended toward the obtuse. Blair[1] stated that where limitation of motion was due to a scar, the ramus may become abnormally broad anteroposteriorly, and he explained this by a failure of the normal resorption of the anterior border of the ramus.

Clinically, patients with condylar growth arrest and mandibular deformity may have disturbances in the eruption and the position of teeth, particularly in the region of the affected ramus. This is true for at least two reasons. First, there is a lack of increase in the height of the mandibular ramus to open the space between the upper and lower jaws into which the teeth erupt and the alveolar processes grow. Second, posterior growth of the ramus is affected, so that length of the body of the mandible is less, with not as much room for the eruption of the teeth. It is well known that the dependence of tooth eruption upon the growth of bone(s) is considerable.

Inflammation

Inflammation on an infectious basis is another important cause of underdevelopment of the mandible. Primary infection of the condylar cartilage is uncommon. More frequent is the spread of regional infection to this area. In the past, otitis media, as a result of an upper respiratory infection, or scarlet fever was a frequent antecedent to suppuration of the temporomandibular region. With the advent of the antibiotics this complication is now seldom seen. Growth arrest may also result, secondary to a dental infection, with spread to the regional tissues and the joint.

Osteomyelitis of the temporomandibular joint is rare. If it does occur during the period of active growth, it may inhibit or decrease condylar growth activity on the affected side, with a resultant asymmetrical mandible.

Radiation damage in this area has also produced growth arrests, as is evidenced clinically and experimentally.

ANKYLOSIS AND CONDYLAR RESECTION

Deformity and ankylosis of the mandible are frequently found occurring together. Because of this, the deformity of the jaw is sometimes mistakenly believed to be a result of the ankylosis. Actually, both the deformity of the jaw and the ankylosis have been caused by the same etiologic agent. Thus, a child may have a middle ear infection which spread to the temporomandibular joint and affected both the condylar growth site and the temporomandibular joint. As a result the ankylosis is manifest early, whereas the growth deformity is not apparent until later.

In patients with almost complete inability to open the mouth, where condylar growth has not been affected, such as in a false or extra-articular ankylosis, there is no deformity of the jaw. In addition, where the temporomandibular joint has been affected on only one side with condylar growth arrest and ankylosis, the characteristic findings are not seen on the opposite side of the jaw.

Blair[1] described the change of the fulcrum and the type of lever of the mandible subsequent to bilateral condylar resection. He believed that, after removal of both condyles, the masticatory muscles would pull the mandible up into the fossa posteriorly and, thus, produce an open bite in the region of the incisors. To offset this he fixed the jaws in occlusion and, after several weeks, felt that a muscular balance was established that closely simulated normal movement.

The condyle plays a vital role in mandibular and facial growth. Before this important growth site is damaged or removed in children, due consideration should be given to the serious deformity which must result. Thus, in children with ankylosis of the temporomandibular joint, it may be desirable to postpone resection of the condyle until maximal mandibular growth has been attained. It should be determined whether or not the growth site of the condyle has been destroyed. This can be evaluated by taking serial cephalometric roentgenographs at 6–12-month intervals. If the study indicates that growth activity is continuing, postponement of surgical intervention should be considered to avoid

a more severe growth arrest. This does not constitute a problem in adults.

Systemic Causes

Hereditary and congenital conditions

Chondrodystrophia fetalis (achondroplasia). In this condition there is a hereditary dysfunction of cartilage characterized by a failure to contribute the normal degree of growth. The result is a dwarf exhibiting short limbs and lack of development of the middle third of the face, with concomitant deep saddling of the nose, relative bulging of the forehead and a relative mandibular prognathism. Since the important growth site of the mandible, i.e. the condyle, also contains cartilage, the last finding seems paradoxical. One explanation may be that the condylar cartilage is covered by connective tissue and, thus, it normally grows appositionally, as well as interstitially.[2] Since, in chondrodystrophy, only interstitial proliferation of cartilage is arrested and not appositional, the epiphyseal cartilages cease to grow altogether. The cartilage in the condyle of the mandible can continue its growth under those circumstances because appositional growth of the cartilage compensates, at least partly, for the loss of interstitial growth.

Another explanation for the relative prognathism is based on the number of growth sites in the skull and mandible. The two main sites of growth in the cranial base are the spheno-occipital and sphenoethmoidal synchondroses, while there is only one in the mandible, i.e. the condylar cartilage. Premature cessation of cartilaginous growth and, consequently, premature synostosis of the bones, causes permanent cessation of growth in the region. Since there are two main growth centers in the cranial base and only one in the mandible, it is quite possible that lack of total incremental growth in the latter region will not be affected as much as the two together in the cranial base.

Mandibular micrognathia (Pierre Robin syndrome) occurs as a congenital anomaly associated with cleft palate, glossoptosis, inspiratory retraction of the sternum, cyanosis, and malnutrition. The mandible

possesses remarkable potentialities for downward and forward movement in patients with mandibular micrognathia. Thus, the glossoptosis is minimized and spontaneous resolution of the respiratory and feeding problems occurs. In most instances, the increment of mandibular growth, as related to total facial growth, is sufficient to overcome the extreme lack of development of the chin that is observed at birth.

Attempts have been made to stimulate the growth of the mandible by a variety of mechanical devices or surgical procedures. For example, a special nursing bottle was designed to force the infant to protrude the mandible to obtain nourishment and, by this protrusion, to stimulate mandibular growth.[4] The nursing care probably enabled the infant to survive until mandibular growth was sufficient to provide a more adequate airway. In another report, continuous traction on the mandible was maintained by circumferential wiring at the symphysis. The authors claimed growth-stimulating properties for this procedure.[5] Mandibular growth probably occurred spontaneously and not as a result of the traction. In this procedure care must be taken that the circumferential wire does not cut through the mandible. Suturing the tongue to the lip has been done to improve the airway.[6] Distraction osteogenesis is the desired technique today.

Micrognathia occurs in offspring whose mothers received X-ray irradiation for hemorrhage, myoma, or carcinoma of the uterus, while pregnant. Several such cases were reported by Leist in 1920. They were associated with microcephalus, micro-obthalmus, and deficiency in the dentition.[7]

Other anomalies. Various other congenital anomalies — usually unilateral but sometimes bilateral — of the temporomandibular joint and related structures have been reported. They range from underdevelopment of only the condyle to underdevelopment of one side of the face with associated malocclusion. The condylar and coronoid processes, the lower ramus, and even part of the mandibular body may be absent. Associated with this, the external ear may be abnormal in configuration, size, and position, or partially or totally absent. The external opening of the auditory canal is sometimes unexposed and the canal, the middle and inner ears, and temporal bone may be deficient.

Inflammatory lesions

In addition to the local and regional causes, the hematogenous and general ones may also retard condylar growth. This is true of the suppurative arthritis of gonococcal origin, which now, however, is seldom seen. The organisms responsible for osteomyelitis at a distant site may spread via the bloodstream to the temporomandibular joint and set up a new focus with resulting ankylosis and growth arrest. Rheumatoid arthritis may also be a cause. In fact, this may be the first joint to manifest clinical symptoms. Evidence indicates that the proliferation of cartilage in the condylar head is inhibited in this disease. This probably occurs in much the same manner as involvement of joints elsewhere in the body. Since the temporomandibular joint is critical to normal mandibular development, a symmetrical lack of growth of the mandible results.

Dietary deficiencies

There are a number of articles dealing mostly with the effects on the growing mandibular condyle of vitamin-deficient diets and of excessive or deficient amounts of hormones. Because these agents (or lack of them) have a systemic effect, the manifestations seen in the condylar cartilage area are only part of the total picture. Congenital anomalies have been produced in young animals when the fetal environment has been influenced by changes in atmospheric pressure,[8] deficiencies in the maternal diet of single nutritional elements,[9–11] excessive intake of vitamin A,[12] and various mechanical and actinic factors.[13,14]

Since growth of the condyle is by endochondral ossification, as in an epiphysis, dietary restrictions, which affect various cartilaginous growth sites, will also alter the growth and development of the mandible. For example, in rachitic children the reduced cartilaginous growth not only produces a shortness of the extremities, but also results in a marked facial disharmony. Delayed eruption and malpositioning of the teeth also occur, since the intermaxillary space required for eruption is decreased as a result of the shorter ramus. In turn, the anterior border of the ramus fails to resorb at the time the teeth are about to erupt. Normal eruption

of the teeth is entirely dependent upon the normal growth of the mandibular ramus, which in turn may be directed by the activity of the condylar cartilage.

Rats fed rachitogenic diets showed an increased thickness of the condylar cartilage and a clubbing of the condyle, with similar findings for the epiphyseal and articular cartilages.[15] Pantothenic acid,[16] tryptophane[17] and riboflavin[18]-deficient diets inhibit normal growth and development of the cartilage in the mandibular condyle of mice. No specific information was reported, however, on mandibular growth.

Endocrine disturbances: Cretinism

The severe and striking effects of hypothyroidism are seen in understature and disproportion. Cephalometric studies of cretins revealed a generalized retardation of growth, within the facial area.[19] The head is too large for the body and the cranial skeleton is larger than the facial skeleton. The synchondroses at the cranial base and the sutures remain open. The teeth are retarded in development and in eruption, but their size is not affected. Therefore, the teeth and the alveolar process seem overly large for the body of the maxilla and mandible. Retardation in anteroposterior facial growth is induced by the lag in the development of the cranial base, which normally carries the upper part of the face forward. The mandibular ramus normally grows posteriorly because of the association of the condyle with the mandibular fossa of the bone.

OVERDEVELOPMENT OF THE MANDIBLE

Local Causes

Bone tissue, despite its hard, calcified nature, is highly adaptive to different degrees of tension and pressure. Local enlargement of the mandible in the child or adult may be a result of intrinsic factors (tumors) or extrinsic factors (enlarged tongue). In these instances the increase in size is a result of increased apposition of bone, which may be accompanied by some resorption of bone.

Intrinsic factors: Tumors

The basic and dual response of resorption and apposition is evident in the reaction of bone to the pressure of growing tumors. Despite the spread of a tumor, the bone does not always become perforated, tending instead to maintain itself with only gradual changes in size and shape. The bone tissue is resorbed in the path of the tumor pressure but, at the same time, the loss and weakening of bone are compensated for by the formation of new bone along the periosteal surface away from the tumor. If destruction of bone proceeds at a greater rate than the compensatory formation of *new* bone, a pathologic fracture may result.

Extrinsic factors: Enlarged tongue

While true macroglossia (local or systemic) is rare, relative macroglossia is not infrequently encountered in children and, particularly, infants. The absolute size of the tongue is not nearly as important as its size relative to the oral cavity. At birth the tongue normally is positioned between the gum pads of the jaws. Since the jaws increase in size more rapidly than the tongue, it is eventually contained within the dental arches. In some instances where there is an overdevelopment of the muscular part of the tongue or in cases of lymphangioma, which may form internally and cause a diffuse general enlargement, the pressure of the oversize tongue against the lingual aspect of the mandible may result in increased apposition of bone on the labial surface.

Idiopathic

Unilateral hyperplasia of the mandibular condyle

This condition is characterized by a slowly progressive unilateral enlargement of the mandible, facial asymmetry, and shifting of the midpoint of the chin to the unaffected side with cross-bite malocclusion. The discrepancy between the two sides of the mandible usually first becomes apparent during the second decade of life. As a result of hyperactivity or persistent activity of the condylar growth site, the ramus and body of that

side are longer and larger than those of the opposite side of the mandible. Concomitant with increased downward movement of the mandible and the teeth which it carries, there is a compensatory eruption of the maxillary teeth and downward growth of maxillary alveolar bone in an attempt to maintain the teeth in occlusion.

For reasons unknown at this time, sometimes trauma, either one condylar growth site becomes more active than the other or at a later period in life the growth activity persists in one, while the other condyle is no longer active. Rushton[20] relates enlargement of the condyle to abnormally rapid chondrogenesis with subsequent ossification. The histological picture is approximately normal. In addition, the condition is self-limiting and, thus, not truly neoplastic. Rushton further states that a diagnosis of chondroma was made during the period when growth was still active and that of osteoma after growth had ceased.

Patients with overgrowth of one side of the mandible seek treatment because of (1) the impaired masticatory function, (2) the asymmetry, and (3) pain. Thus, treatment is directed toward the correction of these three problems. In some instances osteotomy of the condylar neck or ramus of the involved side and repositioning of the mandible will suffice. The treatment of choice is usually resection of the condyle. Sometimes osteotomy of the unaffected side of the mandible is also necessary, to obtain the desired repositioning. Postoperatively, the jaws are fixed in occlusion for several weeks, to avoid or minimize overshifting of the midpoint of the chin in a unilateral resection and opening of the bite anteriorly in a bilateral resection. At postmortem in monkeys after uni- or bilateral removal of the mandibular condyles, fibrous tissue had formed in the resected area (see Chap. 3). It was integrally united with the ramus and articulated with the temporal bone. Thus, the fibrous tissue served as a support for the mandible. Although improvement is obtained with surgical repositioning of the mandible, preoperative and postoperative orthodontic treatment will result in a more exact occlusion. In addition, the orthodontic appliances can be utilized to keep the jaws in occlusion with intermaxillary wires or elastics. The bony overgrowth of the mandibular body and ramus will tend to correct itself slowly by remodeling. The timing of surgical treatment is an important consideration in children. For instance, if the hyperactive condylar growth site is removed or arrested, the once-larger

side of the mandible may eventually fall behind the unoperated-on growing side.

Prenatal unilateral hypertrophy of the face

In prenatal unilateral hypertrophy of the face (and sometimes including other parts of the body), not only are the jaws and teeth larger on one side but also the other facial bones and the soft structures, including the ear. Although this condition is present at birth, the differences become accentuated with growth.

Prognathic mandible

The patient with a symmetrically prominent mandible frequently presents for cosmetic treatment of deformity and improvement of impaired masticatory function. The deformity may be the cause of personality changes. The prognathic mandible is larger and in a more forward position than the maxilla, so that the chin appears to be unduly prominent. In addition, the normal intermaxillary relationship between the teeth is disturbed, so that the mandibular teeth are more anterior to the comparable ones in the maxilla. While there may be considerable morphologic variation within the group of prognathic mandibles, they do have the following characteristic features in common: (1) the mandibular angle tends to be more obtuse, (2) the sigmoid notch forms the arc of a larger circle, (3) the condylar neck is longer and narrower, and (4) the linear distance between the head of the condyle and the gnathion (a point on the chin) is greater than in the normal mandible.

No definite etiologic factors have been implicated. It is possible that some of the skeletal dyscrasias of the face are present at birth and they proceed to unfold with growth. This is probably the case in the development of the *true* prognathic mandible as a result of a hyperactive growth site at the mandibular condyle. In rare instances the size of the mandible is normal, until some later time when pituitary dysfunction (giantism and acromegaly) leads to an overgrowth and very characteristic prognathism.

The primary indications for surgical treatment of the prognathic mandible are the improvement of mastication and esthetics. Many different

surgical procedures have been utilized to reposition the mandible. Surgery and orthodontia complement each other in treatment of the prognathic mandible. The surgery permits extensive repositioning of the jaw. Orthodontic treatment serves to eliminate tooth interference which might prevent a comfortable, balanced bite and, postoperatively, the orthodontic appliance provides a positive means of controlling the jaw relations with the use of intermaxillary rubber bands or wires.

Endocrine Disturbances: Giantism and Acromegaly

Overactivity of the eosinophilic cells of the anterior lobe of the pituitary gland may affect the growth of the jaws. This is well illustrated in giantism and acromegaly.

Giantism

In giantism there is a proportionate overdevelopment of the osseous system before the epiphyses have closed. Some parts of the body complete their growth so soon after birth that even an early onset of the disease has no influence on them. The brain and other higher sense organs are in this category and a disproportion of skull and face is, therefore, found to develop. Secondary to lack of growth of the cranial skeleton, a disharmony between the upper and lower jaws may develop. The upper facial skeleton is at least partly dependent for its growth on that of the cranial base to which it is attached. Giants show a preponderance of growth in the facial skeleton and sometimes a massiveness and protrusion of the mandible. In the jaws there is a marked disproportion between the size of the crowns of the teeth, which show no enlargement, and the size of the jaw bones.

Acromegaly

In contrast to giantism or hyperpituitarism of adolescence, acromegaly or hyperpituitarism of the adult is characterized by the development of striking disharmonies of the body. Statural growth is not affected because the disease sets in after the epiphyses have closed, but the skeleton shows increased density and overgrowth of osteophytic prominences.

The central feature of the acromegalic changes in the skull is the enormous enlargement of the mandible. This is due to the "growth potential" of the mandibular condyle. As in other bones, periosteal appositional growth is stimulated by the growth hormone. This growth does not keep pace, however, with endochondral-like condylar growth. Excessive growth of the condyle, one of the most striking signs of the disease, causes the mandible to grow out of proportion to the maxillae, resulting in a protrusion of the lower jaw or mandibular prognathism, with increases in the mandibular angle. The tongue becomes quite enlarged, which may be responsible for increased apposition of the anterior border of the mandible.

DISTORTION OF THE MANDIBLE

Extrinsic and intrinsic factors affecting the growing condyle can considerably alter the growth pattern of the mandible. Local enlargement of the mandible may occur from intrinsic factors, such as a tumor, or extrinsic factors, such as an enlarged tongue.

In addition to the above, the changes brought about by scar contracture should also be considered. In this group the more prominent change in the mandible is in shape rather than size. Thus, the patient with a scar contracture extending from the mandible to the neck and chest as a result of a burn may eventually develop a distortion of the anterior part of the mandible with an opening of the bite. This bowing develops in spite of the fact that the mandible is a movable bone. The extent and type of distortion will vary, of course, with the contracture.

Another example is that seen in torticollis, or wryneck. In this instance the shortened sternomastoid muscle alters the normal position of the head and an asymmetry develops of not only the mandible but also the entire skull. The length, height, and development of bony and soft parts are less than normal on the side of the torticollis and perhaps greater than normal on the opposite side. The maxillary alveolar part seems unusually high on the unaffected side; and low on the affected side. These findings may be a result of pressure on the ramus, and particularly the condyle, thereby causing a condylar growth inhibition. The hyoid group of muscles may also play a role. Early correction of these extrinsic factors is important, to avoid severe deformities.

OTHER SURGICAL CONSIDERATIONS

Chronic Anterior Dislocation of the Mandible

Gross studies of the temporomandibular joint in monkeys after resection of the mandibular condyle showed considerable change of the mandibular fossa, the postglenoid process, and the articular eminence. From those studies one would expect similar changes after chronic anterior dislocation of the mandible. Very likely there are also changes in the shape and size of the condyle. Thus, it is not surprising that after a certain length of time the dislocation is not reducible. Although some have obtained reduction by means of general anesthesia or elastics and bite blocks, a subcondylar osteotomy may be found to be necessary.

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The Mandible: Clinical Considerations

The accepted timing and techniques used for clinical correction of mandibular anomalies are rooted in the Sarnat animal experimental data described previously in this unit. The shape and size of the fetal mandible change drastically during growth and development. In the neonatal mandible the ramus is wide and short; the coronoid process projects above the condyle; the body projects anteriorly and contains buds and partial crowns of deciduous teeth; the neurovascular canal runs low near the inferior border and the two halves of the body join at the menti as a syndesmosis.[1]

The growth pattern is influenced by the physiologic stress or functional matrix that acts on the bone. The temporalis muscle influences the coronoid process. The masseter and medial pterygoid muscles influence the angle and ramus. The alveolar unit is influenced by the teeth. Interestingly, Sarnat also showed that in the mature mandible, loss of physiologic integrity of the TMJ region resulted in mandible bone resorption and decreased lower face height.[2]

PEDIATRIC MANDIBULAR TRAUMA

Treatment of pediatric mandibular trauma has been influenced by the Sarnat data on mandibular growth. Damage to the condylar cartilages limits the growth potential of the mandible. With such trauma the normal downward and forward growth may be restricted. A bilateral condylar injury may result in micrognathia (small mandible) and a Class II malocclusion. A unilateral injury may result in an asymmetry or lateral deviation

of the mandible. In a child with a condylar fracture aggressive surgical correction with exposure and manipulation of the fractured condylar segment may result in devascularization of the fracture segment. This may further jeopardize the condylar growth site and result in a significant posttraumatic mandibular deformity in the long term. Thus, with pediatric mandibular condylar trauma, it is advisable to proceed with caution.

Typically, for pediatric condylar fractures a closed approach with placement in maxillomandibular fixation is used in the majority of cases. Alternative treatment of the injured condyle may be necessary for (1) fractures into the middle temporal fossa, (2) fractures with significant lateral displacement of the condylar segment, (3) fractures with associated foreign bodies or (4) bilateral condylar fractures with loss of ramal height, particularly panfacial fractures.[3] For these cases endoscopic approaches with more minimal dissection for reduction and fixation may be considered.

MANDIBULAR ASYMMETRY

Mandibular asymmetry may result from growth disturbances. Etiopathogenesis of this asymmetry may be from condylar problems, such as with unilateral condylar hyperplasia (overgrowth) or pediatric condylar trauma with neck shortening; or cranial base problems, such as with torticollis or unilateral craniosynostosis.

With both condylar hyperplasia and condylar shortening from trauma, mandibular asymmetry with a midline incisor discrepancy and mandibular shift when opening may not be truly evident until a patient is close to skeletal maturity. Treatment involves orthodontics (possibly with fixed edgewise appliance therapy) and orthognathic surgery (bilateral sagittal split osteotomy of the mandibular ramus).

Asymmetries translated from the cranial base may be profound and nearly impossible to correct. Torticollis with a tightened, shortened sternocleidomastoid muscle may result in the anterior positioning of the glenoid fossa and shifting of the condylar position. The asymmetry may involve the entire craniofacial skeleton, such that a clinician cannot determine the true midline. Many patients with asymmetric prognathism actually have mild, unrecognized torticollis.[4]

MANDIBULAR DEVIATION WITH UNILATERAL CORONAL SYNOSTOSIS

Our laboratory undertook a study to investigate whether this mandibular asymmetry resolved after correction of unilateral coronal synostosis.[5] With unilateral coronal synostosis, mandibular dysmorphology has been seen clinically.[6] In patients with unilateral coronal synostosis, the nasal root deviates toward the affected side and the chin point deviates away from the affected side. For our study we used familial, nonsyndromic rabbits with unilateral coronal synostosis which were bred at the University of Pittsburgh.[6,7] The animals in the study group underwent "correction" with resection of the affected suture. Control or "uncorrected" rabbits with unilateral coronal synostosis and normal, wild-type rabbits ($n = 36$; three equal groups of 12) were used for comparison.

Our results showed that among the mature, mandibular specimens, wild-type rabbits showed equal side-to-side measurements. The control, uncorrected unilateral coronal synostosis rabbits showed mandibular asymmetry (Fig. 10.1). Data was recorded as follows: on the affected side — longer ramal height (15%), shorter ramal width (13%), longer body height (10%), and shorter body width (13%). By contrast, 10 of 11 corrected unilateral coronal synostosis specimens showed no side-to-side differences.

Serial lateral cephalograms obtained at 10, 25, 42, and 84 days showed no asymmetries in wild-type rabbits, as expected. However, in the uncorrected unilateral coronal synostosis rabbits, progressive asymmetries in the ramal height and mandibular length were documented. By contrast, in the corrected unilateral coronal synostosis rabbits, existing asymmetries at 10 and 25 days improved by 42 days and were not seen by maturity, at 84 days.

There were no asymmetries in condylar shape or condylar volume in any of the three groups. Cranial base measurements showed asymmetries of the uncorrected unilateral coronal synostosis specimens that were consistent with an anteriorly positioned glenoid fossa on the affected side. However, only 1 of 11 corrected unilateral coronal synostosis specimens showed similar cranial base asymmetries. Thus, our data showed that mandibular asymmetries in nonsyndromic, familial rabbits with unilateral coronal synostosis are progressive with growth but improve after correction

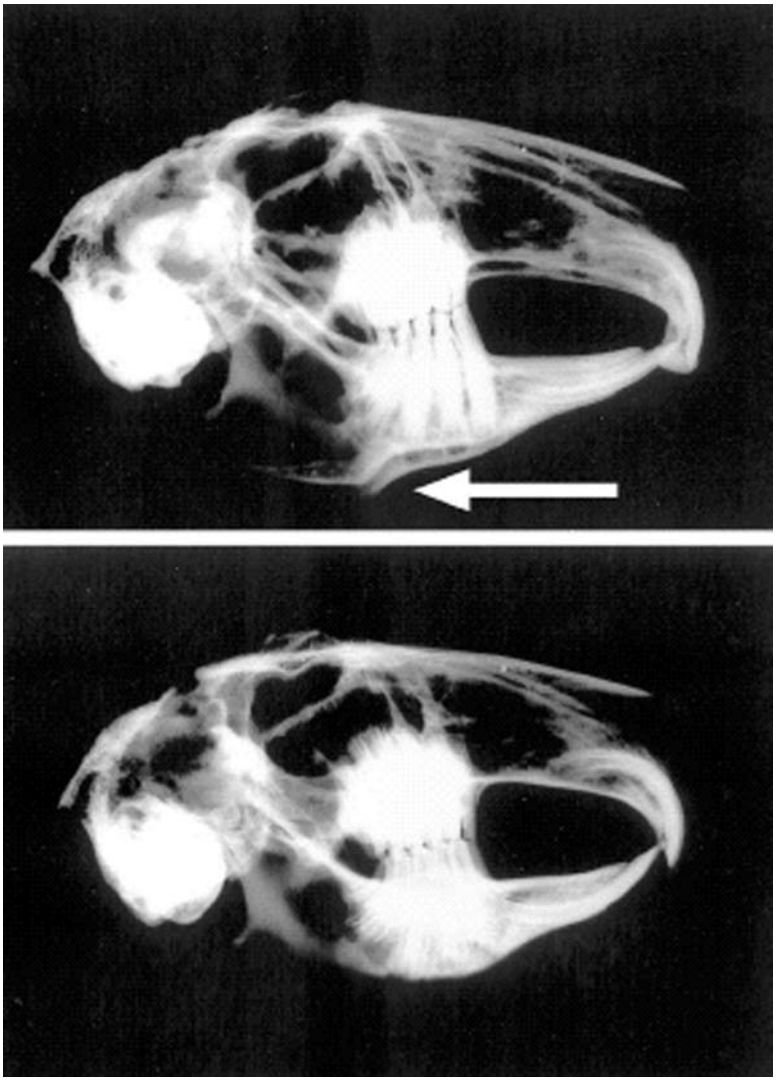

Fig. 10.1 Lateral cephalograms of rabbit skulls (at age 84 days). *Above*: Uncorrected right unilateral coronal synostosis demonstrating overlapping of the inferior mandibular border and mandibular angle, suggesting mandibular *asymmetry*. *Below*: Corrected right unilateral coronal synostosis demonstrating only one line of the inferior mandibular border, representing a symmetric mandible.

of synostosis. Thus, with each removal of fused coronal sutures down to the cranial base we ameliorated facial and mandibular growth disturbances in our experimental rabbits. In humans, clinically, this improvement is not seen in all patients. The reasons for this are under investigation.

PIERRE ROBIN SEQUENCE

Pierre Robin sequence consists of micrognathia, a secondary U-shaped cleft palate, and glossoptosis. With severe micrognathia, the tongue occupies a greater portion of the oropharynx, resulting in glossoptosis. In embryologic development at eight weeks' gestation, the vertically oriented palatal shelves are prevented from collapsing into a horizontal position before fusion in the midline by the intervening tongue.

Patients born with more mild-to-moderate micrognathia are treated conservatively. They have upper airway obstruction that may be safely managed with sideway or prone positioning or with a temporary nasopharyngeal tube. This treatment is based on the expectation of "catch-up" mandibular growth during the first two years of life. With this mandibular body anterior growth, the tongue and epiglottis are pulled away from the posterior pharyngeal wall and the upper airway obstruction is alleviated. Although there is always some growth and functional improvement over time, often subsequent orthognathic mandibular advancement is required at maturity.

By contrast, infants with Pierre Robin sequence with more severe micrognathia may have significant upper airway obstruction problems.[9,10] Although the traditional treatment for management of this severe upper airway obstruction is tracheostomy, neonatal mandibular lengthening with distraction osteogenesis has been successfully used (Fig. 10.2). This newer treatment avoids a tracheostomy and its long-term complications of growth and language delay. The history, biology, and overall process of distraction are important to review, since it has had such a large impact on craniofacial techniques and treatment planning.

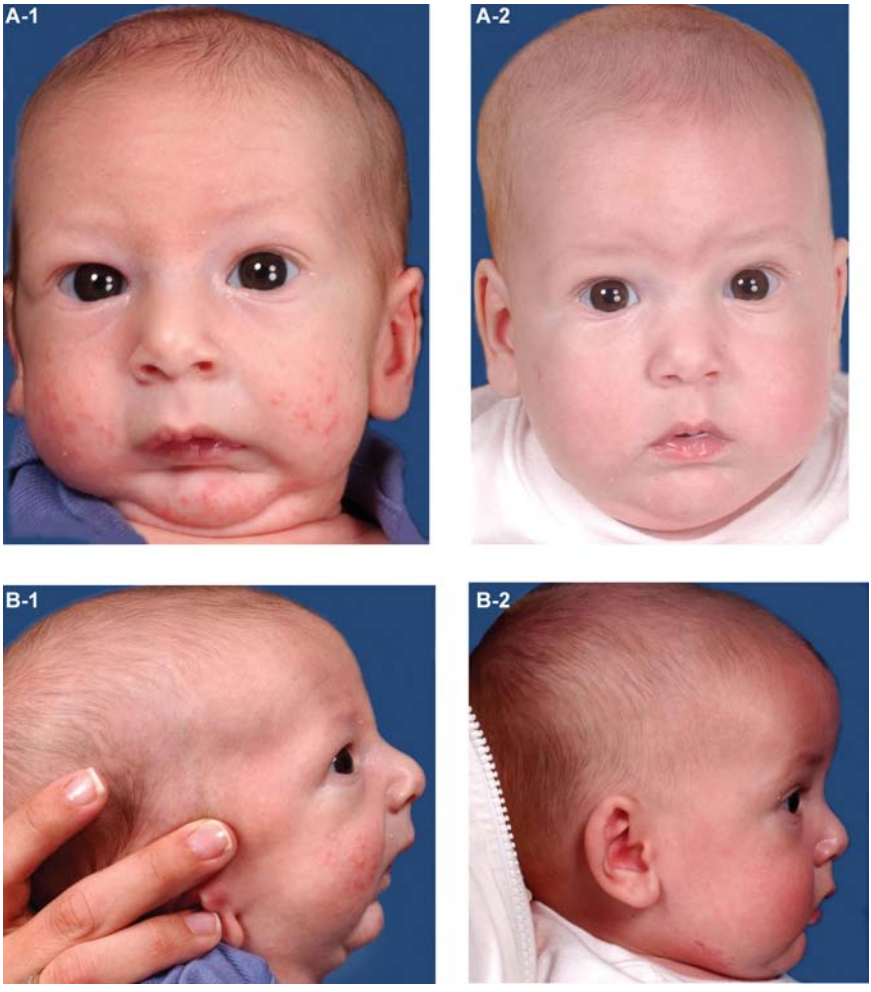

Fig. 10.2 Neonatal mandibular lengthening with distraction osteogenesis: (**A-1**) preoperative frontal view, (**B-1**) preoperative lateral view (after 20 mm of mandibular lengthening), (**A-2**) postoperative frontal view, (**B-2**) postoperative lateral view.

DISTRACTION OSTEOGENESIS

Distraction osteogenesis has become an important technique for craniofacial surgery over the last 18 years. Recent research and development has centered around (1) identifying appropriate indications for the distraction

procedures, (2) perfecting distraction instrumentation and devices, and (3) understanding the biology of distraction within membranous bone. For the craniofacial surgeon, distraction osteogenesis has been a bridge toward tissue engineering techniques. It offers the benefit of reduced morbidity without a need for bone grafting. In addition, there is the theoretic improvement of decreased relapse from less soft tissue recoil postprocedure, due to the gradual lengthening of the distraction technique.

History

The history of distraction osteogenesis resides in the history of fracture repair with the use of continuous traction for the reduction of displaced fractures. Distraction osteogenesis techniques have been modified from the traditional techniques of osteotomies and bone fixation. Early in the 20th century distraction lengthening in the lower extremity was fraught with problems from infectious complications and bony nonunion. Beginning in the 1950's, Ilizarov made great strides in optimizing the distraction process in lower extremities with his external ringed appliances in over 15,000 cases.[11]

The history of distraction in the craniofacial skeleton begins with animal experimentation on the mandible in the 1970's; however, it was not until 1989 that McCarthy initiated the clinical use of distraction with human mandibular lengthening.[12] Since then, distraction has been successfully performed on patients with various craniofacial hypoplasias (craniofacial microsomia, Pierre Robin sequence, Treacher–Collins syndrome, Nager syndrome), temporomandibular joint ankylosis, craniofacial dysostosis (for midface and forehead deficiencies), posttraumatic deformities, and on most bony regions of the craniofacial skeleton (mandible, maxilla, zygomatic/malar, orbital, frontal/forehead, parietal and occipital, sphenoidal, and even the cranial base).

Biology

As with fracture healing, distraction of osteogenesis involves: (1) an initial injury (the osteotomy), (2) a recruitment of cells (including mesenchymal stem cells and preosteoblasts), (3) a mechanical linear force (from the

distraction device to induce and direct the formation of both hard and soft tissues), and (4) callus formation (mineralization of bone with consolidation). The term "osteogenesis" (formation of vascularized bone *de novo*) should be differentiated from the terms "osteoconduction" (creeping substitution of new bone into the peripheral regions of an implant) and "osteoinduction" (new bone induction with the use of growth factors).[13]

There are three phases of distraction: latency, activation and consolidation. Latency is the period immediately following the osteotomy. Typically, the latency for craniofacial distraction is 0–2 days, except with a monobloc distraction procedure, where a 1-week latency period is beneficial (to allow for mucosal healing between the subdural space and nasal sinuses before beginning distraction).[14]

Activation involves rate, rhythm, length, and molding. A standard rate of distraction is 1 mm per day. Any major variation of this may result in fibrous union (rate = too fast) or premature consolidation (rate = too slow). (However, with neonatal distraction faster rates of up to 2 mm per day are necessary.) A rhythm or frequency of turning the distractor arm of two times per day is often used; however, it is yet to be determined scientifically whether this rhythm is superior to a more frequent interval or even continuous distraction. The length of distraction may often be determined preoperatively and is predicted by the size of the defect or the amount of length necessary to correct a functional problem (e.g. upper airway obstruction). Molding the new "generate bone" is possible because of the plasticity of the region prior to consolidation. Molding may be done to close an open bite, correct form or improve symmetry. Guiding the generate bone may be done with multivector distractors, dental elastic bands or other external force.

Consolidation involves the mineralization and hardening of the new bone formed by the distraction osteogenesis process. The study of zones in the distraction site has shown that the peripheral zones (close to the osteotomy sites) begin and end consolidation sooner than the central zones (Fig. 10.3). The time of full consolidation may vary but is generally between 6 and 12 weeks following the completion of distraction. Internal distraction devices are often kept in place for 3 months. External devices are usually removed at 6 weeks, because of their cumbersome nature (Fig. 10.4).

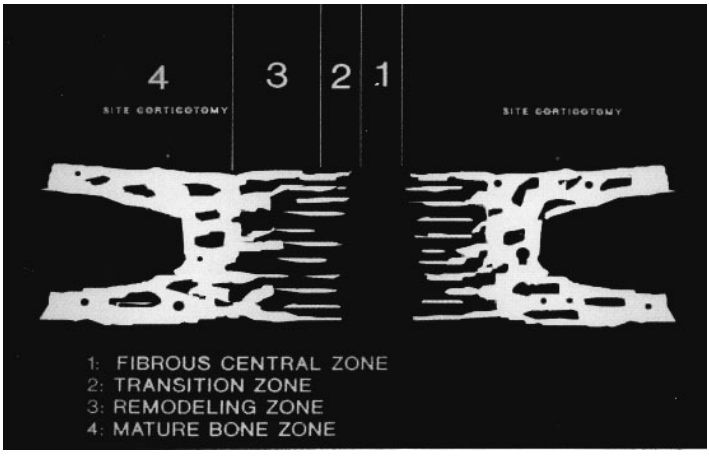

Fig. 10.3 Zones of distraction osteogenesis: 4 = mature bone at the original site of osteotomy; 3 = remodeling region undergoing consolidation; 2 = transition region organized fibrous region beginning ossification; 1 = fibrous region with cells organized along distraction tension lines.

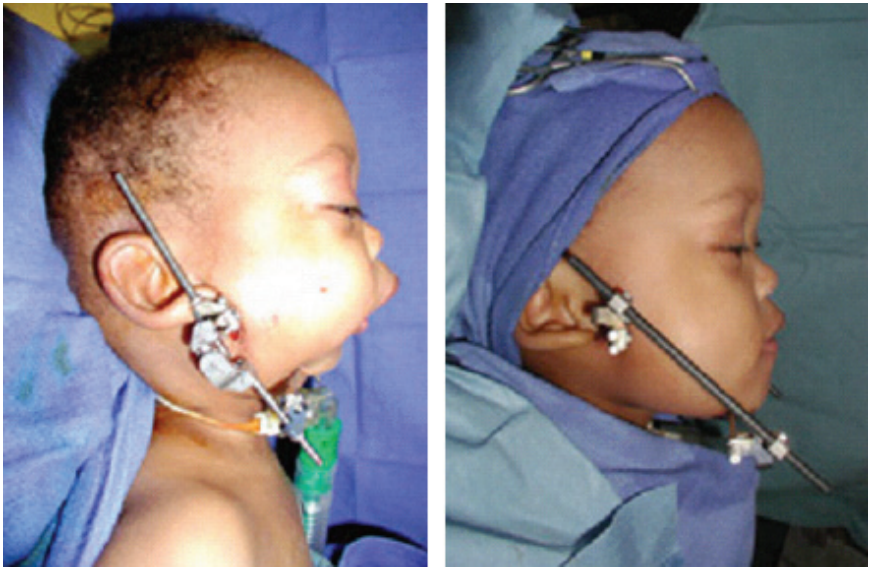

Fig. 10.4 Patient images displaying an external distraction device both pre- and post-distraction. Note the improved chin point.

Slower mineralization and the need for a longer consolidation time occur in older patients, patients with prior exposure to radiation and patients who develop infections.

Mandibular Distraction

Mandibular distraction allows for (1) the formation of vascularized mandibular bone to correct hypoplasias and (2) the expansion of the regional soft tissue envelope. It is commonly used in growing patients with skeletal deformities; however, it may also be used in skeletally mature patients who require extremely large advancements.[15] The use of conventional techniques with large advancements (>10 mm) may result in considerable relapse and undue stress on the inferior alveolar nerve. In general, for shorter advancements in skeletally mature patients, conventional techniques for mandibular advancement (like orthognathic–bilateral sagittal split osteotomy of the mandible, etc.) are preferred. The advantage to an orthognathic procedure is that a patient may obtain optimal occlusion in just one operation.

Indications for mandibular distraction include: micrognathia (with upper airway obstruction, obstructive sleep apnea, or tracheostomy dependency), mandibular asymmetry (craniofacial microsomia), and severe class II malocclusion (Table 10.1). The modified Pruzansky classification system for bilateral or unilateral mandibular hypoplasias is useful in describing severity seen radiographically and in planning treatment options. The four types in the Pruzansky classification include: Grade 1 (only mild hypoplasia) mandibles have a normal configuration but have a reduction in ramal and condylar size; Grade IIa (small but anatomic TMJ) mandibles have a small, malformed condyle but the relation to the glenoid fossa is maintained; Grade IIb (anomalous TMJ) mandibles have no glenoid fossa and the condyle is medially displaced; Grade III (completely absent TMJ) mandibles lack a condyle, ramus and glenoid fossa.[16]

Devices and Vectors

Preoperative preparation for mandibular distractions involves choosing an appropriate device (external or internal) and planning the length and

Table 10.1 Indications for Mandibular Distraction

(1)	Micrognathia
	(a) Upper airway obstruction
	(b) Obstructive sleep apnea
	(c) Tracheostomy dependency
(2)	Mandibular asymmetry
	(a) Craniofacial microsomia
(3)	Severe Class II malocclusion (skeletally mature)

vector of distraction. Preoperative radiographic evaluations may include a panoramic radiograph, a lateral cephalogram and a 3D CT scan (particularly for visualization of the temporomandibular joint region).

External mandibular devices were the first to be designed and used. They offer the advantage of ease of placement and removal. However, external devices are more likely to become dislodged during the distraction process. As mentioned above, shorter consolidation times have been used because of the cumbersome nature of the devices. Although a multiplanar device offers the ability to adjust the distraction vector, less precision may occur because of the increased distance from the osteotomy to the body of the device and because of pin loosening or bending. In addition, with the external devices pin care is necessary and external scarring results from the pins.[12]

Internal mandibular distraction devices offer the advantage of being hidden from sight so that the patients more often return to school during the consolidation phase. Disadvantages include: the application may be technically more difficult, there are more limitations on length and more subperiosteal stripping may be required. Although theoretically this more extensive undermining may decrease blood supply, it has not been shown clinically that bone healing with internal distraction is inferior to external distraction. Internal mandibular devices may be uniplanar, telescopic (a shorter initial rod that lengthens more), have a right angle activation arm (for vertical vector placement), be curvilinear or have another design.

The distraction vector may be horizontal, vertical or oblique. The position of the distraction device (the orientation of the distraction rod), not the osteotomy position, determines the vector. A horizontal vector is

chosen for mandibular body deficiencies, including bilateral micrognathias like Pierre Robin sequence.[9] An oblique or vertical vector is important for lengthening the mandibular ramus in most other cases, as in Treacher–Collins syndrome or craniofacial microsomia. After mandibular lengthening, before consolidation, the generate bone may be molded with external forces (elastic bands) to optimize the final distraction vector.

Neonatal Distraction

The purpose of neonatal mandibular distraction is to correct upper airway obstruction so as to avoid a tracheostomy.[10] Although a tracheostomy may be life-saving for a newborn with micrognathia, it may be complicated by tracheitis, pneumonia, laryngomalacia, bleeding from stomal granulation, subglottic stenosis or long-term problems, such as developmental and speech delays. Once a tracheostomy is placed in a newborn it may take years and multiple surgical procedures to remove it (such as laser ablation for tracheomalacia and tracheal reconstruction).[17] Distraction lengthening of the mandible corrects posterior tongue collapse and elevates the epiglottis, alleviating the need for even a temporary tracheostomy.

Selection of appropriate candidates for neonatal distraction involves a multidisciplinary approach and preoperative tests. The multidisciplinary team always includes a neonatologist, a plastic surgeon, an anesthesiologist and a head-and-neck surgeon, and often includes a pediatric pulmonologist, a pediatric gastroenterologist and a geneticist. Patients considered candidates for neonatal distraction have severe micrognathia and upper airway obstruction. Patients excluded as potential candidates for neonatal distraction require a tracheostomy and have (1) other airway lesions, like a tracheal web, (2) central sleep apnea or (3) severe gastroesophageal reflux. In addition, neonatal distraction is not required if the obstruction is moderate or mild and may be controlled with prone or side positioning. Tongue–lip adhesion or a secured nasopharyngeal tube may also be used in these cases to temporarily control the tongue prolapse. These temporary solutions may be offered to allow time for mandibular growth and improvement of upper airway obstruction. Pierre Robin sequence (micrognathia, glossoptosis, cleft palate) is the most common diagnosis

for patients undergoing neonatal distraction but patients with Treacher–Collins, Nager and other syndromes have also undergone the procedure to avoid a tracheostomy.[9,10]

CRANIOFACIAL MICROSOMIA

Craniofacial microsomia, or otomandibular dysostosis, is a disorder of the first and second branchial arches. Typically unilateral, the asymmetry is manifested as a spectrum of mandibular hypoplasia, deficient soft tissues of the face and microtia (Fig. 10.5). It may be considered a constellation of Tessier's rare facial clefts #6, #7 and #8. Goldenhar's syndrome, or oculovertebral sequence, is a severe variant with colobomas of the eyelid and cervical vertebral anomalies.[18,19]

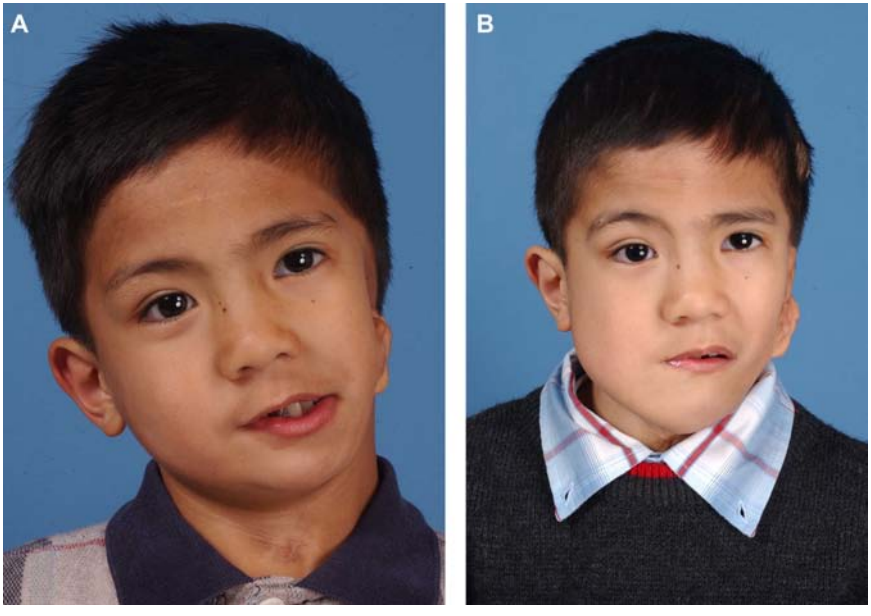

Fig. 10.5 Patient with left craniofacial microsomia or otomandibular dysostosis. This disorder is typically unilateral and manifested as a spectrum of mandibular hypoplasia, deficient soft tissues of the face and microtia. (**A**) Preoperative frontal view, and (**B**) Postoperative frontal view after left mandibular distraction with graft lengthening and TMJ reconstruction.

With Craniofacial Microsomia, the mandibular pathology is located in the ramus and condylar regions. Associated dental structures are also affected. The Pruzansky classification of the mandibular skeletal deficiency, given above, provides useful diagnostic and management nomenclature. The timing of mandibular surgery is planned based on function and growth. Early intervention is necessary if functional impairment (upper airway obstruction) exists. There is an effort to limit the number of surgical procedures required during infancy through adolescent (Fig. 10.6). Thus, patients with craniofacial microsomia typically undergo a mandibular distraction procedure around 6–8 years of age. (If unilateral pathology exists overcorrection of the midline is performed.) Then these patients typically require an orthognathic procedure and orthodontic preparation at skeletal maturity (15–18 years of age).

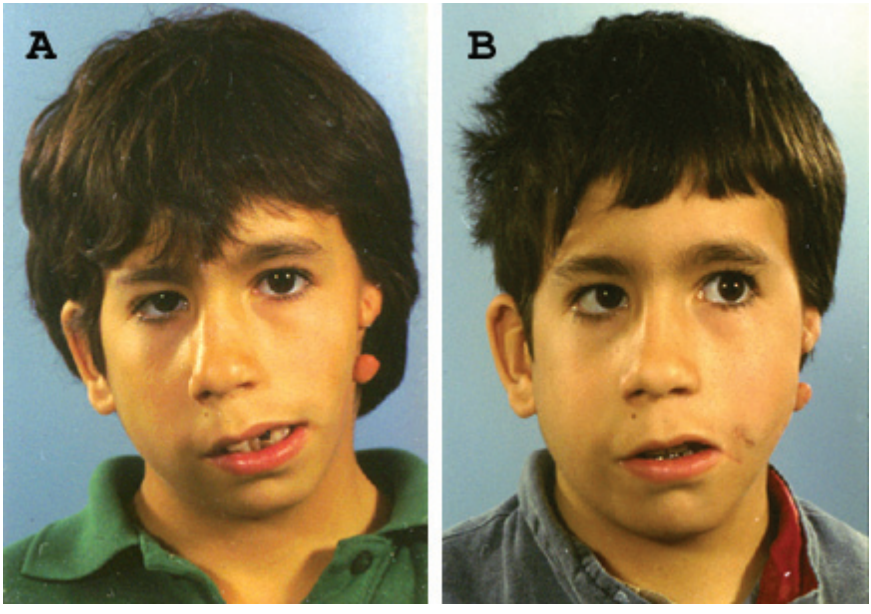

Fig. 10.6 Patient with left hemifacial microsomia: (**A**) predistraction with left mandibular hypoplasia, microtia and macrostomia; (**B**) postdistraction after mandibular lengthening (chin to midline) and macrostomia repair with a Z-plasty. (HK Kawamoto, MD, DDS.)

TREACHER–COLLINS SYNDROME

Treacher–Collins syndrome, or mandibulofacial dysostosis, like craniofacial microsomia, is a constellation of Tessier rare facial clefts #6, #7 and #8. However, unlike craniofacial microsomia, it is typically bilateral (Fig. 10.7).

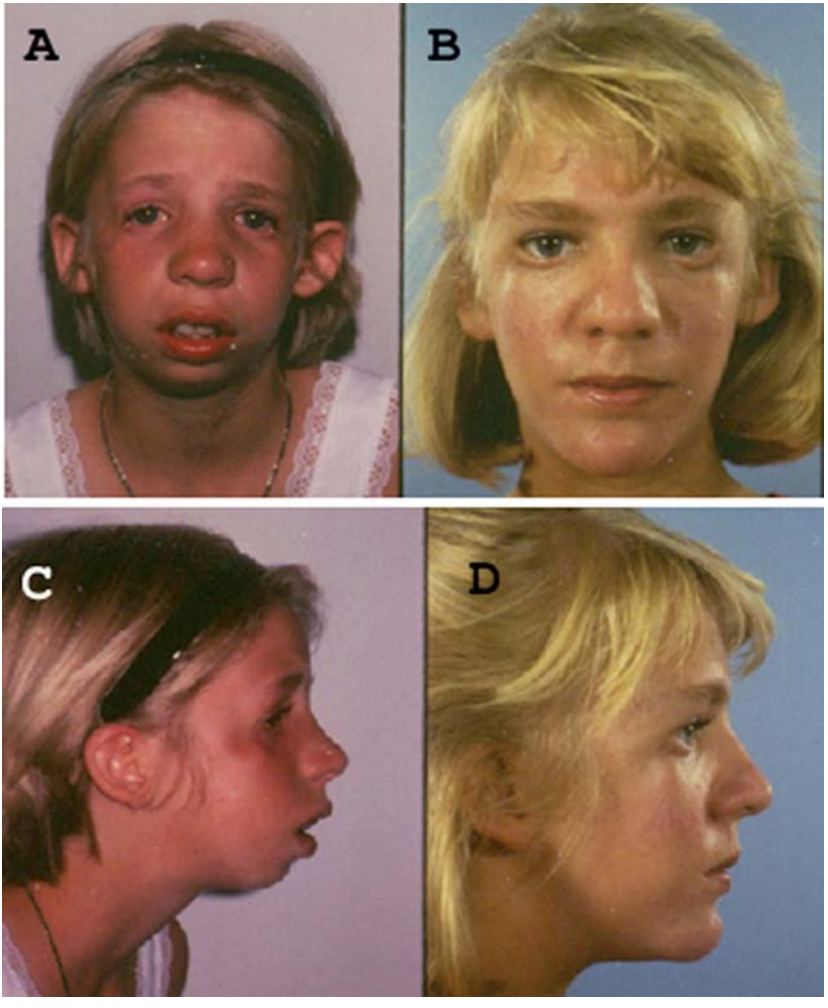

Fig. 10.7 Patient with Treacher–Collins syndrome, or mandibulofacial dysostosis: (**A**) preoperative frontal view; (**B**) postoperative frontal view after the orthognathic procedure (Le Fort I, bilateral sagittal split osteotomy, osseous genioplasty), upper-to-lower eyelid switch flap and fat grafting); (**C**) preoperative lateral view; (**D**) postoperative lateral view. (HK Kawamoto, MD, DDS.)

This familial autosomal dominant syndrome has a spectrum of phenotypic characteristics related to the soft tissue and skeletal hypoplasias. Soft tissue features include: (1) palpebral — antimongonial slant of the fissure, colobomas of the lower eyelid, absent eyelash of the medial 2/3 of the lower eyelid; (2) ear — microtia, conductive hearing loss; and (3) anterior displacement of preauricular hair.

Severe mandibular retrognathia, a steep mandibular plane, an obtuse mandibular angle and an anterior open bite contribute to a facial profile that is "avian." The short ramus, obtuse gonial angle and retrusive chin that points backward results in a micrognathia characteristic of Treacher–Collins syndrome. The strong genioglossal muscle pull contributes to this progressive mandibular dysmorphology and also creates a clinical reconstructive challenge. In the growing Treacher–Collins patient mandibular distraction with a vertical vector aimed at lengthening the ramus is performed (Fig. 10.8). The skeletally mature Treacher–Collins patient may require a

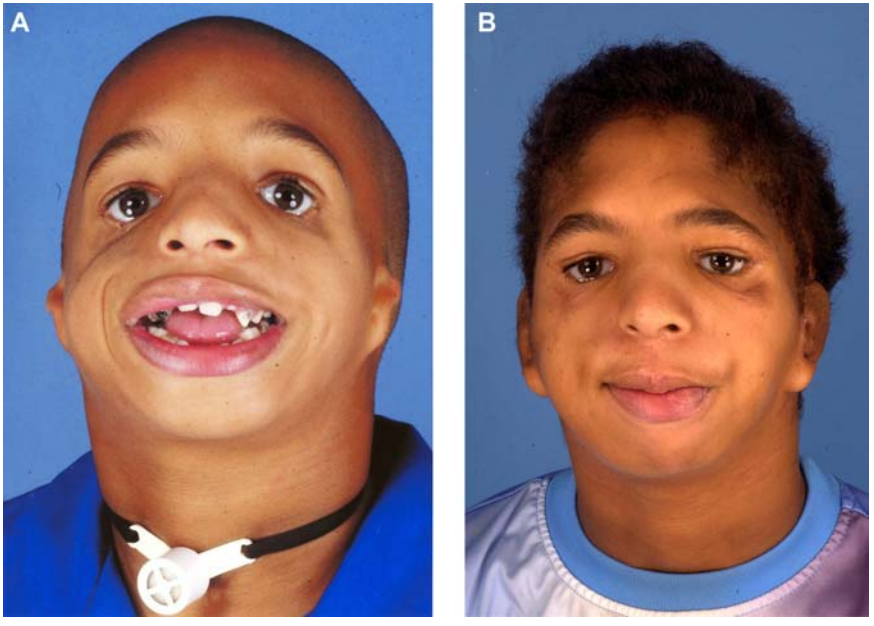

Fig. 10.8 Treacher Collins patient: (A) Preoperative tracheostomy-dependent patient. (B) Postoperative tracheostomy-free patient after mandibular distraction malar reconstruction with cranial bone grafts and eyelid switch flaps.

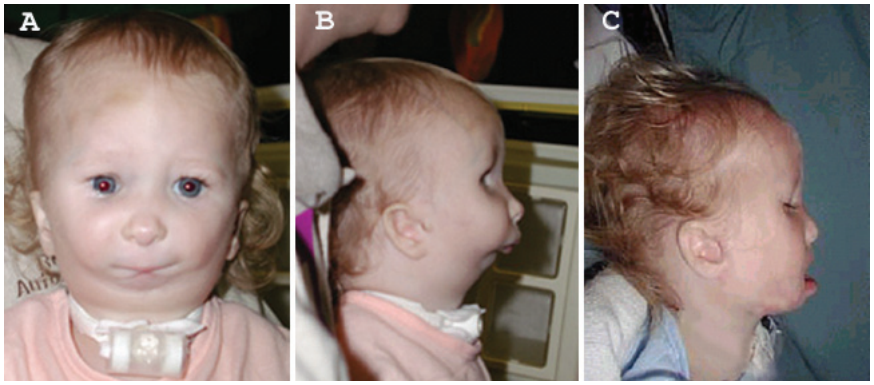

Fig. 10.9 Patient with Nager syndrome: (**A**) frontal view demonstrating facial features similar to those of Treacher–Collins syndrome but more severe; the patient also has a radial club defect of the upper extremity; (**B**) lateral view predistraction with tracheostomy; (**C**) lateral view postdistraction after removal of tracheostomy.

double jaw orthognathic procedure after orthodontic preparation. This orthognathic procedure for the Treacher–Collins "open bite malocclusion" involves a Le Fort I posterior impaction, bilateral sagittal split osteotomy and advancement and an osseous genioplasty advancement. Follow-up studies after mandibular lengthening have reported skeletal relapse and recurrent open bite.[20] Nager syndrome has facial deformity features similar to those of Treacher–Collins syndrome but more severe and with additional cleft deformity of the upper extremity (Fig. 10.9).

GENIOPLASTY DISTRACTION

As mentioned above, both Treacher–Collins and Nager syndrome mandibular hypoplasia may result in posterior collapse of the tongue base and a decreased oropharyngeal airway. Mandibular advancement (with mandibular distraction in the growing patient or an orthognathic procedure in the mature patient) typically improves obstructive sleep apnea and may lead to decannulation of a tracheosotomy. However, in some syndromic patients, upper airway obstruction persists even after advancement. Failure has been attributed to the musculoskeletal milieu and genetics of these syndromic children.

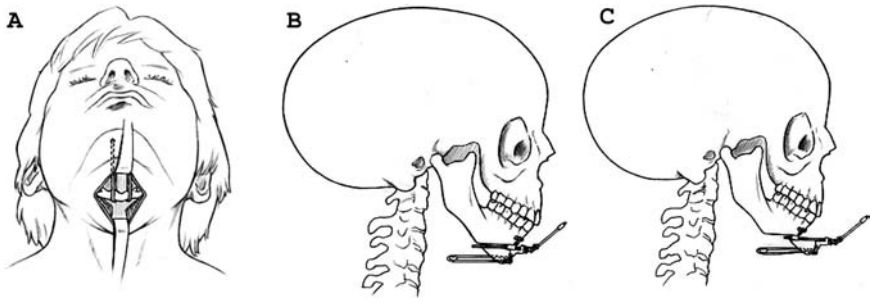

Fig. 10.10 Illustration of the hyoid advancement procedure: (**A**) retraction of the submental incision shows the infrahyoid muscular release and the hyoid advancement via the two fascial slings from the hyoid to the anterior mandible; (**B**) predistraction lateral skeleton view with genioplasty distractor in place; (**C**) postdistraction lateral view with advanced genioplasty segment.

For this subset of Treacher–Collins or Nager syndrome patients with persistent upper airway obstruction after mandibular advancement into proper occlusion, we conducted a study at UCLA involving a new surgical technique.[20] This procedure consisted of a hyoid advancement with genioplasty distraction (Fig. 10.10). The hyoid advancement optimized the epiglottal position (since the hyoid has direct ligamentous attachments to the epiglottis). The genioplasty distraction offered, potentially, a decreased relapse compared to an acute genioplasty advancement. The traditional acute advancement fails in Treacher–Collins and Nager syndrome patients because of the strong genioglossus and geniohyoid muscle pull in the inferior–posterior direction. Distraction offers the advantage of gradual lengthening of soft tissues and avoids the postoperative recoil (Fig. 10.11).[21]

Patients were separated into three groups: Group I (distraction genioplasty, syndromic) ($n = 7$), Group II (acute genioplasty, syndromic) ($n = 8$) and Group III (acute genioplasty, nonsyndromic) ($n = 10$). Groups were age- and gender-matched, with a mean age at the time of operation of 15.1 years. Outcomes of Groups I–III, with regard to skeletal relapse, were assessed by comparing preoperative, postoperative and follow-up cephalometric measurements (ΔX = horizontal advancement and ΔY = vertical change between completion of distraction and follow-up). Outcomes with

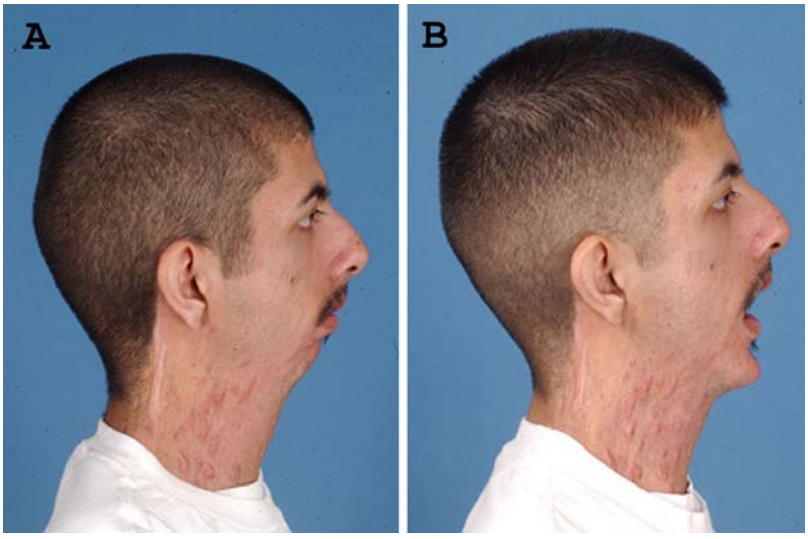

Fig. 10.11 Patient with Escobar syndrome and obstructive sleep apnea: (**A**) preoperative lateral view of the patient with Class I occlusion and retrogenia; (**B**) postoperative lateral view of the patient after genioplasty distraction with hyoid advancement (one-year follow-up). The patient had resolution of obstructive sleep apnea.

regard to airway obstruction for Group I were assessed by comparison of preoperative and one-year follow-up: (1) visual assessment under direct broncholaryngoscopy, (2) sleep studies and (3) the status of tracheostomy dependency.

Our study showed that with Group I patients the epiglottal position was optimized in all patients. Five of 5 (100%) had resolution of their obstructive sleep apnea and 2 of 3 (67%) achieved removal of their tracheostomy. The mean distraction length for Groups I, II and III was 25.1 mm, 14 mm and 8 mm, respectively. Cephalometric measurements showed a horizontal relapse for Groups I, II and III of 1.8 mm (10.4%), 6.8 mm (61.8%) and 0.8 mm (11.3%) with a vertical relapse of –0.8 mm (13.8%), –6 mm (153.8%) and 0.7 mm (35%), respectively. At follow-up for Groups I, II and III, 72.7%, 27.8% and 78.8% of the mechanical device distraction translated into true horizontal (x) advancement and 26.3%, 70.7% and 16.3% translated into vertical (y) inferior migration, respectively (Tables 10.2 and 10.3).

Table 10.2 Distraction Genioplasty with Hyoid Advancement for Treacher–Collins and Nager Syndrome Patients

Patient	Diagnosis	Age (yrs)	Airway Preop	Dental Occlusion	Distraction Length (mm)	Airway Postop	ΔX Postop–Preop	ΔY Postop–Preop	ΔX Follow-up–Preop	ΔY Follow-up–Preop
1	TCS	15	TD	Class I	30	TR	25 ± 2	−7 ± 1	23 ± 2	−8 ± 2
2	TCS	13	TD	Class I	28	TR	23 ± 1	−4 ± 1	22 ± 1	−5 ± 1
3	TCS	14	OSA	Class I	20	Impr	16 ± 1	−4 ± 1	14 ± 1	−5 ± 1
4	TCS	16	OSA	Class I	25	Impr	21 ± 1	−5 ± 1	18 ± 1	−6 ± 1
5	TCS	13	OSA	Mixed	25	Impr	20 ± 2	−5 ± 1	18 ± 1	−6 ± 1
6	Nager	12	TD	Class I	30	TD	24 ± 1	−7 ± 1	21 ± 1	−8 ± 1
7	Nager	21	OSA	Class II	22	Impr	18 ± 2	−6 ± 1	15 ± 2	−6 ± 1
8	Nager	17	OSA	Class I	21	Impr	16 ± 1	−8 ± 1	15 ± 1	−9 ± 1
Mean		15.1			25.1		20.1	−5.8	18.2	−6.6

Yrs = years; mm = millimeters; TCS = Treacher–Collins syndrome; Nager = Nager syndrome; TD = tracheostomy-dependent; OSA = obstructive sleep apnea; TR = tracheostomy removed; Impr = improvement in sleep apnea; Preop = preoperative measurement; Postop = postoperative measurement; ΔX = horizontal change; ΔY = vertical change.

Table 10.3 Genioplasty Lateral Cephalogram Outcomes

Technique	Number of Patients	Age (yrs)	Length (mm)	ΔX (mm) Postop–Preop	ΔY (mm) Postop–Preop	ΔX (mm) Follow-up–Preop	ΔY (mm) Follow-up–Preop	ΔX (mm) Relapse	ΔY (mm) Relapse
Syndromic Distraction (Group I)	8	15.1	25	20 ± 2	−6 ± 1	18 ± 2	−7 ± 1	1.8 (10%)	.8 (14%)
Syndromic Acute (Group II)	7	16.1	14	11 ± 1	−4 ± 1	4 ± 1	−10 ± 1	6.8 (62%)	−6 (154%)
Nonsyndromic Acute (Group III)	10	17.3	8	7 ± 1	−2 ± 1	6 ± 1	−1 ± 1	.8 (11%)	.7 (35%)

Yrs = years; mm = millimeters; Preop = preoperative measurement; Postop = postoperative measurement; ΔX = horizontal change; ΔY = vertical change; Relapse = difference between postoperative measurement and follow-up measurement (Postop − Follow-up); percentages are of total initial advancement (Postop–Preop).

Thus, data from this clinical study suggested that for a subset of Treacher–Collins or Nager syndrome patients: (1) genioplasty distraction with hyoid advancement is effective in relieving obstructive sleep apnea or for removal of tracheostomy; and (2) genioplasty distraction has a lower relapse rate and a better cosmetic outcome than acute advancement. Furthermore, it is a viable adjunct for achieving tracheostomy removal and resolution of OSA among refractory patients in this population. As such, we propose its use.

TEMPOROMANDIBULAR JOINT ANKYLOSIS

Temporomandibular joint (TMJ) ankylosis most commonly has a traumatic or infectious etiology. In the pediatric population, another common cause is congenital ankylosis. Unlike the unilateral fibrous intra-articular adhesions seen in traumatic ankylosis, congenital ankylosis presents with bilateral osseous TMJ unification, mandibular hypoplasia and near-total immobility.[22] While this relationship is not completely understood, it is believed that decreased dynamic movement of the TMJ combined with lack of normal mandibular function results in an absent growth stimulus and intrinsic mandibular hypoplasia.[23]

Congenital TMJ bony ankylosis is a rare pediatric condition that poses a great surgical challenge. The surgical treatment goal is to both release the joint ankylosis and lengthen the mandible with the hope of restoring and maintaining normal TMJ movement and mandibular function. To date, there has been no widely accepted protocol for the simultaneous treatment of congenital TMJ ankylosis and mandibular hypoplasia. Many protocols have been used, with varying success, for the independent treatment of acquired TMJ fibrous ankylosis and congenital mandibular hypoplasia.

Historically, traumatic TMJ ankylosis has been treated with aggressive resection, articular lining with autogenous materials, reconstruction of the condylar segment with a costochondral graft or prosthesis, and early mobilization with physiotherapy.[24] For fibrous ankylosis these methods have proven to be successful. For bony ankylosis, particularly congenital bony ankylosis, results have not been nearly as promising.

Newer treatment modalities have been described in attempts to achieve better results. Stucki–McCormick used transport distraction osteogenesis to successfully treat unilateral posttraumatic TMJ fibrotic ankylosis by creation of a "neocondyle."[25–27] Recently, we conducted a clinical study of congenital osseous TMJ ankylosis using transport distraction osteogenesis and a new device developed by Matthews which allows for TMJ movement in the postoperative phase.[28] In a series of affected patients, we compared two new methods of treatment: transport distraction osteogenesis (TDO) and Matthew's device arthroplasty (MDA).

All patients had CT-scan-documented bilateral TMJ bony ankylosis. Group I (TDO) underwent distraction advancement of the mandible (for micrognathia), followed by resection of the condyles, recontouring of the glenoid fossae with interposition temporoparietal–fascial flaps and TDO of mandibular rami segments. Group II (MDA) underwent all of the above procedures except for TDO. Instead, the Matthew's devices were anchored to the temporal bone and mandibular rami. Hinged arms allowed for motion at the reconstructed TMJ. In both groups, patients underwent extensive postoperative therapy. This therapy involved use of a Therabyte TMJ exerciser and stretcher multiple times daily for six months and return to the operating room every six weeks for six months for stretching under anesthesia. Preoperative, postoperative and follow-up lateral cephalograms were obtained and incisor opening distances were recorded.

Our results showed that all patients but one had severe micrognathia ($n = 9$). For Group I (TDO), the mean age was 6.8 years and the mean advancement was 28.5 mm. For Group II (MDA), the mean age was 8.2 years and the mean advancement was 23.5 mm. In Group I, the mean incisor opening was 1 mm preoperatively, and 27.5 mm postoperatively. However, it relapsed to 14.3 mm by 12.5-month follow-up (48% relapse). The mean incisor opening in Group II was 3.9 mm preoperatively, and 33.4 mm postoperatively, and remained at 30.6 mm after 11.1-month follow-up (8% relapse). One patient in Group I underwent surgical revision because of relapse.

Our data showed that for this small subset of patients with congenital bony ankylosis of the TMJ, both transport distraction and Matthew's device arthroplasty with intensive postoperative therapy improved TMJ function postoperatively. However, Matthew's device arthroplasty was

superior in the long term. A combination of these two treatment strategies may be best. With this combined modality a hinged Matthew's device would have the capability of distracting an intervening transport disk.

SUMMARY

Thus, in correcting traumatic and congenital mandibular anomalies, the clinician may draw on research studies related to growth centers and the influence of physiologic forces. Traumatic injuries may adversely affect growth centers or muscular influences from scarring. Likewise, congenital or syndromic pathology may result in aberrant, or absent, growth centers and abnormal surrounding forces. Distraction osteogenesis with the expansion of the surrounding soft tissue, including muscle, vasculature, nerves and skin, has provided a useful tool for correcting difficult traumatic and congenital mandibular anomalies.

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PART II

THE MIDFACE

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Osteology of the Rabbit Face*

The rabbit face comprises, in part, the mandibular, premaxillary, maxillary, and nasal bones (Fig. 11.1).[1]

The nasal cavity communicates posteriorly with the ventral surface of the skull by the choanae, which, in the rabbit, are incompletely divided (Fig. 11.1). Anteriorly, it opens to the outside by the piriform aperture.

Bilateral division is effected chiefly through a median vertical cartilaginous plate — the nasal septum (Fig. 11.2). This is continuous posterosuperiorly as a synchondrosis with a small crescentic vertical plate of bone, the perpendicular plate of the ethmoid bone, and posteroinferiorly with the presphenoid. Both are sites of endochondral bone formation. Inferoposteriorly, the ventral portion of the cartilaginous nasal septum is supported by and rests in a dorsal groove of a vertical bony plate — the vomer. This forms the septovomeral joint. The vomer, a median, somewhat sickle-shaped vertical plate of bone, separates the ventral portions of the nasal fossae. Anteriorly, the nasal septum bears, on its ventral margin, the paired enclosures of the vomeronasal organ. The septal cartilage extends anteriorly to the piriform aperture and terminates above the basal portion of the incisors (Fig. 11.2A). Information is meager on postnatal growth of the cartilaginous nasal septum (Fig. 11.2B).[2] Normal levels of proliferative

*Excerpted from: Sarnat BG. (1970) The face and jaws after surgical experimentation with the septovomeral region in growing and adult rabbits. *Acta Otolaryngol Suppl* **268**: 1–30.

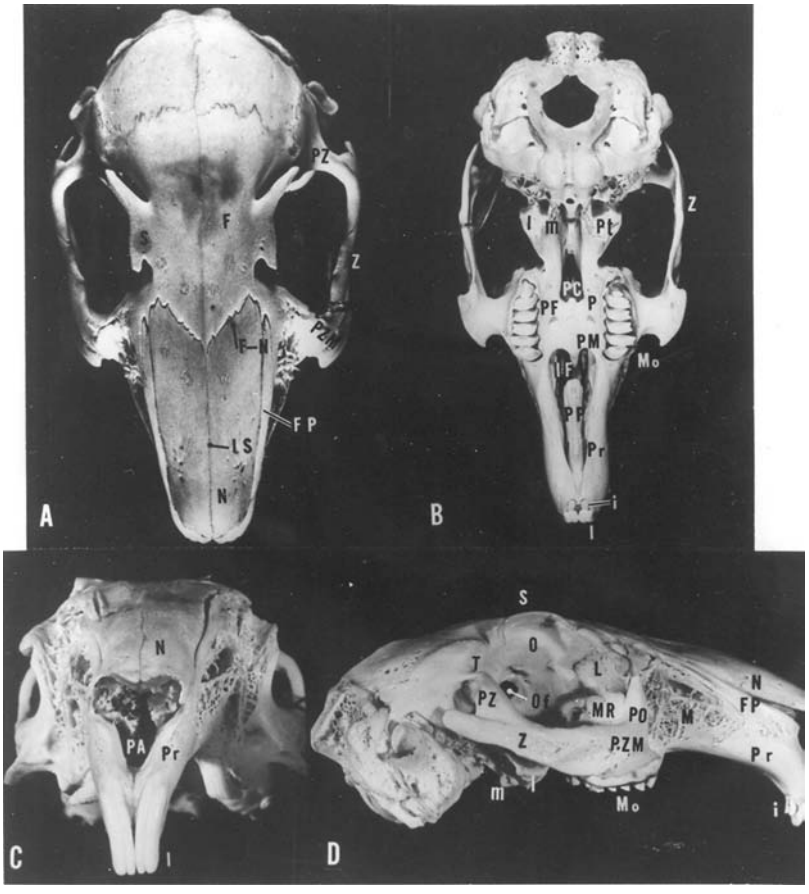

Fig. 11.1 Photographs of a normal adult rabbit cranium. (**A**) Dorsal; (**B**) Ventral; (**C**) Frontal; (**D**) Lateral views. F — Frontal bone; FN — frontonasal suture; FP — frontal process of premaxilla; l — labial incisor; i — lingual incisor; IF — incisive foramen; IS — internasal suture; M — maxilla; Mo — premolars and molars; N — nasal bone; P — palatine bone; PA — piriform aperture; PC — posterior choana; PF — palatine foramen; PM — palatine process of maxilla; PP — palatine process of premaxilla; Pr — premaxilla; Z — zygomatic arch.

cellular activity in the young rabbit's cartilaginous nasal septum were determined by autoradiographic studies with tritiated thymidine (Fig. 11.3). Cellular activity was most pronounced in the anterior and posterior zones (Fig. 11.3).[3]

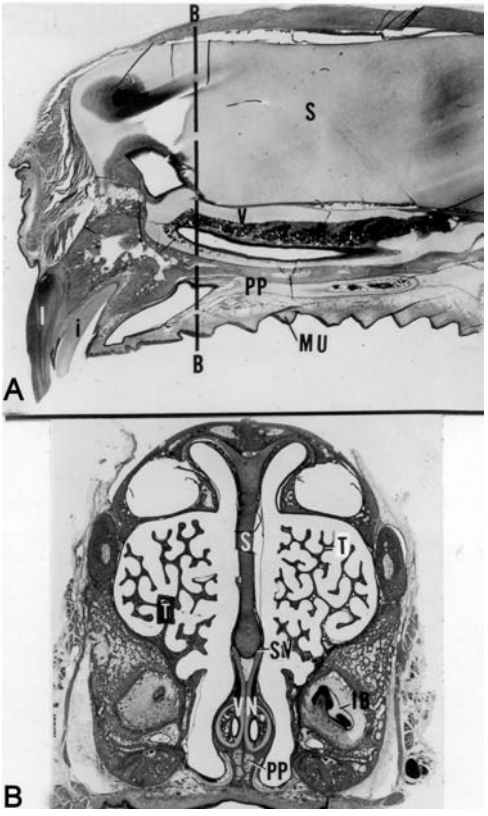

Fig. 11.2 Photomicrographs of (**A**) sagittal and (**B**) transverse (taken at approximately line BB) sections of snouts of 28-day-old unoperated-on rabbits. l — labial incisor; i — lingual incisor; MU — palatal mucosa; PP — palatine process of premaxilla; S — septum; SV — septovomeral joint; T — maxilloturbinate; V — vomer; VN — vomeronasal organ (original ×6). [From: Wexler MR, Sarnat BG. (1961) *Arch Otolaryng* **74**: 305–313.]

The thin and elongated nasal bone forms the roof of the nasal fossa and, in conjunction with its fellow of the opposite side, the dorsal boundary of the piriform aperture (Fig. 11.1C). The posterior border of the nasal bone articulates with the anterior border of the frontal bone, forming the frontonasal suture, a secondary site of active growth in the young rabbit.

The maxillae form the main portion of the upper jaw. Each maxilla consists of a central portion, the body, and of five processes — alveolar,

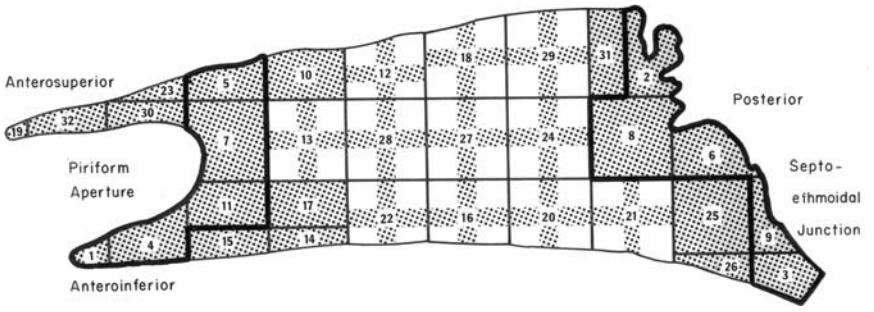

Fig. 11.3 Diagrammatic representation of a longitudinal section of the cartilaginous nasal septum of a three-week-old Dutch rabbit after intraperitoneal injection of tritiated thymidine. The various zones are numbered according to their relative activity (labeling index: zone 1, 3.36%; zone 32, 0.35%). Anteroinferior and posterior areas (heavily outlined) were the most active. Cell counts were made of the stippled areas. [From: Long R, Greulich R, Sarnat BG. (1968) *J Dent Res* **47**: 505.]

palatine, orbital, zygomatic, and spheno-orbital (Fig. 11.1). The ventral portion of the maxilla with the palatine bone forms the hard palate (Fig. 11.1B). This structure is represented chiefly by a bony palatine bridge connecting the two sides of the skull between the premolars and molars. It forms the roof of the oral cavity and a portion of the floor of the nasal cavity. Immediately in front of it, the palatine surface is perforated by a pair of large incisive foramina, which are broadly open to the nasal fossae (Fig. 11.1B). Laterally, where the palatine bones articulate with the palatine processes of the maxillae, are the palatine foramina.

The premaxilla forms the anterior part of the upper jaw. It comprises a central portion, the body, including the alveolar, frontal, and palatine processes (Fig. 11.1). The body forms a portion of the palatal surface of the skull and of the lateral boundaries of the incisive foramen. The frontal process of the premaxilla, a somewhat prominent narrow ridge, extends posteriorly along the lateral surface of the nasal bone and articulates with the premaxillary process of the frontal bone (Fig. 11.1D).

The mandible, the largest element of the facial region, is composed of two portions united anteriorly by the symphysis. Each half comprises a horizontal portion, the body of the mandible, and a posterior, vertical portion, the ramus. The latter serves for the insertion of the muscles of

mastication and for articulation with the skull. The mandibular ramus forms a broad plate, the lateral surface of which is occupied by the masseter muscle, while the medial surface serves as an area of insertion for the pterygoid muscle. The surface of the ramus is greatly increased in its posteroventral portion through the expansion of the bone to form the angle. The elongated articular surface is at the end of the condyloid process. Just inferior to this on the anterior border of the ramus is the coronoid process. The sigmoid notch is between these two processes. The nerve and vessels of the mandible enter at the mandibular foramen on the medial surface immediately behind the last molar.

The body of the mandible bears on its dorsal margin the alveoli of an incisor anteriorly and of the premolars and molars posteriorly. The alveolar process of each premaxilla contains a larger labial and a smaller lingual incisor (Fig. 11.1). The alveolar process of each maxilla contains the premolars and molars. The double set of upper incisors and three upper premolars distinguish the rabbit as a lagomorph from the rodent. The upper incisor occludes labial to the lower one and represents a larger segment of a smaller spiral. The lower incisor, although larger than the upper one, represents a smaller segment of a larger spiral. While the incisors in the rabbit are continuously growing and erupting, they are worn at the edges and thereby maintain occlusion. Because of the thicker layer of enamel on the labial surface and the thinner layer of enamel and softer dentin on the lingual surface, there is a differential in wear, thus producing a sharp bevel. Whereas the basal end of the lower incisor extends to the premolar, the basal end of the upper incisor is considerably anterior to the premolar.

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Normal Growth of the Suture*

INTRODUCTION

Various methods, both direct and indirect, have been employed to study growth of bones.[3] Analysis of the development of the adult size and shape of a bone or a complex of bones such as those forming the skull requires information about the sites and patterns of growth and the environmental influences. Growth of the skull occurs in three principal ways, namely: (1) on its surfaces (subperiosteal), (2) by replacement of growing cartilage (cranial base, mandibular condyle), and (3) at sutures (cranium and face).

The suture is a synarthrosis, found only in the skull (except for the turtle shell). The contiguous margins of the bones are joined by connective tissue which serves as an active site of growth. Growth at the frontonasal suture of the rabbit was determined grossly by the increased amount of separation of metallic implants. The combination of gross and serial cephalometric roentgenographic methods with metallic implants has been used[1,2] and was employed in the present study to determine not only the contributions of the frontonasal, interfrontal, and internasal sutures to the growth of the rabbit snout but also something of the nature of sutural growth.

*Excerpted from: Selman AJ, Sarnat BG. (1955) Sutural bone growth in the rabbit snout: a gross and serial roentgenographic study by means of metallic implants. *Am J Anat* **97**: 395–408.

MATERIALS AND METHODS

Animals

Twenty-five growing female New Zealand albino rabbits were used. Their ages ranged from 42 to 84 days at the beginning of the experiment. These animals were selected primarily because of their rapid growth and large snout, which lends itself to ready implantation and accurate serial roentgenography. However, a disadvantage is the size and complexity of the pinna, which make difficult the insertion of earposts for serial roentgenography. The animals were fed *ad libitum* on a standard rabbit ration.

Anesthesia

The animals were anesthetized by injection into the marginal ear vein of a 1% solution of pentobarbital sodium in distilled water (40 mg/kg body weight). To each dose, 0.25 mg of atropine sulfate was added. General anesthesia was utilized to insert the radiopaque metallic implants and to take serial cephalometric roentgenographs in a specially designed headholder (Fig. 12A.1).

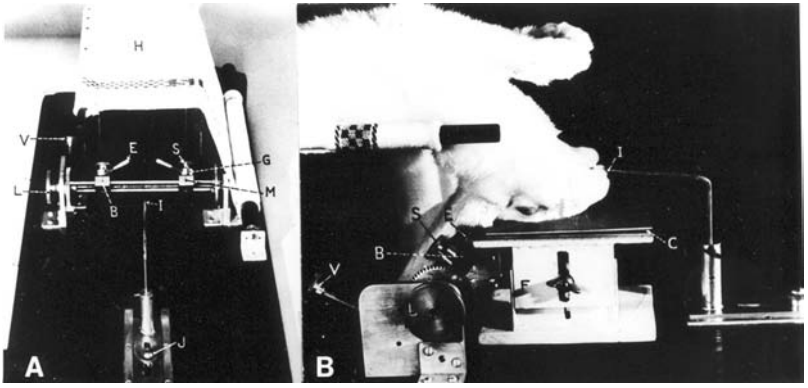

Fig. 12A.1 (A) Specially designed headholder; (B) Head in position on the cassette going into the external ear. B — earpost-bearing block; C — film cassette; E — earpost; F — film elevator; G — earpost guide line; H — hammock; I — incisal pin; J — incisal pin slide-screw; L — horizontal moving gear; M — earpost-bearing block guide line; S — earpost set-screws; V — vertical rotating gear.

Metallic Implants (Direct Measurements)

The anesthetized animal was strapped prone to the operating board. The skin of the dorsum of the snout was clipped free of hair, cleansed with 70% alcohol, and isolated with sterile towels. An aseptic technique was used throughout the surgical procedure. The skin and subcutaneous tissues were incised longitudinally in the midline from the region of the coronal suture to the nasal cartilage. After the wound margins were retracted, the periosteum was incised, elevated from the bone, and the frontonasal, internasal, and interfrontal sutures were exposed.

A dental bur, mounted in a handpiece, was used to prepare two undercut cavities in the cortical plate of each frontal and nasal bone. Into the prepared cavities, dental amalgam was packed. This was used because of its plasticity, tolerance by tissues, and radiopacity. An indentation was made in the center of each implant with the point of a caliper, and the distance between the centers of each pair of implants recorded to the nearest 0.1 mm (Fig. 12A.2). The soft tissues were then replaced and approximated with 4-0 black silk sutures.

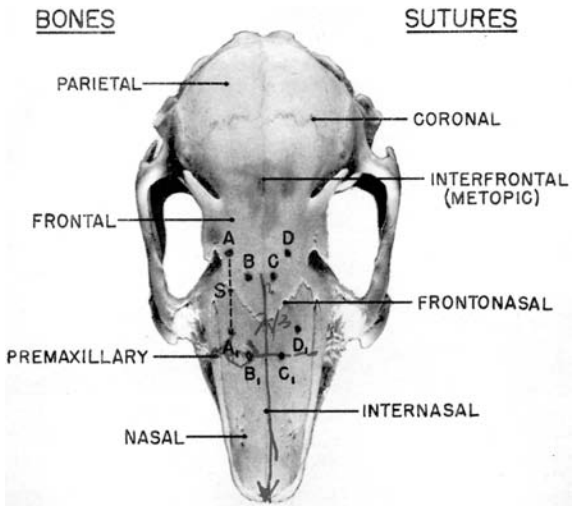

Fig. 12A.2 Dorsal view of a rabbit skull showing sites of implant amalgam (A, B, C, D, etc.) in the frontal and nasal bones. S — point on the frontonasal suture where a straight line crosses between AA_1, etc.

The postoperative survival ranged from 7 to 84 days. The animals were then euthanized by a lethal dose of pentobarbital sodium injected intravenously. The heads were severed and the soft tissues dissected. The distances between the same groups of implants were again determined, as at the beginning of the experiment.

Serial Cephalometric Roentgenography (Indirect Measurements)

To measure distances between the radiopaque implants, a cephalometric roentgenograph of the frontonasal region with the plane porion-interdentale oriented to the horizontal was desired. This view had proven advantageous in the study of animal snouts, and a special headholder had been designed and constructed so as to obtain strictly comparable serial cephalometric roentgenographs.

Immediately after completion of the surgical procedure, a cephalometric roentgenograph was taken. This was repeated in 15 animals at 14-day intervals and at death (Fig. 12A.3). The distances were measured between the estimated centers of the radiopaque images of the metallic implants on the roentgenographs. Measurements between implant images (in frontal and nasal bones) on the roentgenographs are strictly comparable with measurements made directly on the skulls.

RESULTS

Skulls

Of the 200 implants inserted, 7 were missing and 13 were loose. Four of these were associated with infection. Most of the difficulties were encountered in the nasal bones. The remaining 180 implants were well tolerated and invariably covered by a thin layer of bone. Measurements taken between implants in the same bone (frontal or nasal) were the same at the beginning and the end of the experiment.

Increased separation of paired implants at the frontonasal suture

The increased distance between paired implants on either side of the frontonasal suture was determined directly on the skulls by subtracting the

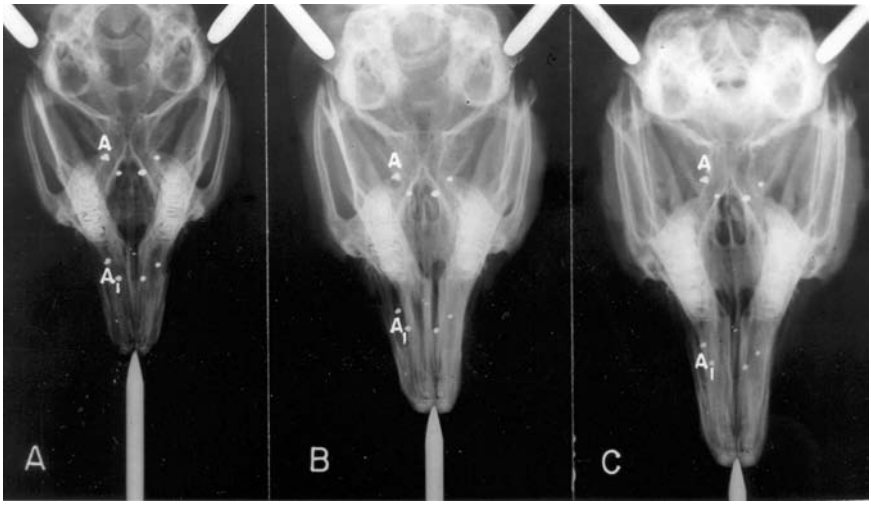

Fig. 12A.3 Ventrodorsal cephalometric roentgenographs of animal No. 21. (**A**) 6 weeks of age; (**B**) 10 weeks of age; (**C**) 16 weeks of age. Note the increase in size and the change in shape of the skull, and the increased longitudinal and lateral separation of the implants on either side of the frontonasal, internasal, and interfrontal sutures (see Fig. 12A.2). However, the distance between implants within the nasal or frontal bones remained constant. The tips of the earposts are in the external auditory canals. The incisal pin is in position.

initial from the final measurement. This difference varied with the age of the animal at the time of implantation, the duration of the experiment, and the individual animal. Thus, in 42-day-old rabbits, the increased amount of separation of the implants after 7 days ranged from 0.3 (No. 20) to 1.3 (No. 73) mm. In another group of rabbits, the increased separation of implants during an 84-day period (42–126 days of age) ranged from 10.6 (No. 10) to 11.9 mm (No. 88).

In addition to the total separation of the paired implants, the individual contributions of the frontal and nasal bones side of the suture to the increased separation of the paired implants were determined. Measurements were taken between each implant (in nasal and frontal bones) and a point on the frontonasal suture at the beginning and the end of the experiment. The point chosen on the suture was found where a straight line crossed between the frontal bone and its corresponding nasal bone implant (Fig. 12A.2). In this way, the respective contributions of the nasal and the frontal aspects of

the suture to the increase in separation of the pegs were determined. Mean percentage values of the frontal and nasal contributions were obtained in a group of 19 animals. These values indicated that the mean frontal contribution was about one-half of the mean nasal contribution at planes AA_1 and DD_1. At planes BB_1 and CC_1, the mean frontal contribution was about two-thirds to three-fourths of the mean nasal contribution.

Increased separation of paired implants at the internasal and interfrontal sutures

The increased distance between paired implants on either side of the internasal and interfrontal sutures was determined by subtracting the initial from the final measurement. The amount of growth was so small (estimated at about one-tenth to one-twentieth of that at the frontonasal suture) that it was within the range of experimental errors.

Serial Roentgenographs

Examination of the serial cephalometric roentgenographs revealed the loss of seven implants at various times. Measurements between the estimated centers of the images of the metallic implants in the same bones (frontal and nasal) showed no change at any time from the beginning to the end of the study (Fig. 12A.3).

There was an increase in separation of the pegs on either side of the frontonasal suture for each 14-day period from 42 to 154 days of age, when the experiments were terminated. The measurements indicated that the animals were in a phase of declining bone growth (Fig. 12A.4). For example, the mean increment of growth from 42 to 56 days of age was about 3.0 mm, whereas from 140 to 154 days it was only 0.3 mm.

DISCUSSION

Implants

Two implants were inserted into each frontal and nasal bone (1) to have an additional implant available for purposes of measurement in the event

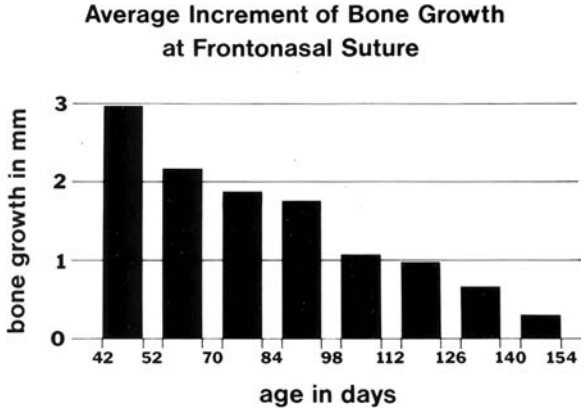

Fig. 12A.4 Average increment of growth of bone at the frontonasal suture at two-week intervals, as determined from implant images on serial cephalometric roentgenographs.

that one was lost, and (2) to determine whether any increase in distance occurred between implants within an individual bone.

Most of the difficulties encountered with the implants (loss, loosening, and infection) were in the nasal bones. This can be explained on the basis of the thinness of these bones. In the preparation of undercut cavities for the reception and retention of amalgam, it was often difficult to avoid penetration into the nasal cavity. Some implants were found at the time of dissection on the mucoperiosteum, possibly as a result of resorption of the inner table of bone. A similar experience was encountered with implants originally placed on the lateral surface of the zygomatic arch, and subsequently found on the medial border (Chap. 15).

Since the design of this experiment also included implants within the same bone, measurements between these implants were taken. The evidence obtained agreed with that of others who do not subscribe to the theory of interstitial growth of bone (Chap. 35). If interstitial growth did occur, with consequent change in distance between implants within one bone, this experiment (determining sutural growth by increased separation of bone implants) would be invalid.

This investigation was concerned essentially with bone growth at the frontonasal suture and was expressed as growth in the length of the rabbit

snout. Bone growth at the frontonasal suture was determined by subtracting the measurement between implants of the preceding period from that between implants of a successive period. From this study, one would conclude that the frontonasal suture made an important contribution to the growth in the length of the rabbit snout, and that most of this was attained by the 154th day of life.

To be unidirectional and/or bilaterally symmetrical, growth must be generally equal in all planes along the suture. At the frontonasal suture, increased separation of paired implants was found to be generally equal in all four planes measured.

In the 42-day-old rabbit, the frontonasal suture was fairly regular in outline and accurate measurements were made from implant to suture. With increase in age, because the suture became more serrated, measurements were only relatively accurate. However, the error in measurement was fairly constant and it was concluded that the findings were essentially correct. Further examination of our data revealed that the increased distance between the implant and the frontonasal suture was greater on the nasal bone side than on the frontal bone side. This would be a result of greater proliferation of connective tissue and apposition of bone on the nasal bone side of the suture. This finding was not anticipated. The total amount of growth at the internasal and interfrontal sutures was considerably less than at the frontonasal suture.

SUMMARY AND CONCLUSIONS

(1) The total amount and biweekly increments of growth of bone at the frontonasal, internasal, and interfrontal sutures were investigated in 25 rabbits from 42 to 154 days of age by means of gross and serial cephalometric roentgenographic studies of the increase in separation of metallic implants on either side of the suture.

(2) At the frontonasal suture, the mean growth of bone was greatest in the 42–56-day age period (3.0 mm) and decelerated in each successive period, until in the 140–154-day age period it was about one-tenth that of the earliest period. The contribution of the frontal side to growth of bone at this suture was about one-half to three-fourths that of the nasal side.

(3) At the internasal and interfrontal sutures, the total amount of growth of bone was estimated to be about one-tenth to one-twentieth that at the frontonasal suture. However, the amount of growth was so small that it was within the limits of experimental error.
(4) The changes in the proportion of the snout were determined by (a) the number of growth sites in a given direction, (b) the rate of bone deposition at a given site, and (c) the length of time over which growth at that site was active. The length of the snout increased more than the width, because the amount of growth was greater in the former dimension.

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Rabbit Snout After Extirpation of the Frontonasal Suture*

INTRODUCTION

The purpose of this experiment was to study the nature of sutural growth and the effects of injury upon it. In a previous report Selman and Sarnat[7] showed that in the 42-day-old rabbit the region of the frontonasal suture was an active site of bone growth. Therefore, this region was selected to study the effects of trauma. The maximal injury was imposed — that of extirpation of the suture.

MATERIAL AND METHODS

Animals

In this study there were 49 (28 experimental and 21 control) growing female New Zealand albino rabbits. Their ages ranged from 42 to 84 days at the time of the surgical operation. Rabbits were selected primarily because of the rapid rate of growth in the region of the frontonasal suture. Thus, one would expect conditions affecting growth at this suture to be reflected in altered growth of the snout. Moreover, the snout readily lends

*Excerpted from: Selman AJ, Sarnat BG. (1957) Growth of the rabbit snout after extirpation of the frontonasal suture: a gross and serial roentgenographic study by means of metallic implants. *Am J Anat* **101**: 273–293.

itself to the placement of metallic implants and accurate serial roentgenography. However, the size and complexity of the pinna make difficult the insertion of earposts for serial roentgenography. The animals were fed *ad libitum* on a standard rabbit ration.

Anesthesia

The animals were anesthetized by injection into the marginal ear vein of a 1% aqueous solution of pentobarbital sodium (40 mg/kg body weight). To each dose, 0.25 mg of atropine sulfate was added. Extirpation of the frontonasal suture, insertion of the radiopaque metallic implants, and serial cephalometric roentgenography were then done.

Extirpation of the Frontonasal Suture

The anesthetized animal was strapped prone on the operating board. The skin of the dorsum of the snout was clipped of hair, cleansed with 70% ethyl alcohol, and isolated with sterile towels. An aseptic technique was used throughout the surgical procedure. The skin and subcutaneous tissues were incised longitudinally in the midline from the region of the coronal suture to the nasal cartilage. After the wound margins were retracted, the periosteum was incised, elevated from the bone and retracted, and the frontonasal, interfrontal, and internasal sutures were exposed (Fig. 12B.1A).

A dental bur, mounted in a handpiece, was used to extirpate the frontonasal suture either unilaterally (in 8 animals) or bilaterally (in 20 animals). The extirpation channel was cut equally out of the frontal and nasal bones, and was about 1.0 cm wide (Fig. 12B.1B). In unilateral extirpations, which were always on the right side, the bur cut extended slightly beyond the midline. In most cases the adjacent premaxillary tip was also cut. Efforts were made in cutting the channel to expose but not damage the underlying endonasal periosteum. This was rarely successful.

Metallic Implants (Direct Measurements)

Two undercut cavities were prepared by means of a dental bur mounted in a handpiece in the cortical plate of each nasal and frontal bone, in both the

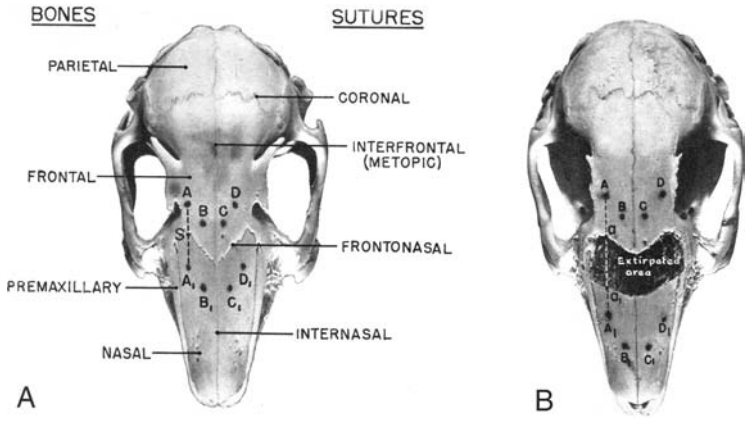

Fig. 12B.1 Dorsal view of rabbit skulls showing sites of implantation of silver amalgam in the nasal and frontal bones. (**A**) Normal animal with the frontonasal suture intact; S — point on the frontonasal suture where a straight line crosses between AA_1, etc.; (**B**) Animal in which the frontonasal suture was extirpated seven days before death; a, a_1 — points on either side of the extirpation site where a straight line crosses between AA_1, etc.

experimental and control groups. These cavities were placed about 1.0 cm from the suture line in the control animals and 0.5–1.0 cm from the channel edge in the experimental animals. Dental amalgam was packed into the prepared cavities. This material was selected because of its plasticity, tolerance by tissues, and radiopacity. An indentation was made in the center of each amalgam implant with the point of a caliper and for each pair of implants the distance between these centers (AA_1, BB_1, etc.) was recorded to the nearest 0.1 mm.

In the control animals a measurement was also made between each implant and the frontonasal suture at the point (S) on the suture where a straight line crossed between the corresponding frontal and nasal implants (Fig. 12B.1A).

In the experimental animals, in addition, the distance between each implant and its adjacent channel border, and the width of the extirpated area were also measured on a line between the corresponding frontal and nasal bone implants (Fig. 12B.1B). The soft tissues were then replaced and approximated with 4-0 black silk sutures.

Serial Cephalometric Roentgenography (Indirect Measurements)

Immediately after completion of the surgical procedure, a cephalometric roentgenograph was taken. This was repeated in 20 experimental animals and 15 control animals at 14-day intervals and at death. The distances were measured between the estimated centers of the radiopaque images of the metallic implants on the roentgenographs. Measurements between implant images (in frontal and nasal bones) on the roentgenographs are strictly comparable with measurements made directly on the skulls.[6]

The postoperative survival ranged from 14 to 84 days. The animals were euthanized by a lethal dose of pentobarbital sodium injected intravenously. The heads were immediately severed and the soft tissues dissected. The distances between the same groups of implants and extirpation borders were again determined as at the beginning of the experiment.

Gross Observations

Of the 168 implants inserted in control animals, 7 were missing, and of the 224 implants inserted in the experimental animals, 8 were missing. Most of the difficulty was encountered in the nasal bones. The remaining implants were well tolerated and invariably covered by a thin layer of bone. Measurements taken between implants in the same bone (frontal or nasal) were the same as at the beginning and the end of the experiment.

The gross appearance of the snout in terms of size and shape, in the animals in which the frontonasal suture had been bilaterally or unilaterally extirpated, was similar to that of the control animals (Fig. 12B.2). No lateral deviation of the snout was observed in the animals with a unilateral extirpation.

Following unilateral or bilateral extirpation, the frontonasal suture did not recover its anatomical form. The channel created by the extirpation contained a dense, fibrous connective tissue in which were occasional splinter-like islands of bone which tended to be larger and longer in the older animal (Fig. 12B.2). Sometimes a new, minor suture was formed by a bone island, at the zone of contact with the border of the frontal or nasal bone. Rarely did an individual bone island extend completely across the

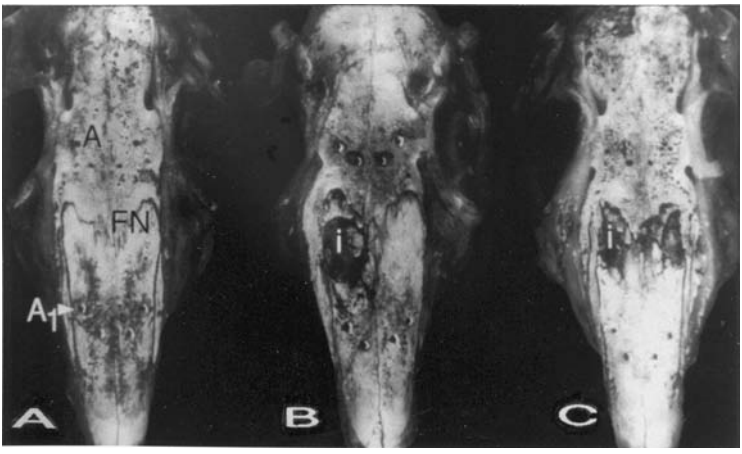

Fig. 12B.2 Dorsal view photographs of three freshly dissected rabbit skulls at death with implants in frontal and nasal bones. All three animals were of the same age and, although subjected to different experimentation, the shape and size of the snout are essentially the same. (**A**) Control animal No. 7. Implants inserted at 42 days of age and a postoperative survival of 70 days. (**B**) Animal No. 29, in which the right side of the frontonasal suture was extirpated at 42 days of age, with a postoperative survival of 70 days. Note the bone islands (i) adjacent to the anterior border of the frontal bone in the dense connective tissue filling the channel. (**C**) Animal No. 11, in which the entire frontonasal suture was extirpated at 42 days of age, with a postoperative survival of 70 days. Note the scattered bone islands (i) and the dense fibrous connective tissue in the channel. There is no semblance of the original suture.

channel. The channel width itself did not become less. Rather, it increased as longitudinal growth proceeded.

Direct Measurement

The observations regarding the gross appearance of the snout in terms of size and shape, and those regarding the extirpated channel, were substantiated by direct measurements. In all animals the direct measurements made between implants at the beginning of the investigation were repeated at death.

Where an extirpation channel was created, three measurements, the sum of which equaled the distance between frontal and nasal implants,

were taken. These consisted of (1) the distance between the frontal implant and the frontal border of the channel (Aa), (2) the distance between channel borders (aa_1), and (3) the distance between the nasal channel border and the nasal implant (a_1A_1). The contribution of each of these to the total increase in length was determined by subtracting the measurement made at the beginning from that at the end of the experiment (Fig. 12B.1).

In addition to the above, measurements could also have been taken from the nasal implants to the anterior border of the nasal bones. Thus, a comparison could have been made of the relative contributions of the frontonasal suture and the free end of the nasal bone to its growth in length of bone. A similar comparison could have been made after extirpation of the frontonasal suture. This was not done since it was beyond the purpose of the present experiment.

Total Longitudinal Growth Between Implants

It was found in each animal that total longitudinal growth was essentially the same in all four planes of measurement, i.e. AA_1, BB_1, CC_1, and DD_1, regardless of whether or not the suture had been extirpated, either bilaterally or unilaterally (Fig. 12B.1).

Further, on the basis of comparable age and duration of experiment, the control group, the bilaterally extirpated group, and the unilaterally extirpated group were compared regarding the total longitudinal growth as measured at AA_1. The differences were found to be without significance (Fig. 12B.1). In the unextirpated region at plane DD, comparability could also be established between the control group of animals and the group of animals with unilateral extirpation of the frontonasal suture.

Components of Longitudinal Growth Between Implants

Using plane AA_1 for measurement, comparability was found between the two experimental groups of animals, i.e. those with unilateral and those with bilateral extirpation of the frontonasal suture, regarding mean frontal bone growth, mean nasal bone growth, and mean increase in the width of the extirpation channel, as measured at Aa, a_1A_1, and aa_1, respectively (Fig. 12B.1B).

Frontal bone growth was relatively unaltered by extirpation of the frontonasal suture. The difference between mean frontal growth in the control and experimental groups, as measured at AS and Aa, respectively, was found to be without significance. Further evidence was seen in the comparability between mean frontal growth on the extirpated and unextirpated sides, as measured at Aa and DS, respectively, in the group of animals with unilateral extirpation of the frontonasal suture.

Nasal bone growth, on the other hand, was affected by extirpation of the frontonasal suture. Although there was no significant difference in mean nasal growth, as measured at a_1A_1, between the two groups of experimental animals, the difference in mean nasal growth between the experimental groups and the control group, as measured at a_1A_1 and SA_1, was found to be significant. Additional evidence regarding nasal bone growth was found in the significant difference between mean nasal bone growth on the extirpated and unextirpated sides, as measured at a_1A_1 and SD_1, respectively, in the group of animals with unilateral extirpation of the frontonasal suture.

A significant difference was established between the amount of frontal and nasal bone growth at the suture in the control group of animals.[7] In this group mean frontal bone growth was shown to be about one-half of mean nasal bone growth in planes AA_1 and DD_1. The difference in frontal and nasal bone growth persists even after extirpation of the frontonasal suture. At plane AA_1 mean frontal growth and mean nasal growth, in both experimental groups of animals, as measured at Aa and a_1A_1, were shown still to be significantly different. At plane DD_1 in both the control group and the group of animals with unilateral extirpation of the frontonasal suture, a significant difference was demonstrable between frontal and nasal growth, as measured at DS and SD_1.

In the group of animals with unilateral extirpation of the frontonasal suture, mean frontal growth and mean channel growth, as measured at plane AA_1, each contributed about one-fourth to the total longitudinal increment, with mean nasal growth contributing about one-half. This was comparable with the findings on the group of animals with bilateral extirpation of the frontonasal suture.

On the unextirpated side in the group with unilateral extirpation of the frontonasal suture, as measured in plane DD_1, mean nasal growth

contributed about two-thirds and mean frontal growth about one-third to the total longitudinal increment. This was comparable with the findings on the control group of animals.

In the older animals, the channel borders were seen to be increasingly irregular and the measurements were, therefore, only relatively accurate. However, the error in measurement was fairly constant and it was concluded that the findings were essentially correct.

Indirect Measurements: Serial Roentgenographs

Examination of the serial cephalometric roentgenographs revealed the loss of 15 implants at various times. Measurements between the estimated centers of the images of the metallic implants in the same bones (frontal and nasal) showed no change at any time from the beginning to the end of the study.

An increase in separation of the implants on either side of the region of the frontonasal suture was obtained for each 14-day period from 42 to 154 days of age, when the experiment was terminated. The measurements indicated the animals were in a declining phase of bone growth.

In each group of animals, the mean of the increments of the four planes of measurement — AA_1, BB_1, CC_1, and DD_1 — were compared and found to be without significant difference. In addition, from the total increment at AA_1 from 42 to 98 days of age, which was calculated for each animal, it was possible to determine the mean total increment for the same period and plane of measurement for each group of animals. The difference between the mean total increments of the experimental and control groups of animals, as measured at AA_1 for the period from 42 to 98 days of age, was found to be without significance. The same strict comparability was determined between the extirpated and unextirpated sides in the group of animals with unilateral extirpation of the frontonasal suture.

DISCUSSION

Implants

Two implants were inserted into each frontal and nasal bone to have an additional implant available for purposes of measurement, in the event

that one was lost. Most of the implants lost were from the nasal bones. This can be explained on the basis of the thinness of these bones.[7] In the preparation of undercut cavities for the reception and retention of amalgam, it was often difficult to avoid penetration into the nasal cavity. Some implants were found at the time of dissection on the mucoperiosteum, possibly as a result of resorption of the inner table of bone. A similar experience was encountered with implants originally placed on the lateral surface of the zygomatic arch and subsequently found on the medial aspect.[1]

The evidence obtained from measurements between implants in the same bone agreed with that of others who do not subscribe to the theory of interstitial growth of bone. If interstitial growth did occur, with consequent change in distance between implants within one bone, this experiment (determining sutural growth by increased separation of bone implants) would be invalid.

Extirpation Site

The frontonasal suture is formed by the overlapping of the anterior margin of the frontal bone with the posterior margin of the nasal bone. The overlapping margins are narrow medially but rather broad laterally. It was necessary, therefore, to make a wide extirpation channel in order to remove all sutural tissue. In no instance following extirpation was there complete, or even nearly complete, bony healing of the extirpation site.

Some Considerations of Sutural Growth

One concept of sutural bone growth describes it as an expansion initiated by a proliferation of the sutural connective tissue.[9] The separation of the contiguous bones is said to be followed immediately by apposition of immature bone along the contiguous borders. This concept is not consistent with the findings of this study and is not supported by investigations of other sutural areas.[2,3]

A wedging or expansive force between frontal and nasal bones by the frontonasal suture is apparently not necessary for growth in that area. Separation of the nasal and frontal bones continued at all times in an amount not significantly different from normal in the absence of the

normal suture. The small islands of bone formed between nasal and frontal channel edges (Fig. 12B.2) were not conceivably adequate for the task of wedging the bones apart. In some animals, furthermore, an island of bone may have formed on one side of a bilaterally extirpated channel and not on the other. Growth in such cases was, nevertheless, equal for the two sides. In unilaterally extirpated cases, growth on the extirpated side was essentially equal to that on the unextirpated side whether or not islands of bone were formed. That the broad, thin, fibrous connective tissue band in the extirpation channel might have caused a widening of the channel does not seem likely.

Creation of the extirpation channel is creation of a bone defect or fracture. Under conditions of relative immobility the dense, fibrous connective tissue might act as a connective tissue model in repair of a bone fracture.[8] However, the movement involved in growth separation of the frontal and nasal bones would seem to be an important factor in preventing their fusion.

An I-shaped metal splint could be inserted across an extirpation channel in an attempt to stop or restrain increase in channel width. The question is whether fusion across the channel would eventually take place under these conditions. It would also be of interest to observe in growing animals the effects of an attempted immobilization of the bones on either side of the intact frontonasal suture by use of the same method. If immobilization were effected in this manner, as proven by failure of the implants to separate, fusion of the suture would indicate that growth compensation was the function of the suture — *per se.*

In the control animals, measurements between implants, and between implants and suture, showed that the frontal bone contributed about one-third and the nasal bone about two-thirds to the total longitudinal growth at the frontonasal suture. After extirpation the frontal bone contributed about a 25–30% increase in channel width and nasal growth contributed about 45–50% to the total longitudinal growth in the region.

Increase in channel width apparently occurred mainly at the expense of nasal bone growth. Frontal growth was relatively unaltered by extirpation of the frontonasal suture. However, nasal growth remained characteristically greater than frontal growth even in the absence of the suture. Such evidence eliminates sutural activity even further as the primary, direct effector of growth.

SUMMARY AND CONCLUSIONS

(1) The total amount and 14-day increments of separation between implants in the frontal and nasal bones after bilateral and unilateral extirpation of the frontonasal suture were studied in 28 rabbits from 42 to 154 days of age for periods as long as 84 days. These were determined directly by gross measurements at the beginning and the end of the experiment and indirectly by means of serial cephalometric roentgenographs taken at 14-day intervals. Twenty-one rabbits with the frontonasal suture intact were used as controls.

(2) The mean total amount of increase of separation of these implants in normal animals was found not to differ significantly from that in animals in which the right half or the entire frontonasal suture had been extirpated. In addition, no significant difference was found in the amount of increase of separation of the implants on the left and right sides of animals in which there had been only a unilateral extirpation of the frontonasal suture.

(3) Whereas in control animals the nasal part of the frontonasal suture contributed about two-thirds and the frontal part about one-third to the increased separation of the implants, in the animals in which the frontonasal suture had been extirpated the nasal part contributed about one-half, the extirpation site one-fourth, and the frontal part one-fourth to the increased separation of the implants.

(4) Grossly, no significant difference was seen in the shape and size of the snouts between the normal and experimental animals (unilateral and bilateral extirpation of frontonasal suture).

(5) Thus, from these experiments it seems that maximal injury to a facial suture, as severe as extirpation, failed to produce a growth arrest.

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Growth Pattern of the Nasal Bone Region*

Two radiopaque implants were inserted into each left and each right nasal bone in five female rabbits. Ventrodorsal cephalometric roentgenographs were taken at 6 and 16 weeks of age. From these roentgenographs, separate tracings were made on matte acetate paper of the left and right nasal bone regions, including the radiopaque implants. The markers of the 16-weeks-of-age tracing were superposed on the markers of the 6-weeks-of-age tracing. The difference between the two established outlines represented the changes in size and shape in two dimensions that had occurred during the 10-week period. Our purpose was to determine the relative growth activity at several borders. The mean increase was about 6.79 mm at the proximal (posterior) border, 6.19 mm at the distal (anterior) border, 2.73 mm at the lateral border, and 1.22 mm at the medial border. Thus, growth at the proximal and distal borders was about the same and about twice that of the lateral border and about five times that of the medial border.

INTRODUCTION AND PURPOSE

Growth of the nasal bone region occurs in two principal ways, namely on its various surfaces and at sutures (frontonasal and premaxillary–maxillary). The purpose of this study was to assay the growth pattern of the rabbit nasal bone region by determining relative amounts of growth at

*Excerpted from: Sarnat BG, Selman AJ. (1982) Growth pattern of the rabbit nasal bone region. *Rhinology* **20**: 93–105, Cottle Award, American Rhinologic Society.

several borders. This was done by a combined method of serial gross and roentgenographic measurements between radiopaque implants inserted within a single bone — the nasal bone.[5] There were several advantages: (1) it was a serial study; (2) there were permanent records; (3) the implants served as stable reference markers from which accurate information could be obtained as to sites, relative amounts, and directions of growth; and (4) the roentgenographic changes that occurred from one period to another could be determined without killing or reoperating on the animal. We have found no such report. In Table 13.1, there is a brief historical review.

MATERIALS AND METHODS

Animals

Five growing six-week-old female New Zealand albino rabbits were used. They were selected primarily because of their rapid growth and a snout which lent itself to ready implantation and accurate serial roentgenography. A disadvantage, however, was the size and complexity of the pinna, which made difficult the insertion of ear posts for serial roentgenography. The animals were fed *ad libitum* on a standard rabbit ration.

Anesthesia

The rabbits were anesthetized by injection into the marginal ear vein of a 1% solution of pentobarbital sodium in distilled water (40 mg/kg body weight). To each dose, 0.25 mg of atropine sulfate was added.

Metallic Implants

The anesthetized animal was strapped prone on the operating board. The skin of the dorsum of the snout was clipped free of hair, cleansed with 70% ethyl alcohol, and isolated with sterile towels. An aseptic technique was used throughout the surgical procedure. The skin and subcutaneous tissues were incised longitudinally in the midline. After the wound margins

Table 13.1 Brief Historical Review of Implant Markers Used in the Longitudinal Study of the Growth of Bones*

Investigator	Year	Material Used	Bones Studied	Animal
Gross (direct) studies				
Hales	1727	holes	tibia	chicken
Duhamel	1743	silver stylets	long bone	pigeon, dog
Hunter	1770	lead shot	tibia tarsometatarsal	pig chicken
Humphry	1864	wires	mandible	pig
Gudden	1874	holes	parietal, frontal	rabbit
Wolff	1885	metal	frontal, nasal	rabbit
Giblin and Alley	1942	wax	parietal, frontal, etc.	dog
Roy and Sarnat	1956	stainless steel wire. black silk suture	rib	rabbit
Gross (direct) and/or serial radiographic (indirect) studies				
Dubreuil	1913	metal	tibia	rabbit
Gatewood and Mullen	1927	shot	femur	rabbit
Troitzky	1932	silver wires	skull	dog
Levine	1948	denial silver amalgam	frontal, nasal	rabbit
Gans and Sarnat	1951	dental silver amalgam	various facial	monkey
Sissons	1953	metal	femur	rabbit
Selman and Sarnat	1953	dental silver amalgam	frontal, nasal	rabbit
Robinson and Sarnat	1955	dental silver amalgam	mandible	pig
Björk	1955	tantalum	various facial	human
Elgoyhen *et al.*	1972	tantalum	various facial	monkey
Sarnat and Selman†	1978	dental silver amalgam	nasal	rabbit

*Modified after Sarnat.

†This report.

were retracted, the periosteum was incised, elevated, and retracted, and the nasal bones were exposed.

A dental bur, mounted in a handpiece, was used to prepare two cavities, with an undercut at the base to facilitate retention in the cortical plate of each nasal bone. Into these cavities, dental amalgam was packed (Fig. 13.1). When prepared, this material was pliable and could be readily handled and inserted into a newly created bone cavity. In addition, it expanded slightly after setting, which aided retention. Two other important characteristics of this material were its tolerance by the local tissue and its radiopacity. An indentation was made in the center of each amalgam implant with the point of a caliper, and for each pair of implants within the same bone the distance between these centers (A_1, B_1, C_1, D_1) was recorded to the nearest 0.1 mm. A direct measurement was also made between each implant and the frontonasal suture at the point S on the suture where a straight line crossed between the corresponding nasal implant (Fig. 13.1). The soft tissues were then replaced and approximated with 4-0 black silk sutures. The animals were killed 70 days later by pentobarbital sodium injected intravenously and the

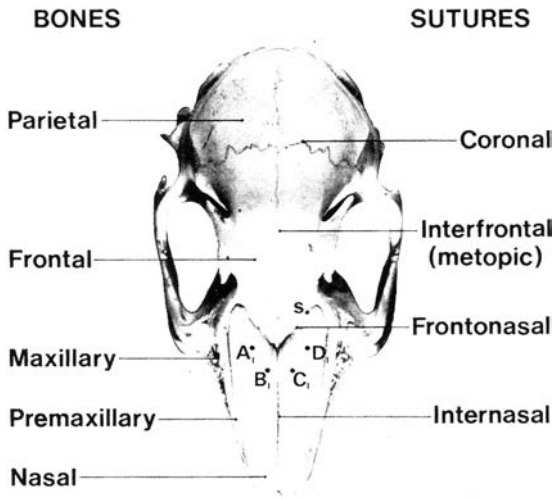

Fig. 13.1 Dorsal view of a rabbit skull showing sites of implantation of dental amalgam in right (A_1, B_1) and left (C_1, D_1) nasal bones. S — point on the frontonasal suture.

measurements repeated. The heads were severed and the soft tissues dissected.

Serial Cephalometric Roentgenography

A special headholder had been designed and constructed to obtain comparable serial cephalometric roentgenographs.[6] An ear post was placed in each external auditory meatus and an incisal pin placed between the maxillary incisors to orient the head in the same position each time the roentgenographs were taken. A ventrodorsal cephalometric roentgenograph was taken of the frontonasal region with the plane porion-interdentale (between the external auditory canals and the point of convergence of the upper incisors) oriented to the horizontal. This view had proven advantageous in the study of the rabbit snout (Selman and Sarnat, 1953).

Immediately after completion of the surgical procedure, a cephalometric roentgenograph was taken (Fig. 13.2A). This was repeated 10 weeks

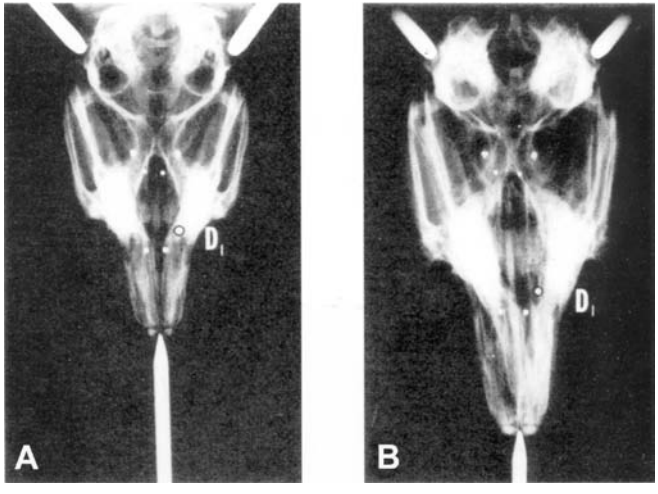

Fig. 13.2 Ventrodorsal cephalometric roentgenographs of a rabbit at 6 (**A**) and 16 (**B**) weeks of age. Note the increase in size and the change in shape of the skull and particularly the snout. D_1 — one of two implants in left nasal bone. The relationship between implants in the same bone did not change during the 10-week period. The tips of the ear posts are in the external auditory canals. The incisal pin is in position.

later at death (Fig. 13.2B). A separate tracing of each left and each right nasal bone region was made on matte acetate paper of the first and last roentgenographs, with special attention given to the position of the implant images and the borders of the nasal bone region. On the roentgenograph a midline was established, extending between the upper incisors and along the septovomeral midpalatal region. The lateral border was the lateral border of the premaxilla. The distal border was the most distal border of the nasal bone. The proximal border was determined by direct gross measurements of the distance of each nasal bone implant to the frontonasal suture at two points (such as D_1 to S) at 6 and 16 weeks of age (Fig. 13.1). From this, the pattern and position of the frontonasal suture were estimated. A base for the serial roentgenographic tracings was obtained by placing the later tracing over the initial one in a position where the two implant images (A_l, B_l, C_l, D_l), recorded on each tracing, superposed. The difference between the two established outlines of the nasal bone region represented the changes in size and shape in two dimensions that had occurred during this period (Figs. 13.3A,B). Selected measurements were made of the differences.

RESULTS

Gross

Of the implants inserted, two were missing (animal No. 26). The remaining implants were well tolerated and invariably covered on the dorsum by a 0.1–0.3 mm layer of bone. Measurements taken between implants in each nasal bone were the same at the beginning and the end of the experiment. Measurements were taken between each implant (in nasal bones) and a point on the frontonasal suture at the beginning and the end of the experiment (Fig. 13.1). In this way the contributions of the nasal aspect of the suture to the increase in the size of the nasal bone were determined at two points.

Serial Cephalometric Roentgenographs and Tracings

Measurements between the estimated centers of the images of the metallic implants in the same nasal bone showed no change at any time from the

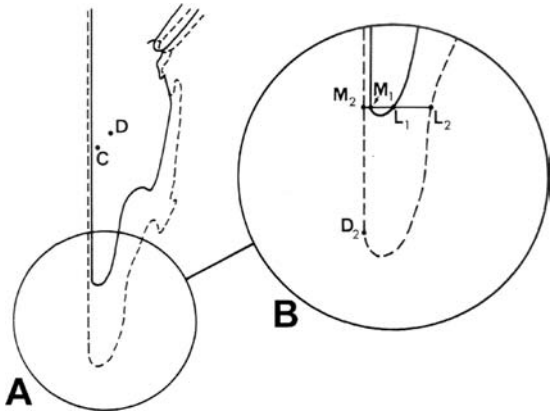

Fig. 13.3 Tracing of the left nasal bone region taken from ventrodorsal cephalometric roentgenographs and superposed on implant images in the left nasal bone. Estimated position and pattern at 6 weeks of age, ---; at 16 weeks of age, … Note the growth pattern of the nasal bone region with the greatest increase in size proximally and distally, less laterally, and least medially. B — enlarged area of Fig. 13.3**A** to demonstrate reference points for measurements. M_1 — most distal point on the medial border at 6 weeks of age; M_2 — represents M_1, on the medial border at 16 weeks of age; M_2–L_2 — line at right angles to medial borders; D_2 — most distal point on the medial border at 16 weeks of age; L_1 — point on the lateral border at 6 weeks of age; L_2 — point on the lateral border at 16 weeks of age; M_1–M_2 — increase in the medial dimension; L_1–L_2 — increase in the lateral dimension; M_2–D_2 — increase in the distal dimension.

beginning to the end of the study (Fig. 13.2; Tables 13.2 and 13.3). Consequently these implants were used as sites of reference for superposing the tracings of the roentgenographs. In this way, not only sites but also the amount of change could be determined during the 10-week period when the roentgenographs were taken (Fig. 13.3). The sites of growth were at all of the borders, and it was possible to compare the relative amounts of growth. The most prolific growth was at the proximal and distal borders, less at the lateral and least at the medial border (Fig. 13.3). The mean increase was about 6.79 mm at the proximal (posterior) border, 6.19 mm at the distal (anterior) border, 2.73 mm at the lateral border, and 1.22 mm at the medial border. Thus, growth at the proximal and distal borders was about the same and about twice that of the lateral border and about five times that of the medial border.

Table 13.2 Approximate Rabbit Nasal Bone Region Growth in mm at Selected Sites Determined from Tracings of Ventrodorsal Radiographs and by Direct Measurements from Implants to the Frontonasal Suture, at 6 and 16 Weeks of Age

Animal No.	Medial Border* (M_1–M_2)	Lateral Border* (L_1–L_2)	Distal Border* (M_1–D_2)	Implant to FN Suture	
7 left	1.4	2.5	5.3	D_1-S	7.9
				C_1-S	7.0
right	0	2.8	4.2	B_1-S	5.7
				A_1-S	8.3
21 left	1.4	2.8	7.8	D_1-S	8.9
				C_1-S	8.7
right	1.4	2.9	7.6	B_1-S	7.4
				A_1-S	8.9
26 left	1.0	2.4	6.6	D_1-S	6.9
				C_1-S	–
right	1.0	2.3	6.6	B_1-S	–
				A_1-S	5.8
28 left	1.1	1.9	4.9	D_1-S	4.5
				C_1-S	3.3
right	1.1	1.9	4.9	B_1-S	4.7
				A_1-S	3.1
35 left	1.2	4.0	6.9	D_1-S	9.0
				C_1-S	7.3
right	1.2	3.8	7.1	B_1-S	8.1
				A_1-S	7.6

M_1: Most distal point on the medial border at 6 weeks of age
M_2: Represents M_1 on the medial border at 16 weeks of age
M_2–L_2: Line at right angles to medial borders
D_2: Most distal point on the medial border at 16 weeks of age
L_2: Point on the lateral border at 16 weeks of age
M_1–M_2: Increase in the medial dimension
L_1–L_2: Increase in the lateral dimension

DISCUSSION

The purpose of this study was to establish the growth pattern of the rabbit nasal bone region in terms of sites, relative amounts, and directions of growth. This is based on the use of fixed reference areas within the nasal

Table 13.3 Statistical Determinations in 5 Rabbits of Nasal Bone Region Growth in mm from 6 to 16 Weeks of Age at the Proximal, Distal, Lateral, and Medial Borders (see Table 13.2)

	Means	Standard Deviation	Standard Error of Mean
Medial border	1.22	0.18	0.08
Lateral border	2.73	0.75	0.33
Distal border	6.19	1.31	0.58
Proximal border (implants to FN suture)	6.79	1.81	0.81

Paired T-test	Probability
Lateral border–medial border	0.009*
Distal border–lateral border	0.002*
Proximal border–lateral border	0.002*
Distal border–medial border	0.001*
Proximal border–medial border	0.002*
Proximal border–distal border	0.367†

*Significant at 1% level
†Not significant

bone in relation to the nonfixed borders. The fixed reference areas were the two images on the serial ventrodorsal cephalometric roentgenographs of silver amalgam implants inserted in each nasal bone (A_1 and B_1; C_1 and D_1). These images, as well as the outline of the nasal bone regions, were transferred to translucent matte acetate paper. The tracings of the 6- and 16-week-old rabbit roentgenographs were superposed on the implant images in each nasal bone. In this way the growth pattern of the distal, lateral, and medial borders was determined (Fig. 13.3). The proximal border (frontonasal suture) was determined at the beginning (6 weeks of age) and at the end (16 weeks of age) of the experiment from gross measurements of the distance between the implants in the nasal bone and the frontonasal suture. Thus, each time, two points were determined on the frontonasal suture. The rest of the suture was estimated from gross studies.

The design of this experiment included measurements between implants within the same bone. Since evidence showed a constant relationship between these implants, we concluded that there was no interstitial growth

of bone. If interstitial growth did occur, with consequent change in the distance between implants within the same nasal bone, this experiment would be invalid. Thus, an essential start is a fixed stable reference site from which dependable measurements of growth may be made.

The accuracy of the results was limited by a variety of factors, such as similar repositioning of the head for serial roentgenographs, a true ventrodorsal view, duplicability of tracing of roentgenographs, and superposition of tracings. In this roentgenographic study changes were determined in two planes of space without consideration of the increasing curvature of bone with growth of this region. Of all the determinations, those at the frontonasal suture were the least accurate. Although no two animals exhibited identical quantitative growth, the general growth pattern was similar. The length of the rabbit nasal bone is highly variable.[2]

Growth of the nasal region occurred by the addition of bone at the internasal, premaxillary–maxillary, and frontonasal sutures and at the free distal and lateral borders. Dorsal, but not ventral, surface changes were observed.

John Hunter[1] proposed that resorption was as characteristic of bone growth as apposition.[a] However, in this study apposition was determined for a given period. In evaluating the growth pattern of the mandible, it was possible to determine not only the total amount of apposition along the posterior border but also the total amount of resorption along the anterior border of the ramus.[4]

Contiguous bones which are identical, or mirror images, are joined by a suture with identical bone growth activity on both sides, such as the sagittal or internasal suture. The essentially straight internasal suture of the growing rabbit joins symmetrical nasal bones which taper. Constancy of the equal amount of bone growth on either side of the suture maintains the symmetrical bone and straight suture form. The particular anteroposterior shape of the snout, i.e. narrower anteriorly and wider posteriorly, raises a question as to the growth gradient all along the internasal and premaxillary–maxillary sutures as well as the lateral borders of the premaxilla. Progressive decrease anteriorly in

[a] Another Englishman, Lewis Carroll, in *Alice in Wonderland*, described 12 decreases and increases in size.

the rate of sutural bone growth accentuates this tapering. Anterior sutural growth of the snout is arrested earlier than posterior sutural growth.[3]

The deformity of the snout, including less large nasal bones, after resection of the nasal septum in growing rabbits could be the result of a lack of growth rather than a lack of support by the nasal septum. Does growth of the nasal septum drive the snout forward, with sutural accommodation of the related bones? Did resection of a large part of the septum trigger closure or cessation of activity of the suture complex in the growing nasal bone region? Does normal interaction of the various growth patterns in a bone complex require maintenance of normal spatial relations of the individual units in the complex? Further investigation is indicated, such as a study of nasal growth as in this report after septal resection.

Clinical Comment

Precise analogies cannot and should not be made between rabbits and human beings. The amount of increase in separation of the implants on either side of the frontonasal suture indicated that this was a site of considerable growth. Since growth at this region was not affected after resection of the frontonasal suture, it was considered to be a secondary growth site. The proximal, frontal end of the nasal bone in rabbits is probably the most prolific of the four growth sites studied. Since severe trauma to this growth site did not result in a clinical deformity, this information may be relevant in regard to an osteotomy as part of a rhinoplastic procedure in a child or adolescent.

Thus, one might assume that, in children, trauma to the nasal bones, providing that they are repositioned, will not result in severe deformity.

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Rabbit Nasal Septum*

INTRODUCTION AND PURPOSE

The septovomeral region is considered to be an important growth center.[1,2] The relationship of trauma to this region to nasal and facial development is of clinical interest. A group of experiments was designed to test the effects upon growth of the face of varying degrees of surgical resection and trauma to different parts of the septovomeral region in both growing and adult rabbits. The information obtained is reviewed and summarized in this report in relation both to basic concepts of growth of bones and to possible clinical significance.

REVIEW OF THE LITERATURE

Hilton[1] in 1845 described the role of the vomer in the downward and forward growth of the maxillae and the deepening of the nasal fossae. Fick[3] in 1858 removed a portion of the cartilaginous nasal septum through a trephine opening of the nasal bones in growing dogs, cats, pigs, and goats. At autopsy the hard palate was greatly shortened anteroposteriorly and he stated that growth of the hard palate was dependent upon the growth of the nasal septum. Landsberger[4] in 1929 resected in part the anterior portion of the nasal septum in dogs two weeks of age, and killed them

*Excerpted from: Sarnat BG. (1970) The face and jaws after surgical experimentation with the septovomeral region in growing and adult rabbits. *Acta Otolaryngol Suppl* **268**.

six months later. From his findings, he concluded that the growing septum was an important factor in pushing the floor of the nasal cavity downward. Selman and Sarnat reported that although the frontonasal suture was a site of rapid growth,[5] its extirpation in the rabbit failed to produce a growth arrest of the snout.[6]

MATERIALS AND METHODS

Animals

Different experiments were designed to determine the effects of varying amounts of surgical resection and trauma to the septovomeral region in five groups of growing and one group of adult New Zealand albino rabbits (Table 14.1). Additional rabbits served as operated-on and unoperated-on controls. The rabbit was selected because of the rapid increase in length of the snout.

Anesthesia

A solution of 1% procaine hydrochloride (0.5–2 cc) was injected submucosally in the sulcus between the upper incisors and the lip. First, the adult rabbits were injected intramuscularly with pentobarbital sodium (30 mg/kg) and propiopromazine hydrochloride (Tranvet) (7.5 mg/kg).

Surgical Procedure

The animals were secured on an operating board. The face and snout were cleansed with an antiseptic solution. An about 1.5 cm transverse incision was made through the mucosa between the upper incisors and the lip. The tissues were elevated from the premaxilla, entrance was gained to the nasal cavity, and the septum and septovomeral joint were exposed. This was the extent of the surgical procedure for the animals which served as operated-on controls. In a group of growing animals maximum amounts of the anterior portion and body of the cartilaginous nasal septum, including mucoperichondrium, were resected.[7] The vomer was left intact. A similar procedure was followed in a group of adult rabbits.[8] In a final group of

Table 14.1 Summary of Various Surgical Experiments on the Septovomeral Region in Growing and Adult Rabbits
Sarnat BG, Wexler MR (1969). Logitudinal development of upper facial deformity. *Br J Plast Surg* 22: 313–323, Elsevier

Special Procedure	Number of Animals				Type of Study	Findings
	Control (Operated and Unoperated)	Experimental	Approx. Age at Surgery (weeks)	Approx. Post-operative Survival (weeks)		
Growing Rabbits						
Resection of septovomeral region	6	18	4–7	17	Cross-sectional	Severe deformity of snout and incisors
Resection of large amount of cartilaginous nasal septum	10	15	3	15–21	Cross-sectional	Severe deformity of snout and incisors
Resection of large amount of cartilaginous nasal septum	7	26	2 and 3	1–21	"Longitudinnai"	Gradual development of severe deformity of snout and incisors

(*Continued*)

Table 14.1 (*Continued*)

Special Procedure	Number of Animals				Type of Study	Findings
	Control (Operated and Unoperated)	Experimental	Approx. Age at Surgery (weeks)	Approx. Post-operative Survival (weeks)		
Resection of linear horizontal segment of cartilaginous nasal septum	12	6	3	16	Cross-sectional	Moderate deformity of snout and incisors
Dislocation of cartilaginous nasal septum from vomerine groove	7	10	5–7	16	Cross-sectional	No deformity of snout and incisors. Deformity of septovomeral region
Adult Rabbits Resection of large amount of cartilaginous nasal septum	8	9	Adult	16	Cross-sectional	No gross deformity of snout or incisors. Local defect of septum

growing rabbits, cartilaginous nasal septum, vomer, and premaxilla were removed.[5] The mucosal wound margins were approximated and sutured with No. 4-0 black silk. These animals, except for the one experiment with adult rabbits, were operated-on at 2–7 weeks of age, weaned at 6–7 weeks of age, and killed 16–20 weeks later and studied. In addition, in another experiment, where large amounts of cartilaginous nasal septum were resected, the animals were studied at death from 4 to 145 days.[7]

In most instances the animals were euthanized by injecting pentobarbital sodium into the heart. Immediately after death, the heads were severed from the body and a portion of the soft tissues was resected. The heads were then fixed in either 70% ethyl alcohol or 10% formalin. Subsequently, further dissection was done and the heads were sectioned just to the left of the midline in the parasagittal plane with a small hacksaw. The skulls were never boiled, since this would destroy the remaining cartilaginous nasal septum.

Photographs and Roentgenographs

Antemortem and postmortem photographs were taken of the heads in the dorsal, lateral frontal, and parasagittal views. Although every effort was made to obtain comparable photographs, this was not always possible.

Lateral roentgenographs were taken of the sectioned skulls with a standard roentgen apparatus at a target–film distance of 100 cm operated at 50 and 100 mA, 58–68 kV, and an exposure time of ½–¾ of a second. Tracings were made of selected roentgenographs.

RESULTS

Growing Rabbits

Resected septovomeral region and/or cartilaginous nasal septum (large amounts)

Antemortem observations

As early as four days after resection of cartilaginous nasal septum, there was a reversal of the incisal relationship, with the upper incisors being lingual to the lower (Figs. 14.1–14.3).[7] Subsequently, the sharp

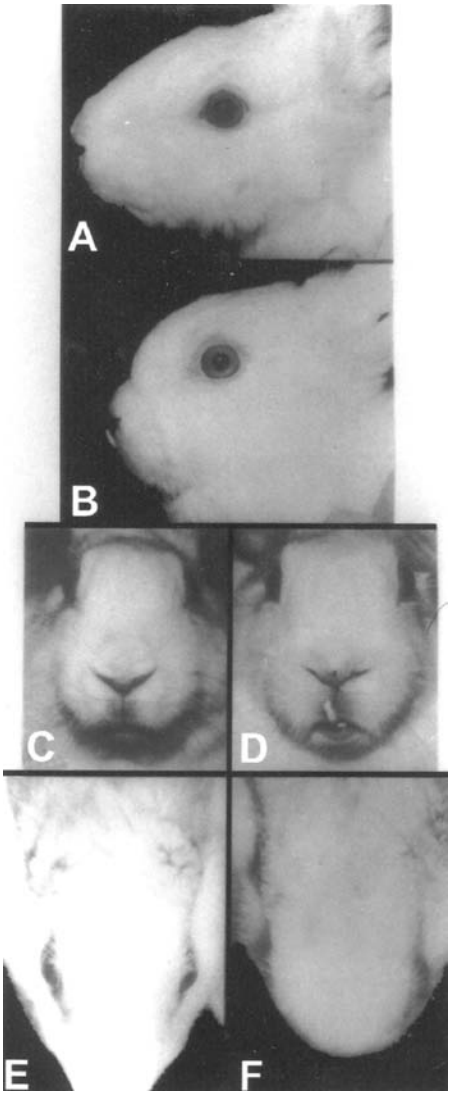

Fig. 14.1 Antemortem lateral, frontal, and dorsal (retouched) view photographs of rabbit No. 4, in which a minor amount of nasal septum was removed, and of rabbit No. 18, in which a major amount of nasal septum was removed, at 21 days of age. Note the extreme contrast in facial appearance. Animal No. 4 has a relatively normal, long, tapered face, whereas animal No. 18 has a short, stubby, rounded face with an indentation above the nostrils (lateral view) and an overerupted lower incisor. [From: Sarnat BG, Wexler MR. (1966) *Am J Anat* **118**: 755–767.]

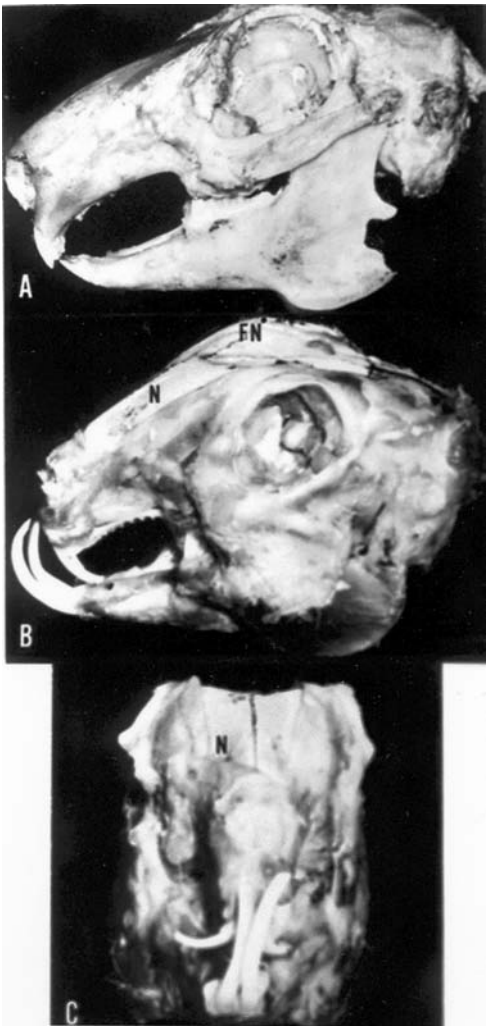

Fig. 14.2 Postmortem photographs of lateral view (**A**) of unoperated-on control rabbit No. 23, and lateral (**B**) and frontal views (**C**) of operated-on littermate rabbit No. 21. A portion of the septum and vomer were removed at 28 days of age. Postoperative survival was 118 days. Both animals were killed at 146 days of age. In (**B**) note the shorter snout, upper jaw, and face, acute angulation, and peaking at the region of the frontonasal suture (FN) and sharp downward direction of nasal bones (N). Contrast this with the longer snout and smoothly curved dorsum of the unoperated-on rabbit in (**A**). Also note the malalignment and overgrowth of all incisors in (**B**) and (**C**). [From: Wexler MR, Sarnat BG. (1961) *Arch Otolaryngol* **74**: 305–313.]

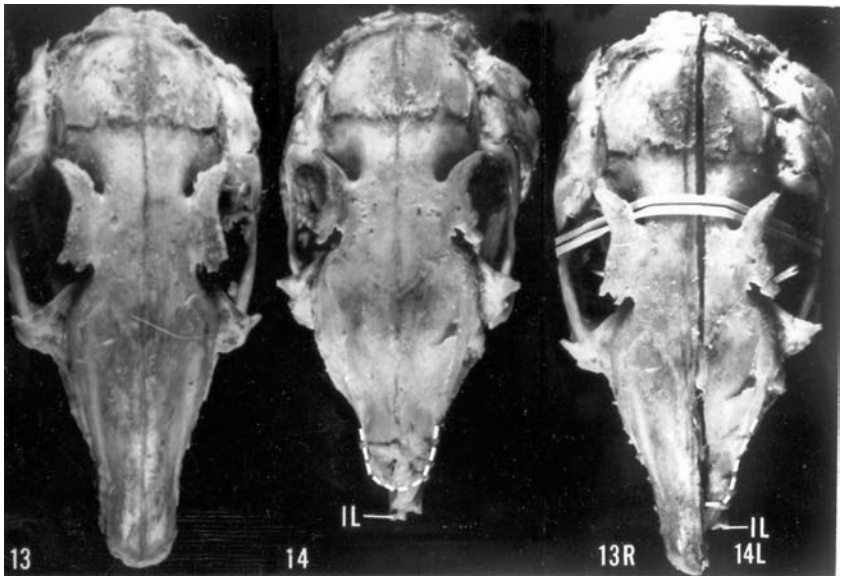

Fig. 14.3 Postmortem dorsal view photographs of the skulls of littermate rabbits No. 13 (operated-on control) and No. 14 (resected nasal septum) with a postoperative survival of 110 days. In No. 14 note the lack of development of the snout. In the right-hand photograph, the right side of the skull of control rabbit No. 13 and the left side of the skull of experimental rabbit No. 14 were approximated along the posterodorsal and occipital borders. Note that the differences are limited essentially to the snout area. IL — lower incisor. White outlines — anterior part of the snout. [From: Sarnat BG, Wexler MR. (1966) *Am J Anat* **118**: 755–767.]

incisal edge on the labial surface was not maintained. Overeruption and fractures of the incisors were frequent in the experimental animals with a longer postoperative survival. At times food would become lodged between the spread incisors. These factors sometimes made ingestion difficult. In a few of the experimental animals, the weight was less and the fur was not as smooth when compared with the controls.

The face of the experimental rabbit was shorter, in contrast to the long, smoothly curved, tapered face seen in the operated-on and unoperated-on control animals (Fig. 14.1). The snout became progressively stubby, along with the appearance of a pronounced indentation

above the tip of the nose. This was suggestive of the face of a bulldog and was prominent less than three weeks postoperatively.

Postmortem observations

Changes noted in the dissected skulls of the experimental animals were limited to the snout in the region anterior to the orbits, zygomas, and molars. Although the findings were not always consistent, generally the degree of change varied directly with the amount of septum resected and the postoperative survival period.

The following description is characteristic of the most severe deformities seen in animals with the longest postoperative survival. The snout, when seen from the side, was tapered and shorter than that of the unoperated-on control. Whereas the snout in the control animal was the prominent part of the anterior face, this was reversed in the experimental rabbit. There was a deflection of the snout in a forward direction, beginning anterior to the frontonasal suture. This was in contrast to the smoothly curved dorsum of the control animals (Figs. 14.1 and 14.4). From below, the palate and the incisive foramen were shorter. From in front, the nasal aperture was smaller. The snout when viewed from above was considerably shorter than that of the littermate control animal (Fig. 14.2).

The nasal bones were considerably shorter and narrower than those of the control animals and converged toward the premaxilla, with the nasal height and volume much reduced. The premaxilla and its frontal process were also shorter. The end of the snout was tapered in the dorsoventral direction (Fig. 14.3).

Examination of the parasagittally sectioned crania revealed in the experimental animals the extent of the septal defect in relation to the remaining septum and deformity of the snout, and in the control animals the relation of the extent of the nasal septum to the snout (Fig. 14.6). The site of the beginning of the downward deflection of the nasal bones was correlated with the posterior border of the septal defect, which was anterior to the frontonasal suture. Whereas in the control animal the nasal bones and hard palate were about parallel, in the experimental animal anterior projections of lines from the surfaces of these bones would soon

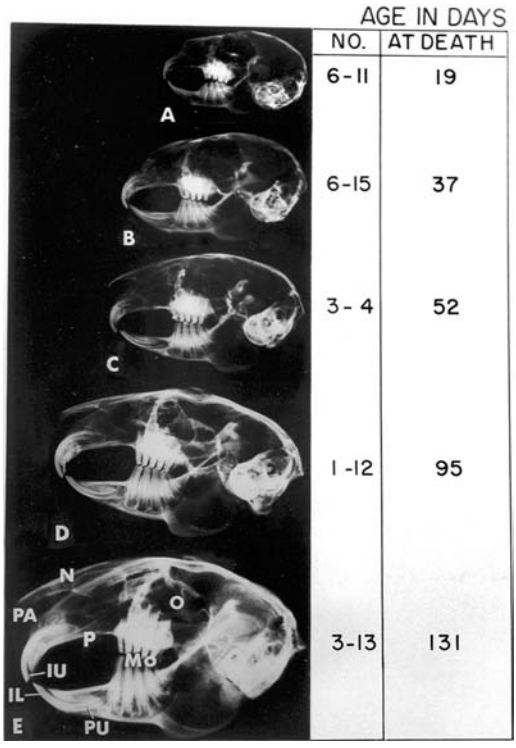

Fig. 14.4 Reproduction of lateral roentgenographs, arranged according to age from 19 to 131 days at death, of parasagittally sectioned skulls of rabbits with the cartilaginous nasal septum intact. Note the downward smooth curve of the anterior dorsum; the length and anterior extension of the nasal bone; the size of the piriform aperture; the length of the palate; and the form, position, and relationship of the incisors. IL — lower incisor; IU — upper labial and lingual incisors; Mo — premolars and molars; N — nasal bone; O — orbit; P — palate; PA — piriform aperture; PU — pulpal cavity. Contrast these with experimental animals in Fig. 14.5. [From: Sarnat BG, Wexler MR. (1969) *Brit J Plast Surg* **22**: 313–323.]

intersect. The postmortem gross findings of the facial skeleton at 18, 35, 55, 91, and 131 days of age are summarized in Table 14.2.

The left (experimental, No. 14) and right (control, No. 13) sides of the parasagittally sectioned skulls of littermate animals with the same survival period were approximated along the posterosuperior and occipital borders. This demonstrated the extreme differences in the size of the snouts (Fig. 14.3).

Table 14.2 Postmortem Gross and Roentgenographic Findings on the Face in Selected Rabbits 18–131 Days of Age After Resection of Cartilaginous Nasal Septum (see Figs. 8, 10, and 11) Sarnat BG, Wexler MR (1969). Logitudinal development of upper facial deformity. *Br J Plast Surg* 22: 313–323, Elsevier

Number	Age at Death (days)	Postoperative Survival (days)	Anteroposterior Curvature Dorsal Surface of Snout	Size of Nasal Aperture	Relation of Anterior Border of Nasal Bone to Upper Incisor		Palatal Length (from Medial Surface of Upper First Premolar to Lingual Incisal Alveolar Crest)	Relation of Upper Face to Mandible
					Anteriorly	Superiorly		
8–14	18	4	Within normal range	Within normal range	Within normal range	Within normal range	Within normal range	Within normal range
8–22	35	14	Slight flattening	Within normal range	May be somewhat less than normal	Within normal range	May be somewhat less than normal	Upper face somewhat less prominent
8–25	55	34	Loss of anterior curvature	Less than normal; soft tissue depression above upper incisal area	Less than normal	Decrease	Decrease	Upper face somewhat less prominent

(*Continued*)

Table 14.2 (*Continued*)

Number	Age at Death (days)	Postoperative Survival (days)	Anteroposterior Curvature Dorsal Surface of Snout	Size of Nasal Aperture	Relation of Anterior Border of Nasal Bone to Upper Incisor		Palatal Length (from Medial Surface of Upper First Premolar to Lingual Incisal Alveolar Crest)	Relation of Upper Face to Mandible
					Anteriorly	Superiorly		
8–20	91	70	Extreme depression of anterior border	As above but more extreme	Considerable decrease	Decrease	Decrease	Upper face much less prominent
3–14	131	110	Severe depression of anterior border	As above but more extreme	Severe decrease	Severe decrease	Severe decrease	Upper face severely less prominent

The upper incisors were usually in lingual occlusion with the lower incisors — the reverse of the normal. The upper and lower incisors were overerupted, in malposition, fractured, and deviated. The sharp labial bevel was frequently absent or reversed. The postmortem gross dental findings at 18, 35, 55, 91, and 131 days of age are summarized in Table 14.3.

Roentgenographic observations

Examination of the roentgenographs of the parasagittally sectioned skulls yielded findings not seen on the gross specimens. Differences between the control (Fig. 14.4) and experimental (Fig. 14.5) animals were demonstrated in the lateral roentgenographs of the parasagittally sectioned skulls. Comparisons were significant not only between the two groups but also within each group, with increase in the postoperative survival period. The postmortem roentgenographic (and gross) facial and dental findings on the control animals and those rabbits which had cartilaginous nasal septum resected are summarized in Tables 14.2 and 14.3.

In the younger experimental animals, the anterior dorsum of the skull was flat. With increase in postoperative survival this region was shorter, more posterior and closer dorsoventrally to the upper incisors than in the control rabbits (Figs. 14.4, 14.5). Other findings on the experimental animals were larger pulpal cavities in the incisors, an increase in the proportion and amount of erupted to unerupted incisors, and lesser amounts of alveolar bone supporting the incisors.

Tracings of the roentgenographs and superpositioning of these tracings further illustrated the differences. In the parasagittal view the basal end of the upper incisor was in close proximity to where a portion of the septum was resected.

Adult Rabbits

Resected cartilaginous nasal septum (large amounts) in adult rabbits in antemortem observations of the snout and incisors revealed no gross differences between the control and experimental rabbits. In a few of the latter group a clear nasal discharge was noted at times. Postmortem gross

Table 14.3 Postmortem Gross and Roentgenographic Dental Findings on Selected Rabbits 18–131 Days of Age After Resection of Cartilaginous Nasal Septum (see Figs. 8, 10, and 11) Sarnat BG, Wexler MR (1969). Logitudinal development of upper facial deformity. *Br J Plast Surg* 22: 313–323, Elsevier

Number	Age at Death (days)	Post-Operative Survival (days)	Relationship and Occlusion of Upper and Lower Incisors	State of Incisal Eruption	Fracture of Incisors	Lateral Deviation of Incisors	Incisal Bevel	Pulpal Size	Alveolar Bone Supporting Incisors
8–14	18	4	Relationship slightly reversed from normal; upper incisors just lingual to lowers incisors but in occlusion	Within normal range	0	0	Within normal range	Within normal range	Within normal range
8–22	35	14	Upper incisors definitely lingual to lower incisors and not in occlusion	Overeruption	0	0	Within normal range	Within normal range	Within normal range

(*Continued*)

Table 14.3 (*Continued*)

Number	Age at Death (Days)	Post-Operative Survival (Days)	Relationship and Occlusion of Upper and Lower Incisors	State of Incisal Eruption	Fracture of Incisors	Lateral Deviation of Incisors	Incisal Bevel	Pulpal Size	Alveolar Bone Supporting Incisors
8–25	55	34	Upper incisors markedly lingual to lower incisors and not in occlusion	Marked overeruption	Occasional	+	Some reversal from normal with lingual surface being more prominent	Some increase over normal	Considerably less than normal
8–20	91	70	Upper incisors markedly lingual to lower incisors and not in occlusion	Marked overeruption	Not unusual	++	Increased reversal	Further increase	Considerably less than normal
3–14	131	110	Upper incisors markedly lingual to lower incisors and not in occlusion	Less apparent because of fractures	Frequent	+++	Frequent reversal or absent	Considerable increase	Considerably less than normal

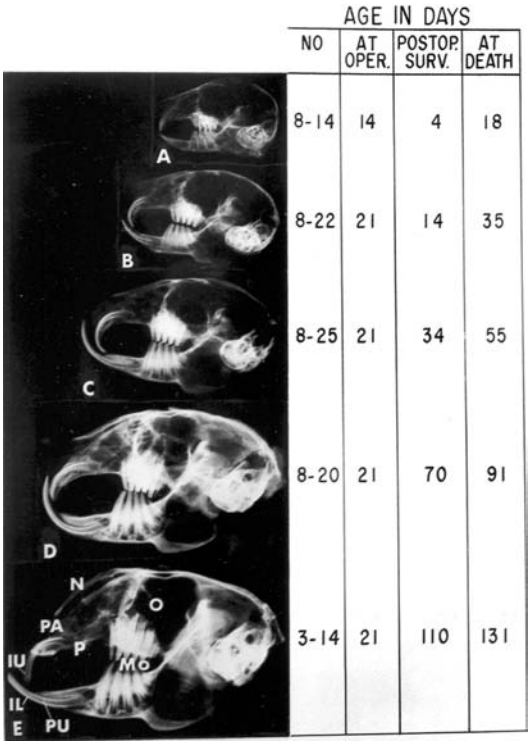

Fig. 14.5 Reproduction of lateral roentgenographs, arranged according to postoperative survival, of parasagittally sectioned skulls of rabbits which had the cartilaginous nasal septum resected at 14 or 21 days of age, with a postoperative survival of 4–110 days. Note the flat anterior dorsum with increasing downward deflection in an anterior direction, with increasing postoperative survival. The deflection begins at the posterior site of resection. Contrast these with control animals in Fig. 14.4. Note the shorter snout, nasal bone, and palate and the smaller piriform aperture. Also note in (**A**) that the upper incisal edge is just lingual to the lower one. This is more extensive in the animals with longer postoperative survival. Also in contrast with Fig. 14.4, the incisors are considerably overerupted and longer and not in occlusion. IL — lower incisor; IV — upper incisor; Mo — premolars and molars; N — nasal bone; O — orbit; P — palate; PA — piriform aperture; PU — pulpal cavity. [From: Sarnat BG, Wexler MR. (1969) *Brit J Plast Surg* **22**: 313–323.]

examination of the lateral and parasagittal views of the face, jaws, and incisors likewise showed no gross differences between the control and experimental rabbits (Fig. 14.6). Inspection of the nasal septal region in the experimental animal (Fig. 14.6B) disclosed a large defect.

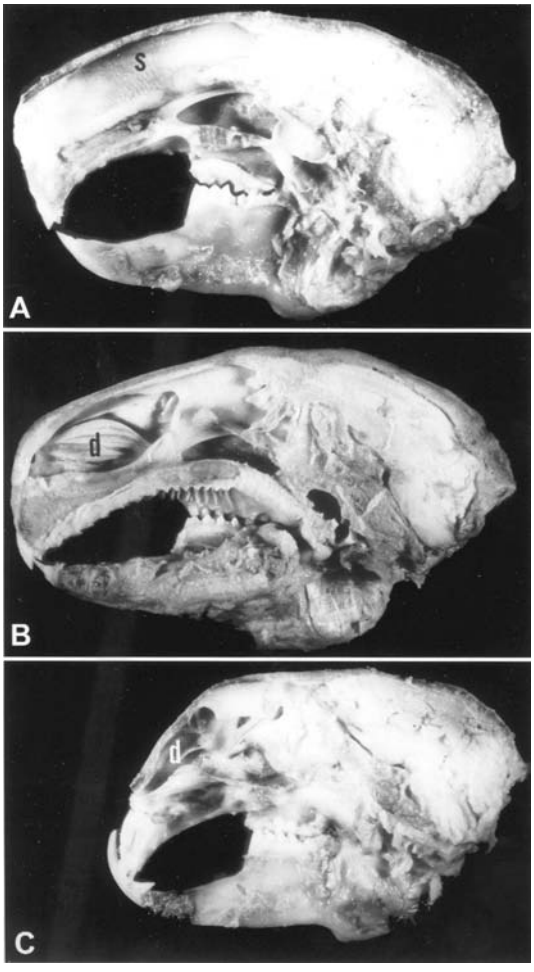

Fig. 14.6 Postmortem photographs of the right halves of left parasagittally sectioned rabbit skulls. (**A**) Operated-on control animal No. 13. No cartilaginous nasal septum was resected. (**B**) Cartilaginous nasal septum was resected in this experimental adult animal, No. M-1. Compare with (**A**) and note the similarities of size, shape, and regularity of incisors. Also note the regularity of the dorsal curvature uninfluenced by the underlying septal defect, d. (**C**) Cartilaginous nasal septum was resected in this experimental animal, No. 11, at three weeks of age, and it was killed at about four months of age. Note the growth arrest of the snout and the malocclusion of the incisors. Also note the deflection of the snout in an anterior direction, beginning in the region of the septal defect, d. S — septum. [From: Sarnat BG, Wexler MR. (1967) *Arch Otolaryngol* **86**: 463–466.]

DISCUSSION

The Face and Jaws After Surgical Experimentation with the Septovomeral Region

Young rabbits were used to impose injury during a period of rapid growth. Resection of the septovomeral region in growing rabbits elicited a prompt and early response manifested by a deceleration of growth of adjacent bones. A similar response was obtained, moreover, when large amounts of only cartilaginous nasal septum were resected with particular care taken not to injure the septovomeral joint. The severity of the growth arrest became strikingly apparent with a longer postoperative survival.

Antemortem, the snout of the unaffected animal was long and tapered with a smoothly curved dorsum (No. 4, Fig. 14.1). This was in contrast to the snout of the affected animal, which was short, stubby, rounded, with a sharp deflection of the dorsum in an anterior direction and an indentation above the nostrils (No. 18, Fig. 14.1). Postmortem, the dissected skull of the control animal had an appearance comparable with that antemortem. This was not as true with the experimental animal, because the soft tissue masked the findings.

The response to resection of cartilaginous nasal septum varied with the age of the rabbit, the amount (and site) resected, as well as the duration of the postoperative survival. Although an attempt was made to standardize the surgical procedure, the same amount of cartilaginous nasal septum was not resected from comparable sites in all animals. The degree of change varied from relatively small to extreme, depending on these factors. Severe deformities involving many lateral facial structures were produced by removing portions of this midline structure, the cartilage of the nasal septum.

In a few animals which expired at the time of, or shortly after, surgery, postmortem examination revealed that about 60–75% of the cartilaginous portion of the septum was removed. In animals with a four-month postoperative survival, the surgical defect represented about only 30–40% of the septum. The defect may have remained nearly the same in actual size but, proportionately, it became smaller with continued growth of the cartilaginous nasal septum. Histologic investigation of

the septal border may provide information regarding the regenerative activity at this site.

Questions arose as to the role of the cartilaginous nasal septum and its sites of activity in relation to the growth and form of the snout. Is the snout deformity a result of lack of growth of the cartilaginous nasal septum or lack of support?

In a different experiment, large amounts of cartilaginous nasal septum were resected in adult rabbits.[8] After a postoperative survival of 16 weeks, study of the dissected skulls showed a large septal defect but no deformity of the snout (Fig. 14.6B).

Increase of the cartilaginous nasal septum in height, length, and thickness is by both interstitial and perichondrial growth. The relative contribution of each is not known. A study of the proliferative activity of chondrocytes with tritiated thymidine indicated the highest activity to be in the anteroinferior and posterior parts of the cartilaginous nasal septum (Fig. 11.3). Although the central zone of the cartilaginous nasal septum had a relatively low rate of proliferation, this rate would result in doubling of the cell population in about four weeks. Assuming that a significant increase in septal mass accompanies increased chondrocyte numbers, then deformities of the snout might well be anticipated as a consequence of surgical ablation of the central zone early in life.

Dental Changes

Concomitant with lessened growth of the snout, a relative mandibular prognathism resulted with lack of occlusion of the upper and lower incisors. The incisors overerupted in bizarre forms as a result of continuous growth and eruption as a logarithmic spiral coupled with a decreased rate of attrition. The relation of the upper incisors lingual to the lower ones and overeruption of the incisors proved to be early clinical signs of a developing deformity of the snout. This was noted as early as four days postoperatively (Fig. 14.5). In other experimental rabbits where snout length was not as severely affected, occlusion was relatively normal.

Another possible cause of this deformity is that the basal ends of the incisors, adjacent but lateral to the septovomeral region, were traumatized at the time of surgery. No dental deformities were noted (i) in the

operated-on control animals in which the surgical procedure was carried out up to removal of cartilaginous nasal septum, (ii) in rabbits in which the cartilaginous nasal septum was dislocated but not resected, or (iii) in adult rabbits in which large amounts of cartilaginous nasal septum were resected.[8] Consequently, it was concluded that the malocclusion was related to failure in anterior growth of the snout and not to trauma to the growing tooth at the time of the original surgery. Malocclusion may occur on an inherited basis.[9] Injury to growing rodent incisors may lead not only to overeruption but also to disturbances in enamel formation.[10] The latter was not found in this experiment.

Along with these face, jaw, and dental abnormalities, it is possible that there were other anatomic and physiologic alterations of the nose, temporomandibular joints, and the rest of the masticatory and respiratory systems.

Clinical Considerations

Findings on experimental animals may be of assistance in understanding normal and abnormal growth of bones in the human being. Deformities of the nasal septum and associated structures seen clinically in the adult have been considered to be manifestations of severe nasal injury incurred during an earlier period. Since the above experimental findings confirm this thesis, it would be advisable that young children who have sustained injuries to the cartilaginous septum and nose be treated and observed not only for the immediate but also for late deformities. In addition, they should be followed for deformities of the teeth, jaws, and face.

In a child with a complete bilateral cleft palate, the upper face may be unable to obtain a full expression of downward and forward growth because of lack of contact of the palatal shelves with the ventral-free actively growing septovomeral region (Fig. 14.7).[11] Furthermore, trauma to the septal region, during cleft palate or septal surgery, might have an untoward effect upon growth of the nose and upper jaw and face. Injury to the midpalatine or transpalatine sutures, which are secondary growth sites, is of less import.[12]

In surgical procedures related to the nasal bones and septum in the actively growing child, one would not anticipate a growth arrest in relation

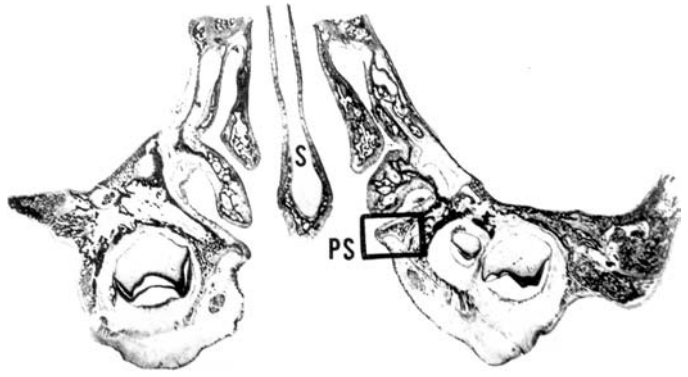

Fig. 14.7 Frontal section through the upper jaw of a newborn human being with a bilateral cleft palate. PS — palatine shelf; S — septum. [From: Weinmann JP, Sarnat BG, Sicher H. (1958) *Oral Surg Oral Med Oral Pathol* **11**: 20–25.]

to trauma to the nasal bones. However, some deficiency of growth might result if there is sufficient trauma to the cartilaginous nasal septum. This statement in regard to differential reaction is based upon the absence of gross deformity of the snout in rabbits after either extirpation of the frontonasal suture or temporary dislocation of the nasal septum, but the presence of deformity of the snout after resection of cartilaginous nasal septum.

SUMMARY AND CONCLUSIONS

A series of surgical experiments on the septovomeral region of young growing and adult rabbits has been reviewed and summarized. The purpose was to relate this information to basic concepts of growth of bones and to possible clinical significance.

After resection of the septovomeral region and/or large amounts of only cartilaginous nasal septum in young growing rabbits, there was, as early as four days postoperatively, a deceleration of growth of the snout, a reversal of the incisal relationship, and an overeruption of the incisors. At postmortem in the experimental animals, as contrasted with the controls, the snout was shorter and smaller, with a resulting severe relative mandibular prognathism. The nasal and premaxillary bones were smaller,

as were the nasal cavity and piriform aperture. At the posterior border of the septal defect there was considerable downward deflection of the nasal bones in an anterior direction. This was in contrast to the smoothly curved dorsum of the control animals. The extent and severity of the deformity varied with the amount of cartilaginous nasal septum resected, the age of the animal at the time of resection, and the length of the postoperative survival. It is concluded that after resection the remaining cartilaginous nasal septum is unable to attain its full expression of growth. The relationship of the cartilaginous nasal septum to growth of the snout can be compared with that of the orbital contents to the growth of the orbit and the brain to the growth of the cranium.

When large amounts of cartilaginous nasal septum were resected in adult rabbits, neither snout nor dental changes were observed.

The cartilaginous nasal septum is important in the growth and development of the upper face of the rabbit. This information if applicable to human beings is of particular clinical significance in young patients with injuries to this area or with bilateral complete cleft palates.

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Growth of Multiple Facial Sutures*

INTRODUCTION

The purposes of this experimental study on the Macaca rhesus monkey were: (1) to compare the relative amounts of sutural growth in selected areas of the face by means of metallic implants; (2) to compare the roentgenograph with the direct method of measuring growth by means of metallic implants; and (3) to study the direction of growth of certain components of the facial skeleton by superpositioning tracings of serially taken roentgenographs.

There is no report showing the role played by external facial sutures in the growth of the face using direct measurements (taken on the skull) in combination with indirect measurements (taken on the roentgenograph). The sutures studied were the frontomaxillary, frontozygomatic, zygomaticomaxillary, zygomaticotemporal, and premaxillomaxillary ones.

MATERIAL

The Macaca rhesus monkey was selected because it was the only readily available animal closely related to man. Although the anatomic details were not identical to those of the human being, it was felt that important information could be obtained in regard to normal growth of the face.

*Excerpted from: Gans BJ, Sarnat BG. (1951) Sutural facial growth of the Macaca rhesus monkey: a gross and serial roentgenographic study by means of metallic implants. *Am J Orthod* **37**: 827–841. Prizewinning article, American Association of Orthodontists.

Eight monkeys (five males and three females) ranging in age from about 8 months to 2 years were obtained from the Frank Buck farms in Florida. Since all animals were born in freedom, it was necessary to rely on the dentition to determine their approximate ages. These animals were divided into three groups on the basis of age. The youngest group, consisting of four animals, had a complete deciduous dentition and was estimated to be about 8 months of age. The intermediate group of two monkeys had the four permanent first molars and was estimated to be 18 months of age, while the oldest group of two animals was believed to be about 24 months of age because of the presence of the permanent central and lateral incisors as well as the permanent first molars. The experimental period ranged from seven to ten months.

METHODS

Anesthesia

The animals were anesthetized with an intraperitoneal injection of a 3% solution of sodium pentobarbital (1/2 cc per pound body weight) to insert the metallic implants and to take cephalometric roentgenographs.

Metallic Implants (Direct Measurements)

A surgical approach was developed to implant amalgam in the bone on each side of the following sutures: frontozygomatic, frontomaxillary, zygomaticomaxillary, zygomaticotemporal, and premaxillomaxillary (Fig. 15.1). A sterile technique was utilized throughout the operative procedure. After the animals were secured to the operating table, the left side of the head and face was shaved. The surgical field was painted with 3% tincture of iodine, followed by 70% alcohol, and then isolated with sterile towels.

The incisions were planned so as to avoid the facial nerve. Interference with the motor nerve supply to the facial musculature would disturb function and therefore affect the experiment.

The zygomaticotemporal and frontozygomatic sutures were exposed by overlying, horizontal, extraoral incisions. The frontomaxillary suture was exposed by a midline, vertical, extraoral incision. The zygomaticomaxillary

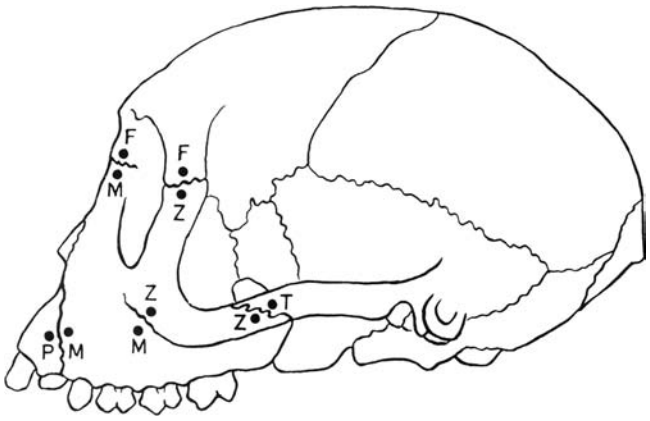

Fig. 15.1 Diagram of lateral view of a monkey skull showing facial sutures studied. Amalgam which was implanted on each side of the sutures is shown as a large black dot. F — frontal bone; M — maxilla; P — premaxilla; T — temporal bone; Z — zygoma.

and premaxillomaxillary sutures were exposed intraorally by incisions which followed the plane of these sutures. When the periosteum was reached, it was incised and elevated to expose the bone. A No. 35 inverted cone dental bur, mounted in a dental handpiece, was used to prepare cavities in bones adjacent to the selected suture lines. Amalgam was packed into the prepared cavities because of its radiopacity, pliability, and tolerance by tissues. An indentation was made in the center of each implant with the point of a caliper, and the distance between each pair of implants recorded. The soft tissue was then replaced and sutured with 000 black silk.

The trauma at the time of surgical operation and insertion of implants may have influenced sutural growth. All sites of implantation were exposed in a similar manner. Inasmuch as the same procedure was used at all times, the effects should be similar. The purpose of this investigation was to determine trends rather than the exact amounts of growth at individual sutures.

Cephalometric Roentgenographs and Tracings (Indirect Measurements)

During the course of the experiment, cephalometric roentgenographs were taken on the Broadbent–Bolton cephalometer at monthly intervals

(Fig. 15.2A). The animals were oriented in the Frankfurt horizontal plane. An ear post was placed in each external auditory meatus, with the lower border of the left orbit touching the orbital marker. The exposure time was 1 s for the lateral films and 1½ s for the frontal films at 20 Ma. and 68 KYP. The distance between the centers of each pair of implants was recorded directly from the roentgenographs.

To have comparable serial roentgenographs, the position of the head in the cephalometer must be constant. An attempt was made to position the heads as accurately as possible. The orbital landmark was palpated through the skin. Some variation was introduced into the vertical position of the head. This was of no consequence in the lateral roentgenographs. Regardless of the vertical orientation of the head, as long as the ear posts are in the external auditory meati the lateral films are comparable (Fig. 15.2B).

Individual tracings were made of the serial roentgenographs for each animal. Tracings of the original and final roentgenographs were superposed on the outlines of sella turcica and the most superior portion of the anterior cranial fossa defined by the roofs of the orbits (Fig. 15.2C).

Variation in the distance of the implants from the film and the variation in angulation of paired implants to the central ray of the X-ray tube were at least two factors responsible for some distortion. A minimum of distortion occurs with implants lying in a plane perpendicular to the central ray of the X-ray tube. Implants placed in the frontomaxillary, frontozygomatic, and zygomaticotemporal sutures fall into this category. However, implants placed in the area of the zygomaticomaxillary and premaxillomaxillary sutures lie in a plane oblique to the central ray of the tube and consequently show distortion. This error is avoided in measurements taken directly on the skulls.

Preparation of Material

The animals were euthanized by an intraperitoneal dose of sodium pentobarbital 7–10 months after the start of the experiment. The heads were then severed and the soft tissues dissected. Selected skulls were bleached in a solution of albone C (30% H_2O_2). One skull was cleared by placing it in

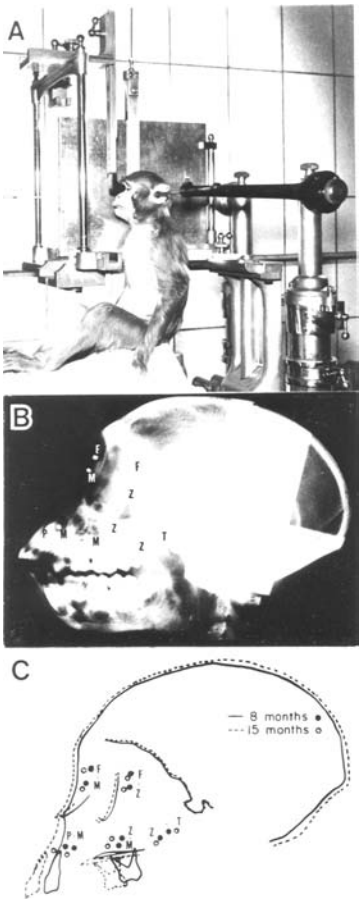

Fig. 15.2 (**A**) Anesthetized Macaca rhesus monkey in position in the cephalometer for taking lateral and frontal roentgenographs; cassette in position for a lateral roentgenograph. (**B**) Lateral cephalometric roentgenograph of a monkey skull with radiopaque amalgam implants on each side of facial sutures studied. F — frontal bone; M — maxilla; P — premaxilla; T — temporal bone; Z — zygoma. (**C**) Superposed tracings of serial cephalometric roentgenographs, demonstrating movement of implants with total growth of the face in the monkey. F–M — frontomaxillary suture area implants; F–Z — frontozygomatic suture area implants; P–M — premaxillomaxillary suture area implants; Z–M — zygomaticomaxillary suture area implants; Z–T — zygomaticotemporal suture area implants. Position of the implant at the beginning of the study ○; position of the implant at the completion of the study •. Note the downward and forward movement of all the implants, except for the one placed on the temporal side of the zygomaticotemporal suture, which moved posteriorly. Also note the stability of the facial pattern.

70% alcohol for two days, in 95% alcohol for one week, and in absolute alcohol for one week. It was then placed in a solution of methyl salicylate. This method makes the bone translucent and permits excellent visualization of implants.

FINDINGS

Examination of Skulls

Tissue reaction to individual implants

Of the 80 implants inserted, 1 was lost and 73 remained firmly within the facial skeleton. Evidence of infection was seen in only one animal. The thin plates of bone were resorbed and some metallic implants were found lying free in the connective tissue. Fifty-nine implants were found to be partially or completely covered by a thin plate of bone, while 14 were completely visible.

Amalgam implants placed on the lateral surface of the frontal bone could no longer be seen from the lateral view. They were now visible only on the medial surface of the frontal bone which forms the lateral wall of the orbit. Pegs placed at the zygomaticotemporal suture on the lateral surface of the zygomatic process of the temporal bone were similarly visible only from the medial surface of the zygomatic arch.

Separation of paired implants

Measurements of the distance between sutural implants taken on the skulls revealed that separation of implants at the zygomaticotemporal suture exceeded that of all other regions studied. Next in amount of separation were the implants in the area of the zygomaticomaxillary suture. Separation of paired implants at the frontozygomatic, frontomaxillary, and premaxillomaxillary sutures was considerably less. Variations in the increased distance between paired implants were noted. In several animals the separation of implants at the frontomaxillary suture exceeded that at the premaxillomaxillary suture. In others the reverse was true. This lack of consistency, as well as the small amount of increase in the separation of paired sutural implants at the frontomaxilliary,

frontozygomatic, and premaxillomaxillary sutures, made it difficult to place these areas in a definite order. In the two older groups of animals, the implants were separated to a lesser degree than was observed in the younger group, the only exception being the implants at the premaxillomaxillary suture.

Examination of Roentgenographs

Individual implants

Analysis of serial frontal roentgenographs revealed that the implants originally placed on the lateral surfaces of the zygomatic processes of the temporal and frontal bones were now closer to the medial surfaces.

Paired implants

Measurements taken on the roentgenographs followed closely those taken on the specimens. Implants at the zygomaticotemporal suture showed the greatest amount of separation. Implants at the zygomaticomaxillary suture were next. The small amount of separation of implants in the other three areas precluded their placement in a definite order.

Rate of separation

In all three groups studied, the rate of separation of implants at the zygomaticotemporal suture exceeded that in all other areas. In the youngest group of animals, the rate of separation of implants at the zygomaticotemporal and zygomaticomaxillary sutures exceeded that of the other two groups. In the middle group, the rate of separation at the frontomaxillary and frontozygomatic sutures exceeded that of the other two groups, while in the oldest group the rate of separation at the premaxillomaxillary sutures exceeded that of the other two groups.

Examination of Superposed Tracings of Serial Roentgenographs

The tracings of the roentgenographs were superposed on sella turcica and the most superior outline of the anterior portion of the cranial

fossa as defined by the roofs of the orbits. This revealed a downward and forward movement of all implants except those on the temporal side of the zygomaticotemporal suture, which moved downward and posteriorly (Fig. 15.2C). The findings on the oldest group of animals were similar, with the exception of the implants in the zygomatic process of the temporal bone. These appeared to be stationary throughout the study.

DISCUSSION

Appositional Growth

Local tissue reaction to the metallic implants used in this study proved to be minimal. Of the 80 implants inserted, 73 were retained, many of which were covered by a thin bony plate, demonstrating lateral surface growth of the facial bones. The most striking area of surface growth was the zygomatic arch and the lateral wall of the orbit.

Sutural Growth

The greatest amount of separation of paired implants occurred in the areas of the zygomaticotemporal and zygomaticomaxillary sutures. These areas contribute primarily to the anteroinferior growth of the face. The zygomaticotemporal suture lying as it does in the general plane of the junction between the visceral and the cranium reflects the growth of this area. The zygomaticomaxillary suture, lying anteriorly but in a plane parallel to that of the craniofacial hafting zone, contributes to the downward and forward movement of the middle face.

The two sutures observed in this study which contribute most to the downward growth of the face are the frontomaxillary and frontozygomatic ones. Although growth was evident in these areas, it did not account for the entire vertical growth of the face. The floor of the nose was found to have descended to a lower level than could be accounted for by growth of the frontomaxillary and frontozygomatic sutures. The same was true of the occlusal plane of the teeth. This difference was attributed to surface resorption and apposition.

The premaxillary segment of the facial skeleton was relatively inactive except during eruption of the permanent central incisors, and particularly just prior to the eruption of the permanent canines.

The rate and total amount of growth in the areas of the frontomaxillary, frontozygomatic, and premaxillomaxillary sutures were significantly lower than the rate and total amount of growth in the zygomaticotemporal and zygomaticomaxillary sutures. The greatest difference in the measurements of the distance between the paired sutural implants at the beginning and the termination of the experiment was found at the zygomaticotemporal suture. The frontozygomatic, frontomaxillary, and premaxillomaxillary sutures were relatively inactive.

Total Facial Growth

The regularity of the growth process in maintaining the basic pattern with which ontogenetic growth proceeds should be stressed. The outlines of the occlusal planes of teeth, observed in either the deciduous or the permanent dentition, descended in a plane parallel to the original one. The same was true for the plane of the floor of the nose. The outline of the facial profile was likewise shifted but not distorted with growth. The oldest group exhibited the beginning of formation of the supraorbital ridge. Although no two animals exhibited identical quantitative growth, the general pattern of growth was similar. This study suggests that sutural growth of the face varies in different age periods as follows: (1) the anteroposterior growth is most active in the age group from about 8 to 15 months; (2) the vertical growth is most active in the age group from about 18 to 34 months.

Comparison between the Roentgenographic and Direct Methods of Measuring Growth

Harmonious growth of the craniofacial complex takes place in three planes of space. There is a vertical, a lateral, and an anteroposterior component. Whether growth is measured on the skull or on serial roentgenographs, the true direction of this development is extremely difficult to observe, not only because the various sutures grow at different rates

but also because of their position in space. It is likely that with growth the position of the sutural planes relative to each other is changed. Growth of the face, therefore, does not follow straight lines, but with the rotation of the sutural planes, the bones of the face follow various curves. Measurements of this growth, taken either on the skull or the roentgenographs, show only the linear enlargement. Although this study concerns itself with the growth of the face, it is fully realized that an inseparable coordination exists in the growth of the face and the skull as a whole.

The advantage of the direct method of measuring growth is that it gives accurate information about total growth, while the advantage of the roentgenographic method is that it permits serial study of the rate and relative direction of growth. Because they complement each other, the two methods for studying bone growth were combined.

SUMMARY AND CONCLUSIONS

(1) This report is based on 8 growing Macaca rhesus monkeys in which 80 metallic implants were used to study growth of the frontomaxillary, frontozygomatic, zygomaticotemporal, zygomaticomaxillary, and premaxillomaxillary sutures. The experimental period varied from 7 to 10 months.
(2) Direct measurements between each pair of implants were made at the time of placement and upon completion of the study.
(3) Frontal and lateral serial cephalometric roentgenographs were taken at monthly intervals on the Broadbent–Bolton cephalometer. The increased distance between the centers of paired implants was recorded to show the rate of growth at each suture.
(4) Tracings of the lateral roentgenographs were superposed on sella turcica and the superior outline of the orbits to study the change in position of the implants with growth.
(5) *Examination of the skulls*

    (a) The greatest increase in the distance between the paired sutural implants was seen at the zygomaticotemporal suture. It was readily and relatively accurately measurable. This was less true of the

zygomaticomaxillary suture. The frontomaxillary, frontozygomatic, and premaxillomaxillary sutures were relatively inactive.

(b) Appositional growth was most prominent on the zygomatic arch and zygomatic process of the frontal bone. In these areas implants initially placed on the lateral side were now visible *only* from the medial side.

(c) Only the total amount of growth could be determined from direct measurements.

(6) *Examination of roentgenographs*

(a) Sutural growth of the facial bones varied in different age periods as follows: the anteroposterior growth was most active in the age group from about 8 to 15 months; the vertical growth was most active in the age group from about 18 to 34 months.

(b) The rate of separation of paired implants was greatest at the zygomaticotemporal suture.

(c) Roentgenographic studies gave information not only about total growth but also about the rate of growth.

(d) The roentgenographic method of measuring growth was not entirely accurate because of (i) difficulties in the proper positioning of the animals in relation to the X-ray tube, (ii) variation in the distance of the implants from the film, and (iii) variation in angulation of paired implants to the central ray of the X-ray tube.

(7) *Examination of tracings*

(a) All metallic implants moved in a downward and anterior direction except for those on the temporal side of the zygomatic arch, which moved downward and posteriorly. In the oldest animal this implant remained stationary.

(b) Outlines of the occlusal plane and floor of the nose descended in a plane parallel to each other. In the youngest group the bony profile of the face was shifted anteriorly, maintaining the original outline, while in the intermediate and older groups there was a trend toward "snouting." The oldest animal exhibited the beginning of formation of the supraorbital ridge.

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Maxillary Sinus*

INTRODUCTION

In the human being, the maxillary sinus may decrease[1] or increase[2] in size after extraction of the maxillary teeth. Because of these conflicting statements, an investigation was undertaken to determine the change in volume of the maxillary sinus of the adult dog after the extraction of teeth adjacent to the maxillary sinus.

In a previous report,[3] it was determined by means of metallic casts that there was no significant difference between the volumes of the right and left maxillary sinuses of dogs. In this work, the plan was to compare the volumes of the left and right maxillary antra in dogs in which teeth adjacent to the left maxillary sinus had been extracted. The antrum of the unoperated-on side served as a control for the one adjacent to the site of extraction. This method offered only one opportunity to make a cast of each sinus. No such study was found in a review of the literature.

BRIEF DESCRIPTION OF THE GROSS ANATOMY OF THE MAXILLARY SINUS OF THE DOG

The maxillary sinus of the dog is essentially a deep depression of the nasal surface of the maxilla. It comprises the dorsal, lateral, and ventral

*Excerpted from: Rosen MD, Sarnat BG. (1955) Change of volume of the maxillary sinus of the dog after extraction of adjacent teeth. *Oral Surg Oral Med Oral Pathol* **8**: 420–429.

walls of the sinus. The medial wall is formed anteriorly and, for most of its extent, by the lateral lamina of the ethmoid bone.[4] The posterior part of the medial wall of the antrum is formed by the vertical plate of the palatine bone. Its opening, the ostium, is large and oval, with the long axis situated vertically and at the anteromedial end of the sinus. The roof and the floor of the sinus diverge dorsally and ventrally behind the confines of this opening. The medial and lateral walls diverge also, to a lesser amount. All the walls meet posteriorly in a rounded fundus. The antrum is superior to the maxillary third and fourth premolars and the first molar. Measurements of a normal antrum in the adult dog are as follows:

	Height (mm)	Width (mm)	Length (mm)	Volume (cc)
Miller[4]	20	10	20	—
Eller[5]	22	5	32	2.3
Rosen and Sarnat[3]	23	9.5	30	2.1

BRIEF GROSS DESCRIPTION OF THE MAXILLARY DENTITION OF THE DOG

Each quadrant of the dog's dentition is composed of three incisors: one canine, four premolars, and two molars in the maxillary (Fig. 16.1), and an additional molar in the mandibular quadrants. Thus, the dental formula for the upper and lower quadrants is written as follows: I 3/3, C 1/1, PM 4/4, M 2/3.

The maxillary incisors have single roots flattened mesiodistally. The canine has a single root which curves distally, is oval in cross section, and is the largest in all dimensions. The first premolar has a single root. The second and third premolars have two roots each, situated mesiodistally in relation to each other. All of these roots are circular in cross section. The maxillary fourth premolar and first and second molars each have three roots, essentially round in cross section. Their roots are situated as follows: two buccally (one mesially and one distally) and one palatally opposite the mesiobuccal root in the fourth premolar and about equidistant between the two buccal roots in the molars, forming a triangle.

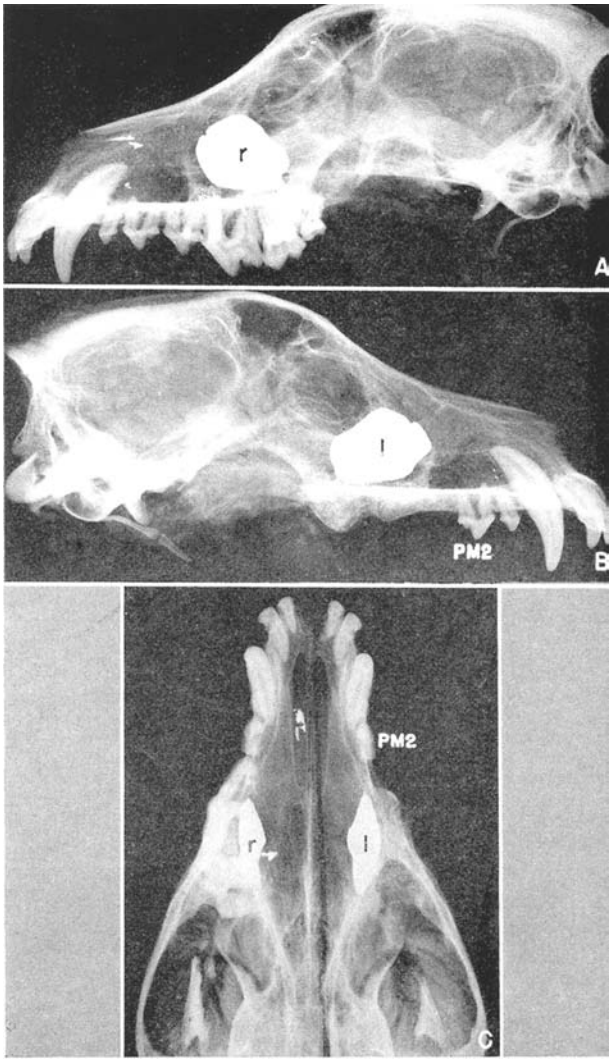

Fig. 16.1 Roentgenographs of the skull of an operated-on dog, No. 15, with casts reseated. The left maxillary third and fourth premolars and first and second molars were extracted 12 months before death. At postmortem the volume of the left maxillary sinus was determined to be 1.7 cc, and that of the right maxillary sinus was 1.3 cc. (**A**) Lateral view of the unoperated-on right half of the skull; (**B**) Lateral view of the operated-on left half of the skull; (**C**) Dorsoventral view; r — cast of the right maxillary sinus; l — cast of the left maxillary sinus. Note that the upper central incisors are absent. They were removed to facilitate a midsagittal sectioning of the skull.

MATERIAL AND METHODS

Ten young, adult, apparently normal, mongrel dogs with complete dentitions were selected at random from the general animal hospital supply without regard to either sex or breed. The dog was selected for this experiment because it was readily available and had a maxillary sinus of sufficient size to facilitate the contemplated casting procedure.

General anesthesia was used for the dental extractions. It was obtained by injecting an aqueous solution containing 0.06 g morphine sulfate subcutaneously and by injecting, one-half to one hour later, 0.33 cc of a 3% pentobarbital sodium solution per pound of body weight intraperitoneally. This was supplemented with a local infiltration of about 2–3 cc of 1% procaine hydrochloride with epinephrine 1–50,000 solution to aid in hemostasis and to obtund more profoundly reflexes arising in the periosteum of the maxilla. Either all or only certain maxillary teeth on the left side were extracted. All multirooted teeth were sectioned by means of not only a carborundum disk but also a chisel and mallet prior to removal. Care was taken to minimize trauma at all times and not to destroy the buccal plate of the alveolar process. The individual roots were then loosened with the use of a straight elevator and delivered by means of a pair of forceps. After the removal of the teeth, a buccal mucoperiosteal flap was elevated and brought over the alveolar wound as much as was possible and closed with 000 chromic gut sutures. The animals were fed the standard hospital dog ration of a mixture of Purina Dog Kibbled Meal (one part), Miller's Puppy Meal (two parts), and freshly ground horse meat (one part).

After about one year, all the animals were exsanguinated and decapitated immediately after death, their cranial contents were macerated, and the heads were fixed in 10% formalin. After complete fixation, the heads were sectioned in the midsagittal plane with a band saw. To facilitate this procedure, it was necessary to extract both upper central incisors (Fig. 16.1C). The ostium of each half was exposed by dissection. The specimens were rinsed in water and the sinuses flushed to remove any debris. The sectioned heads were then allowed to dry at room temperature until drops of moisture no longer could be recovered from the antra by vibration. Handy and Harman low fusing metal type "D" at about 95°C was

then cast into each maxillary sinus via its normal ostium. This metal was selected because its casting range was below the boiling point of water. Thus, it was possible to avoid pitting of the castings which might result from the vaporization of any moisture present in the maxillary sinuses. The cast was delivered by removal of the medial wall of the sinus and the excess metal was trimmed at the level of the ostium. From these casts, by means of their weights and the specific gravity of the metal (9.58), the volumes of the sinuses were determined. The casts were reseated in all specimens, and lateral- (Figs. 16.1A, B) and dorsoventral-view (Fig. 16.1C) roentgenographs were taken.

Those dimensional changes resulting from fixation with formalin, drying in air, use of metal for the cast, and determination of the level of the ostium may have contributed to a final inaccuracy in each measurement. All specimens were treated similarly, and special effort was expended to prepare the two halves of each head in an identical manner.

FINDINGS

In two of the dogs in which the maxillary teeth were extracted, the volumes of the left and right maxillary sinuses differed by less than 3%. In the remaining eight dogs, the differences ranged from 4.6% to 27.1%. In seven of these eight dogs, the maxillary sinus was larger on the left side, from which the teeth were extracted. In only one animal was the maxillary sinus larger by more than 3% on the unoperated-on right side (No. 12, 4.6%). The lateral and dorsoventral roentgenographs taken of all specimens, with their casts reseated, were not adequate for determining volumetric changes.

The percentage difference in volume between the left and right maxillary sinuses was plotted for each of ten normal dogs[3] and the ten dogs whose left maxillary teeth were extracted. There was a shift to the left, designating increased left maxillary sinus volume in the dogs which had their left maxillary teeth extracted.

DISCUSSION

The growth and development of a living organism result from an interaction of genetic and environmental influences. The physiologic stability of

the components of the adult organism is the result of many interrelated factors, prominent among which is the normal functional use of each component organ. The general hypertrophic effects of excessive use or the atrophic effects of disuse of an organ are well recognized. Modifications in the functions of a part are reflected in alterations in the form of that part.

The functional use of the dentition in mastication is accompanied by the production of forces which are brought to bear on that which is being masticated and which, in turn, react to the dentition and its supporting structures. To maintain these reactive forces within physiologic limits, the maxilla and its cranial attachments are utilized in such a manner as to spread and thereby diffuse and reduce the forces exerted on the dentition. In the maxilla, masticatory forces are transmitted from the teeth to the alveolar process via the periodontal membrane. The alveolar process transmits these forces in two principal directions. The palatine process of the maxilla receives part of the forces and transmits them transversely to the palatine process of the maxilla of the opposite side. The remainder of the force is transmitted and dissipated via the facial surface of the maxilla to the cranium and its vault by three buttresses (frontomaxillary, zygomaticomaxillary, and pterygomaxillary).[2]

The maxillary sinus occupies the interval between the palatine process of the maxilla and the facial surface of this bone, and is situated at the base of the alveolar process. Thus, it lies at the crossroads, as it were, of the pathway of forces from the teeth as they are transmitted to the cranium, and away from their site of origin.

The extraction of maxillary teeth in this region serves to reduce the functional forces transmitted along the trajectories enumerated previously. The alveolar process is dependent upon the presence of teeth, regardless of whether or not they are active in mastication.[6,7] After the extraction of teeth, the normal rate of resorption in the alveolar process continues, but the rate of apposition of bone is reduced as a consequence of the absence of functional stimulation. The result is a net reduction in the mass of the alveolar process.

This sequence of events occurs along all the bony pathways concerned with the distribution of masticatory stresses. At least two modifying factors also operate. The first is distance. The greater the distance from the site of original masticatory stresses, the less the effect their variation will

have on the bony architecture. Second, at these more distant sites other stresses, such as those resulting from origins or insertions of muscles, are encountered. Variations in masticatory stresses could affect the architecture of the more distant sites maximally, therefore, only by that percentage of the total forces that they contribute. The floor of the maxillary sinus bears an intimate relation to the teeth. It is so situated that the forces of occlusal action are still powerful at its site, and can still affect its architecture. In addition to this, much of the walls of the antrum, and especially the region of its floor, are devoid of muscular attachment. Thus, the masticatory forces contribute most of the functional forces transmitted by this region. After the extraction of maxillary teeth the sinus is bounded by walls in which the functional forces are reduced, and therefore by walls wherein bulk is reduced. The reduction in bulk of the walls contributes to the enlargement of the sinus.

The site of maximum enlargement of the maxillary sinus is probably at its floor, since this region is most closely associated with the functional changes in the dentition. A somewhat lesser effect is probably found in the external wall of the sinus. However, it was not possible in this investigation to determine with any accuracy the specific sites of change of form. The roentgenographic material did not lend itself to accurate study of changes in either volume or form.

In the human being, the maxillary sinus often bears an intimate relation to the maxillary teeth, the roots of which invaginate into the sinus. These intrasinus projections are often associated with concomitant ridges that cross the sinus and may even form septa in the sinuses. The removal of these teeth and the resorption of their supporting bony invaginations could contribute to an enlargement of the sinus. In the dog, the roots of the maxillary teeth most closely associated with the antrum do not intrude upon the sinus in this manner, even in these largest antra. It must be assumed, therefore, that the sinus floor and possibly its lateral wall were resorbed and the enlarged sinus occurred because of a general change in the functional pattern of the bone and not because teeth projected into the antrum. In a study of roentgenographs of a patient born without teeth or tooth buds, it was of interest to note the extremely fragile appearance of the facial skeleton and the very high degree of pneumatization. All sinuses were extensive and were contained within very thin walls.[7]

The continuous eruption of teeth (accompanied by their supporting bone) which are without antagonists suggests an alternate investigation in which the influence of the extraction of mandibular teeth upon the opposing maxillary teeth and volume of the maxillary sinus may be studied.

CLINICAL APPLICATION

Surgical preparation of the jaws in the human being prior to the construction of artificial full dentures is a frequent need. Occasionally a maxillary tuberosity is encountered in which alveolectomy is indicated, but in which a large antrum has resulted in such thinning of the tuberosity wall that surgical correction is not advisable. The results of this investigation suggest that alveolectomy should be performed preferably at the time of extraction rather than at a later date. The loss of maxillary posterior teeth many years before the need for a complete artificial denture may allow for excessive pneumatization of the maxillary tuberosity by the antrum if the correction is left until the later date.

SUMMARY AND CONCLUSIONS

The purpose of this investigation was to compare the volumes of the left and right maxillary sinuses in the dog after extraction of teeth adjacent to the left maxillary sinus.

In ten normal adult dogs with complete dentitions, the upper left third and fourth premolars and first and second molars were extracted in seven, and the entire superior left quadrant of teeth in the other three. These dogs were euthanized 6–12 months later, and their heads were immediately severed, fixed, and sectioned in the midsagittal plane. A low-fusing-point metal was poured into the maxillary sinus of each half via its exposed ostium. The casts were then delivered by removal of the medial wall of the sinus, and the excess was trimmed at the level of the ostium. From these casts, by means of their weight and the specific gravity of the metal, the volumes of the sinuses were determined.

In two of the experimental dogs, the volumes of the left and right maxillary sinuses differed by less than 3%. In the other eight dogs, the differences ranged from 4.6% to 27.1%. In seven of these eight animals,

the maxillary sinus was larger on the left side, from which the teeth were extracted. In only one animal was the maxillary sinus larger by more than 3% on the unoperated-on side. From this limited preliminary study, it was concluded that the extraction of teeth adjacent to the maxillary sinus caused it to increase in size. The possible mode of action was discussed.

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The Palate*

INTRODUCTION

The purpose of this experiment was to determine grossly (1) the effects of reduced vascularity upon the hard palate, (2) the effects of trauma by total removal of the sutural growth sites of the hard palate upon palatal and facial growth in the normal rhesus monkey, and (3) something about the nature of sutural growth. The following was done to accomplish this: (1) complete unilateral removal of the palatal mucoperiosteum and severance of the descending palatine artery, and (2) production of complete surgical clefts of the soft and bony palate. No such report has been found in the literature. This experiment was not meant to be comparable with that of the problem of the cleft lip and palate patient with an underdeveloped and undersized maxilla. However, it was felt that this approach would offer an important and basic contribution to the general subject of the effect of decreased circulation and trauma, and to the specific subject of the effect on palatal, sutural, and facial growth.

*Excerpted from: Sarnat BG. (1958) Palatal and facial growth in Macaca rhesus monkeys with surgically produced palatal clefts. *Plast Reconstr Surg* **22**: 29–41. Winner of the Senior Award First Prize in the 1957 contest sponsored by the Foundation of the American Society of Plastic and Reconstructive Surgery and Beverly Hills Academy of Medicine.

MATERIAL AND METHODS

Because the growth activity of the face is greatest during early life, the youngest Macaca rhesus monkeys obtainable were used for this experiment. Their age at the beginning of the experiment was estimated, according to the primary dentition, to be about 8 months. They weighed from 4½ to 6 pounds. A total of 14 monkeys were included in this report: 7 unoperated-on controls, two animals in which the mucoperiosteum was completely removed from the left side of the hard palate, and 5 animals in which not only the mucoperiosteum was removed from the left half of the hard palate but also a complete surgical cleft was produced. Unilateral surgical procedures were performed, so as to be able to compare the operated-on and unoperated-on sides in the same animal.

The animals were anesthetized by an intraperitoneal injection of a 3% aqueous solution of sodium pentobarbital (½ cc/lb of body weight). Using a sterile surgical technique, the mucoperiosteum was incised on the left half of the hard palate along the posterior border, then anteriorly close to the midline on the right side and along the lingual border of the alveolar process. The descending palatine artery at its exit from the major palatine foramen was isolated, ligated, cut, and permitted to retract. The foramen was plugged with dental amalgam. The remaining mucoperiosteum was then elevated and removed completely. The palatal aponeurosis was dissected from the posterior part of the hard palate on the left side only. In addition, in five animals the exposed left bony palate was resected with a dental tapered fissure bur. This included the median and left transverse palatine sutures, the major palatine foramen, and nasal mucoperiosteum. Care was taken not to disturb either the alveolar process or the teeth. Thus, complete communication was established between the oral and nasal cavities. Bleeding was controlled and the animals were returned to their cages with the palatal wounds exposed. The postoperative survival period ranged from 1 to 34 months. An attempt was made to obtain approximately comparable unoperated-on controls. This was based upon the dental age, because the chronologic age was not known.

Upon the death of the animal, the head was severed and fixed immediately in a 10% solution of formalin. After removal of the mandible and the tongue, a photograph was taken of the oral palatal surface (Fig. 17.1, upper row). The skull was then dissected and additional photographs were

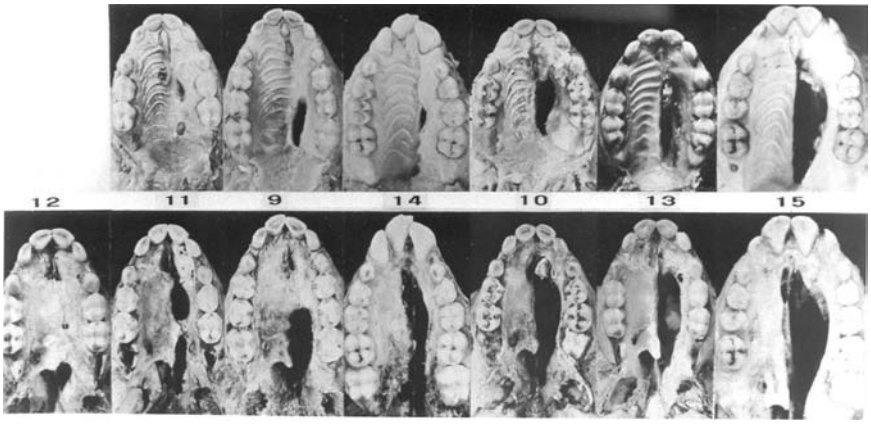

Fig. 17.1 Postmortem photographs of the oral palatal area of operated-on monkeys arranged in approximate order of increasing defect in the bony palate. Animals Nos. 9 and 10 had only the mucoperiosteum removed from the left half of the palate and ligation and cutting of the descending palatine artery at its exit from the major palatine foramen. The remaining animals had the left hard palatal area resected. The upper row of photographs was taken prior to the removal of the soft tissues. The lower row of photographs is of the corresponding animals after removal of the soft tissues. Note how the soft tissues mask the underlying bony defect. The rugal pattern is absent in the scarred epithelial surface of the healed operated-on side. Note in the lower row — animals Nos. 12, 11, and 9 — that there has been partial bony healing of the palatal defect and that the suture line is eccentric, toward the operated-on side. The major palatine foramen is not evident on the operated-on (animal's left, reader's right) side. In animal No. 14 the upper left permanent central incisor is malposed because of the absence of the adjacent permanent lateral incisor. There is no gross asymmetry of the maxillary arch.

taken of the denuded hard palate (Fig. 17.1, lower row). In addition, the soft tissues of the unoperated-on and operated-on sides of the oral hard palate in three animals were prepared for microscopic study.

FINDINGS

Postoperative Findings

During the first few postoperative days, the monkeys with palatal clefts had a drainage of fluid from the external nose. Subsequently this disappeared and no other untoward effects were noted. Examination of the palates,

about one month postoperatively, revealed that the surgically exposed bone was now covered by soft tissue with a smooth epithelial surface devoid of rugae. The surgically produced clefts of the hard palates, with communication between the oral and nasal cavities, persisted in varying degrees.

Postmortem Findings

Soft tissues of the hard palate

At postmortem, examination of the soft tissue revealed the absence of rugae on the operated-on side (Fig. 17.1). In addition, the rugal pattern on the unoperated-on side was not regular, the form varied, and some of the rugae extended beyond the midline. This was in contrast to the regular and bilaterally symmetrical rugal pattern in the unoperated-on animals. The size of the clefts ranged from a narrow slit with overlapping of epithelial covered tissue (animal No. 14) to an extensive cleft (animal No. 15) including the boundaries of the surgical procedure. No definite correlation could be made between the size of the cleft at postmortem and the postoperative survival.

Bony palate

In dissection of the soft tissue from the hard palate, the normal mucoperiosteum which contained the rugae was readily elevated from the bone. The scar tissue, which had no rugae, was thinner and was separated from the bone with more difficulty. Nothing unusual was noted of the soft palate. In two animals (Nos. 9 and 10), although only the mucoperiosteum was removed, clefts of the hard palate were found. In every animal the extensiveness of the bony palatal defect was masked by the overlying soft tissues (Fig. 17.1). The palatal defects were classified according to their extent and listed in order of postoperative survival (Table 17.1). In those instances where the palatal defect had been bridged by bone (animals Nos. 11 and 12), a suture was found. However, this suture was not in the midline but eccentric on the operated-on side. This was also found in animal No. 9 when only the mucoperiosteum was removed at the time of surgical interference. The bone in this area was thinner and more fragile than the bone on the

unoperated-on side. There was no evidence of the major palatine foramen on the operated-on side. No gross asymmetry of the palatal arch was noted although there were, of course, unilateral variations of the hard palate.

Other structures

A gross comparison of the left (operated-on side of the palate) and right (unoperated-on side of the palate) sides in regard to maxillary teeth (position, deformity), mandibular teeth, occlusion of maxillary and mandibular teeth, maxillary development, and mandibular development revealed no differences. In only one animal was there a malpositioning of the teeth. This was limited to the upper left permanent central incisor as a result of absence of the upper left permanent lateral incisor (animal No. 14). The lateral and frontal aspects of the skulls appeared similar to those of unoperated-on control animals of comparable age.

DISCUSSION

Healing After Palatal Surgery

In this group of seven operated-on animals, it was difficult to correlate the palatal findings with either the type of surgical procedure or postoperative survival. Regardless of the type of unilateral surgical operation, there was no asymmetry in maxillary dental arch size or shape.

In two animals (Nos. 9 and 10, Fig. 17.1), although only the mucoperiosteum was removed, extensive clefts of the bony palate were found at the time of death (8 and 14 months postoperatively). However, the palate at 1 month postoperatively appeared to be intact in these two animals. The loss of bone in the hard palate could possibly have been a result of the surgical trauma, the reduced vascularity incident to removal of the oral mucoperiosteum and ligation of the descending palatine artery or subsequent infection. The bony palate on the operated-on side was thinner and more fragile than on the unoperated-on side.

The findings on the above animals could not be distinguished from those on the animals in which not only the mucoperiosteum was removed but also a complete cleft of the entire left half of the bony palate was produced.

The findings on the latter group ranged from complete persistence of the cleft (animal No. 15) to nearly complete closure (animal No. 12). Interestingly enough, the animal with complete closure had a postoperative survival of only 4 months, whereas the animal with the wide open cleft had a postoperative survival of 34 months. It was not determined in this experiment whether or not part of the tongue was ever lodged in the cleft so as to retard or prevent its closure. In those animals where there was a regrowth of bone and the palatal shelves had rejoined forming a new suture, it was not in the midline but on the operated-on side (animals Nos. 9, 11, and 12; Fig. 17.1). Apparently bone had grown faster from the intact palatal process than the alveolar margin. In every animal the soft tissue contribution to the closure of the cleft was greater than that of bone. The fact that the mucoperiosteum and alveolar bone were intact anteriorly and the soft palate was intact posteriorly no doubt played a role in the healing of these clefts. It would be of interest to determine the extent of healing were these clefts to extend completely through the alveolar process and the hard and soft palates.

Clinically, in the surgical closure of a cleft palate it is well known that if a midline separation of the mucoperiosteal flaps occurs, the separation will gradually become smaller. Complete closure of this opening will not occur, of course, if the margins become epithelized. Thus, both clinically and in animals, palatal clefts or defects on a traumatic basis tend to become smaller even when there is no underlying bony support. An interesting observation was made by Adams[13] when he found bony union of the repaired cleft of the hard palate. He stated, "this was an unexpected finding, since all previous teachings and beliefs were that following repair of complete cleft palate by the use of mucoperiosteal flaps one could expect only a soft tissue repair of the defect." [See: Yin *et al.* (2005) *Plast Reconstr Surg* **115**: 1239–1244 and (2006) *Plast Reconstr Surg* **117**: 2505–2506.

The effects of tension (expansion) and pressure by means of orthodontic appliances on surgically produced clefts (2–3 mm in width) of the left side of the hard palate and alveolar bone in two Macaca rhesus monkeys about three years old were studied by Harvold.[14] The animals were killed eight weeks after the procedure. Examination of the palate subjected to tension (expansion) revealed complete healing of the cleft of the alveolus and hard palate with no asymmetry of the upper jaw. However, examination of the palate subjected to pressure revealed no healing of the bony cleft and deformity of the upper jaw.

Palatal and Facial Growth After Palatal Surgery

Complete extirpation of the median palatine and transverse palatine sutures in the experimental animals did not influence maxillary arch size or shape. Thus, it might be assumed that either these sutures do not make an important contribution to maxillary growth or other growth sites adjusted to the altered conditions. In this regard, the jaws of these animals were in occlusion at the beginning of the experiment and the mandible may have guided maxillary growth. Of course, in a congenital cleft of the hard palate there is no median palatine suture and in the complete unilateral cleft the bony fragments are separated so that these sites of growth are not present. Unilateral extirpation of the frontonasal suture in growing rabbits produced no asymmetry of the snout.[5] On the other hand, removal of the mandibular condyle in growing and adult monkeys produced a severe deformity of the mandible, midface, and ventral portion of the skull.[9] Thus, it seems that trauma is not as serious in terms of a growth arrest to a growing suture as it is to endochondral bone growth. The findings of this experiment do *not* substantiate the thesis that decrease in vascularity to the palate or injury to the sutural growth sites will affect palatal or facial growth.

Maxillary Underdevelopment: Some Possible Causes

Probably the most common and difficult maxillary deformity to cope with is that of the patient with a cleft lip and cleft palate and lack of development and compression of the middle third of the face after a BROPHY procedure. The mandibular prognathism may be only relative because of underdevelopment of the middle third of the bony face, or sometimes the mandible is larger than normal. Prevention of this "dish face," which is difficult to correct, should be our goal.

Genetic and prenatal

Lack of maxillary development may well be due to multiple factors. Experimentally, the cleft palate (and other anomalies) is the result of either a genetic factor or the activity of an environmental noxious agent

(riboflavin deficiency, low oxygen tension, ACTH, etc.) during prenatal development. Associated with this may be some variation from the normal of the facial growth pattern. Three factors seem to determine what form the defects will take: (1) the time at which the agent injures the embryo; (2) the nature of the agent, which determines what tissue it will attack; and (3) the capacity of the developing tissue to repair itself.[15] Until the causative agents of facial clefts and the facial deformity which is sometimes associated with them have been eliminated, we shall have to content ourselves with improvement of methods of treatment.

Surgical interference

Another possible cause of the lack of development of the middle third of the face in the cleft palate patient and the one with which this report is primarily concerned, has been ascribed to the effect of trauma at the time of surgical closure of the cleft palate. For the purposes of this discussion, the compression and restraining operations on the maxillae (Brophy and others) will not be dwelled upon, since the procedures do not bear directly on this work and the end results are so well known.

The effect of other surgical procedures upon bone growth could be considered in relation to damage to the sutures, to the periosteum and appositional growth, and to decreased vascularity. It was demonstrated in this experiment that even though complete removal of the mucoperiosteum caused a loss of palatal bone, facial growth was not affected grossly. In addition, the vascularity of the oral surface of the operated-on side of the palate was presumably reduced, since the major palatine foramen and the blood vessels usually coursing through it were not found. It would be of interest to determine on a clinical basis whether there is any loss of palatal bone after raising a mucoperiosteal flap. In other words, the clinical findings could and would probably be as variable as they were in these experimental animals.

The effects of various surgical procedures upon the cleft palate in regard to facial development have been given considerable attention. Generally, the consensus is that the severity of the growth arrest of the middle third of the face may be dependent upon both the particular type of cleft palate and the time, type, and frequency of surgical operations.

On the other hand, it was stated that in one series the cleft palate patients showed only minor retardation in the anteroposterior growth of the maxilla with under- or overdevelopment of the mandible. Neither crowding of teeth nor crossbite was related to surgical trauma, but rather to the severity of the original palatal defect.[16] More recently, clinical reports have not only questioned the validity of earlier ones on the effect of palatal surgery upon facial growth, but also found that when palatal clefts are closed surgically at an early age by the von Langenbeck procedure, facial growth is similar to that in the control group of normal children.[17]

Considerable difference of opinion exists in regard to when the cleft palate should be closed and by what surgical or prosthetic procedure.[18] This can readily be understood when one considers the multiplicity of variables. Since congenital clefts of the lip and palate are not all alike, they should not be considered as a single, fixed clinical entity in terms of classification and treatment. Therefore, in evaluating results of a particular surgical procedure, the minimum requirement is an accurate anatomical description of the cleft, complete and accurate preoperative and postoperative serial records over a proper period of time, and comparison of like cases only. Unfortunately, some of the opinions expressed are based upon clinical impressions, which are not usually substantiated by accurate measurements.

So much emphasis has been placed on the effect of surgical trauma upon maxillary and facial growth in the repair of the cleft palate that other factors have been given less and possibly too little attention. An important factor is the surgical closure of the cleft lip and the resulting effect upon the cleft palate. It is well known that after surgical repair of a cleft lip the maxillae tend to approximate each other and the palatal cleft is less prominent. The united upper lip, especially if it is tight, could restrain the maxillae from attaining not only their full growth potential but also their proper position. This is noted in particular after the repair of certain, bilateral clefts of the upper lip. Utilization of the maximum amount of the prolabium would result in a less tight but possibly not as esthetically pleasing lip. A tight upper lip could thus have a similar effect to a compression and restraining operation on the maxillae, such as the Brophy procedure for closure of a cleft palate.

Scar tissue

In addition to the trauma sustained at the time of surgical closure of the cleft palate, in certain procedures there may be subsequent formation of scar tissue, which has been considered as another cause of the growth arrest. On this basis criticism has been leveled against the surgical procedure wherein mucoperiosteal palatal flaps are raised from the bone. It has been claimed that the massive scar tissue across the palatal arch has a restraining effect upon palatal and maxillary growth. The question to be answered, however, is: specifically what growth sites are affected and what direct evidence is there to substantiate this often-made claim? In this experiment a cleft was created but no mucoperiosteal palatal flaps with a raw superior surface were raised and sutured in the midline, so that the question of the restraining effect of scar tissue could not be considered.

Need for Further Study

Additional experiments would be of value if extended to include not only a cleft of the hard palate but also one of the incisor alveolus and the soft palate; in other words, a complete unilateral cleft palate. To evaluate properly the effects of various cleft palate surgical procedures, it would be desirable to obtain animals born with these clefts and operate on and observe them during growth periods comparable with that of the human being.

SUMMARY AND CONCLUSIONS

It was not the purpose of this experiment to evaluate or in any way point out the advantages or disadvantages of any of the surgical procedures employed in the treatment of palatal clefts. Rather, it was the purpose of this experiment to determine the effects upon palatal and facial growth of unilateral (1) removal of the oral mucoperiosteum and ligation of the descending palatine artery to decrease the blood supply and (2) resection of the hard palate to eliminate the median palatine and transverse palatine sutures as possible growth sites.

To carry out this study, 7 young growing normal Macaca rhesus monkeys were operated on, with a postoperative survival ranging from

1 to 34 months. An approximately comparable group of 7 normal unoperated-on monkeys were used as controls.

It was found that a smooth, thinner epithelial scar, in contrast to the thicker normal mucoperiosteum with its palatal rugae, covered the operative site in varying amounts. In every instance the soft tissue covered a greater area of the palatal defect than the bone.

In the two animals (Nos. 9 and 10) in which only the mucoperiosteum was removed and the descending palatine artery ligated, extensive defects were found in the hard palate and also the covering soft tissue. In those animals in which in addition the bony palate was resected, the complete surgical cleft of the hard palate persisted in varying degrees, from slight to complete. No correlation was made between the extensiveness of the palatal surgery or the length of postoperative survival on the one hand and the extent of the palatal cleft on the other hand.

A comparison of the skulls of (1) the operated-on and unoperated-on sides with each other and of (2) the operated animals with approximately comparable unoperated-on controls revealed no significant gross differences in growth and development of the hard palate, maxillary arch, mandibular arch, maxillomandibular relationship, (arch size and shape, occlusion and tooth relationships), or total face.

Thus, within the limits of this experiment, it is concluded that unilateral traumatic surgery in the form of (1) elevation and removal of the mucoperiosteum and severance of the descending palatine artery, and of (2) resection of the hard palate and adjacent sutures, did not produce in either the palate or the face a growth arrest which was grossly apparent. This experiment suggests that the surgical trauma incident to the raising of mucoperiosteal palatal flaps is not the cause of lack of maxillary and facial growth by the production of either a sutural growth arrest or decreased blood supply to the area.

After total removal of the midpalatine suture, surprisingly a new suture did form.

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CHAPTER 18

The Midface: Clinical Considerations

SARNAT'S GROWTH STUDIES IN CLINICAL PRACTICE

Sarnat's growth studies on facial sutures, the septum, and the palate have helped shape clinical thought on facial trauma and the timing of midface reconstruction and cleft surgery. Serial cephalograms were used in rabbit studies on facial sutures to show that even maximal injury or trauma (with complete extirpation) to the nasofrontal suture does not lead to growth arrest.[1] By contrast, injury to the septal/vomer region (with resection) led to problematic midfacial growth.[2] Sarnat also found that in mature animals, septal resection was not problematic. He concluded that "the relationship of the cartilaginous nasal septum to growth of the snout can be compared with that of the orbital contents to the growth of the orbit and the brain to the growth of the cranium."

These research data suggest that clinically, in a child, nasal bone trauma is not as detrimental to growth as septal trauma. In addition, when one is planning midfacial surgery in the syndromic patient with midface hypoplasia, the Sarnat studies are informative. Le Fort III advancement and monobloc advancement both involve transection of the septal-vomer region.[3] Thus, these procedures will affect future midface growth and should be delayed, when possible, until later in childhood. If there are not functional issues involving airway, visual, or intracranial pressure, then these procedure may be delayed until 8–12 years of age. In addition, Le Fort I advancement, common in cleft patients with maxillary hypoplasia, also involves injury to the septal-vomer regions, which may affect further nasomaxillary growth.[4]

Sarnat found that in rhesus monkeys palatal trauma with mucoperiosteal elevation was not the cause of maxillary or facial growth arrest by suture growth arrest or decreased blood supply to the area.[5] Clinically, up to one-third of cleft palate patients develop maxillary hypoplasia requiring Le Fort I advancement at maturity.[6] This is most likely due to a combination of intrinsic growth problems and surgical scarring. Sarnat also found that total removal of the midpalatal suture resulted in a new suture formation.[5] This is analogous to the formation of a new cranial suture after removal.[7]

MIDFACE HYPOPLASIA

Midface hypoplasia may be seen with craniosynostotic syndromes, in cleft patients and in posttraumatic or postsurgical patients. This abnormal positioning of the facial skeleton may result from fused facial sutures, intrinsic growth disturbances, or growth disturbances related to trauma or postsurgical scarring.

Dysostotic syndromes associated with midface hypoplasia include Apert syndrome (acrosyndactyly), Crouzon syndrome, Saethre–Chotzen syndrome, Jackson–Weiss syndrome, Pfeiffer syndrome, Carpenter syndrome, Antley Bixler syndrome, craniofrontonasal dysplasia, and others.[8] Patients with midface hypoplasia have dysmorphic features and may have serious functional problems, such as respiratory problems related to upper airway obstruction and ocular problems (ocular keratitis, corneal ulcers, globe herniation, blindness).[9] The timing of the correction of this deformity often depends on the severity of the functional problems. Typically, midface advancement at 8–12 years of age is recommended for the best result and to minimize future procedures. However, when upper airway obstruction or ocular exposure becomes significant, earlier intervention is warranted.

Monobloc Distraction

In the past, correction of patients with midface and forehead retrusion involved either (1) staged procedures with fronto-orbital advancement followed by Le Fort III advancement or (2) monobloc (one unit) advancement.[3] Traditionally, these procedures involve bone grafting and rigid fixation. The monobloc procedure is advantageous, because it avoids a second major

procedure; however, the risk of serious complications (meningitis, CSF leak, frontal bone flap necrosis) is considered too high for many institutions to advocate its use. These infectious complications may be caused by the large nasofrontal dead space and communication between epidural and ethmoidal sinus tissues left after the acute advancement of the facial-forehead unit.

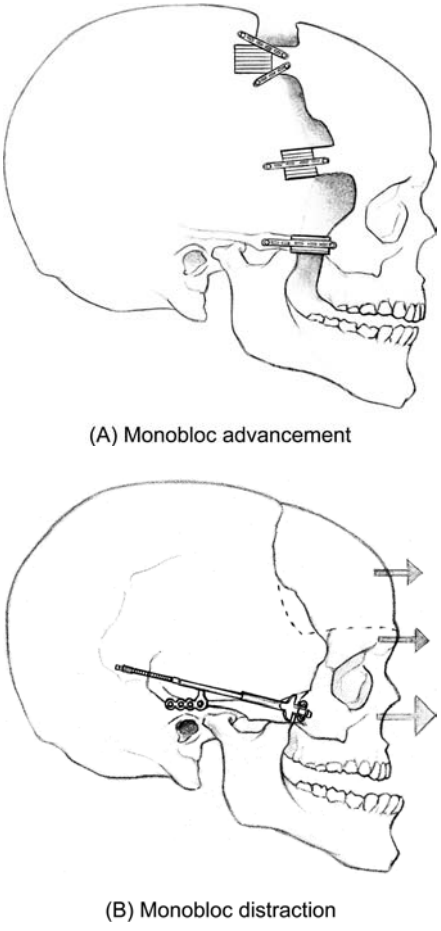


Fig. 18.1 (A) Illustration of the procedure used in Group 1 patients (conventional monobloc), demonstrating monobloc osteotomy and immediate advancement using bone grafting and rigid fixation. (**B**) Illustration of the procedure used in Group 3 patients (monobloc distraction), demonstrating gradual lengthening of the monobloc segment with distraction osteogenesis using internal devices.

To determine if the technique of distraction osteogenesis after a monobloc osteotomy may lower the risk of complications, we conducted a clinical study at UCLA.[3] With this technique remucosalization of the nasofrontal area (for 4–7 days) is allowed before gradual advancement of the forehead and midface. To see if distraction of the monobloc segment offered decreased morbidity, we compared clinical outcomes of patients who underwent conventional monobloc advancement to patients who underwent monobloc distraction.

In our study, Group 1 patients (conventional monobloc) underwent traditional monobloc advancement with bone grafting ($n = 12$) (Fig. 18.1). Group 2 patients (modified monobloc) did not have VP shunts and underwent the above procedures with placement of a pericranial flap and fibrin glue over the midline defect ($n = 11$). Group 3 patients (monobloc distraction) underwent advancement of the monobloc segment by distraction osteogenesis using internal distraction devices ($n = 24$). Complications assessed for included meningitis, CSF leak, frontal bone flap loss, wound infection, and others. For each group, we assessed complications including

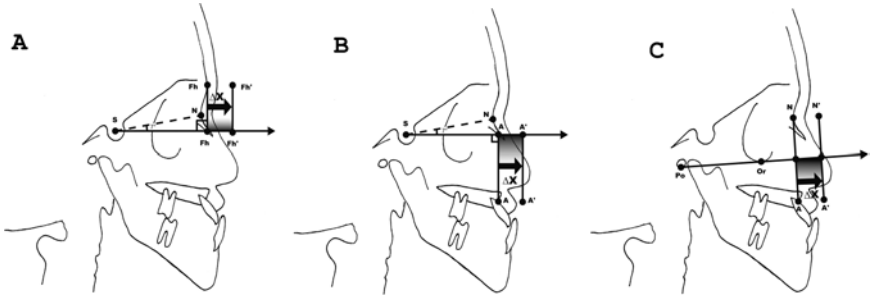


Fig. 18.2 Illustration of a lateral cephalogram tracing. (**A**) Forehead horizontal change (Δx) was measured by drawing the horizontal plane [a line originating at S (sella) and extending 7° below the S–N plane] and measuring the distance along this line between S and the perpendicular intersection of the Fh point. (Fh′ = Fh point after advancement.) (**B**) Maxillary horizontal change (Δx) was measured by drawing the horizontal plane (a line originating at S (sella) and extending 7° below the S–N plane) and measuring the distance along this line between S and the perpendicular intersection of the A point. (A′ = A point after advancement.) (**C**) Midface horizontal change (Δx) was measured by drawing the Frankfort horizontal (porion through orbitale) and measuring the distance along this line between the porion (Po) and the perpendicular intersection of the nasion (N) to the A point (A) line. (N–A′ = N–A after advancement.)

meningitis, CSF leaks, frontal bone falp loss, wound infections, and others. To access horizontal changes after advancement in follow-up, the preoperative, postoperative, and follow-up lateral cephalograms were used. We compared three levels for horizontal change: (1) forehead Δx, (2) midface Δx, and (3) maxillary Δx (Fig. 18.2).

Patients ranged between 5–22 years of age (mean 8–11) in all three groups at the time of the operation. Diagnosis was similar among the three groups: Group 1 (conventional monobloc); Group 2 (modified monobloc); Group 3 (monobloc distraction): Apert syndrome (25%, 9%, 20%), Crouzon syndrome (42%, 36%, 50%), Pfeiffer syndrome (17%, 27%, 20%) or another syndrome, like Saethre-Chotzen, Carpenter, Antley-Bixler (17%, 27%, 8%) (Figs. 18.3–18.6).

Our results showed that Group 3 patients (distraction monobloc) had the lowest complication rate (8%), followed by those in Group 2 (modified monobloc) (43%) and Group 1 (conventional monobloc) (61%) ($p < 0.05$) (Fig. 18.7). Thus, gradual advancement of the forehead and midface with distraction after a week of healing resulted in significantly less meningitis, CSF leakage, and wound infections. Group 1 patients lost over 500 cc more blood and had a hospitalization almost 10 days greater than that of patients in Group 3. In addition, Group 1 was the only group with moderate or significant frontal bone flap loss. The complication profile seen in the patients treated by conventional and modified monobloc was consistent with previously reported results.[9] The improved perioperative complication profile of the monobloc distraction group underscored the less invasive and less morbid nature of the procedure when compared to conventional or modified advancement.

Patients in Group 3 (distraction monobloc) achieved greater advancement (12.6 mm) than those in Group 2 (modified monobloc) (9.4 mm) or Group 1 (conventional monobloc) (9.1 mm) ($p < 0.05$) (Figs. 18.6–18.9). Relapse was least in Group 3 (8%) compared to Group 2 (67%) and Group 1 (45%) (Tables 18.1–18.3).

From this study we concluded that monobloc advancement by distraction osteogenesis (1) had less morbidity and (2) achieved greater advancement with less relapse, when compared to conventional methods of acute monobloc advancement with bone grafting. Thus, the technique of monobloc distraction was superior to conventional methods of acute monobloc advancement and should be considered a reasonable

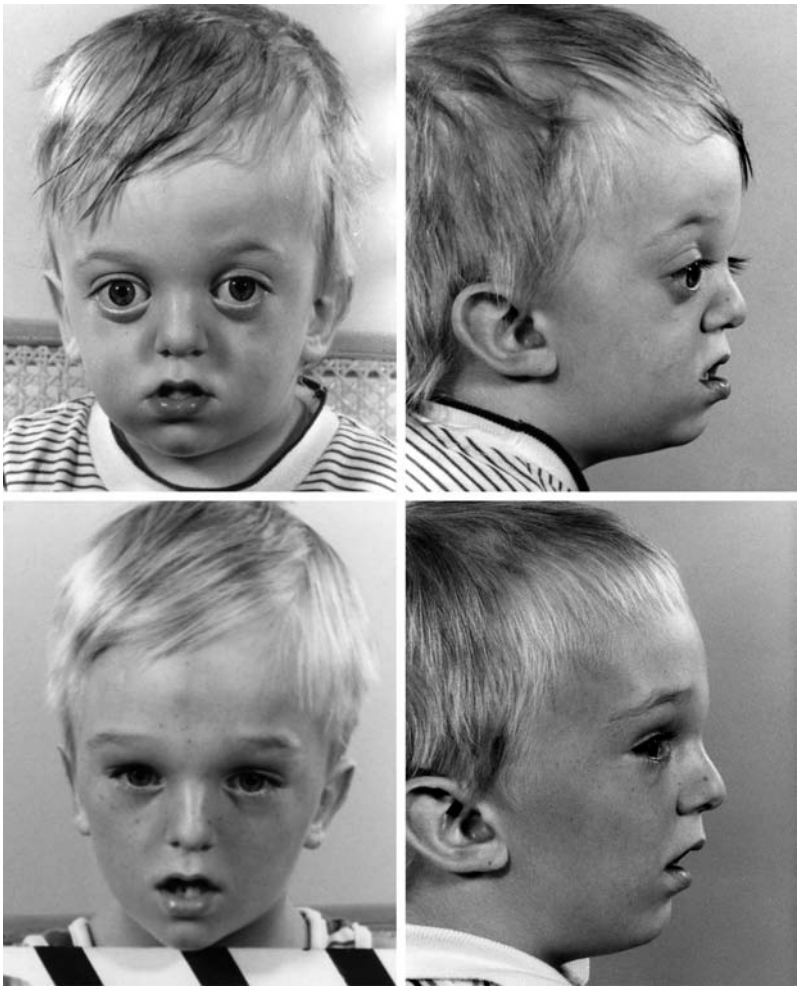


Fig. 18.3 Group 1 (conventional monobloc) patient with Crouzon syndrome. *Above*: Preoperative images before conventional monobloc advancement at age seven. *Below*: Postoperative images after the conventional monobloc procedure demonstrating correction of forehead and midface retrusion (H. K. Kawamoto).

alternative to staged fronto-orbital advancement followed by Le Fort III advancement.

When midface hypoplasia exists but the forehead and orbits are in a relatively normal position, advancement at the Le Fort I level is required.

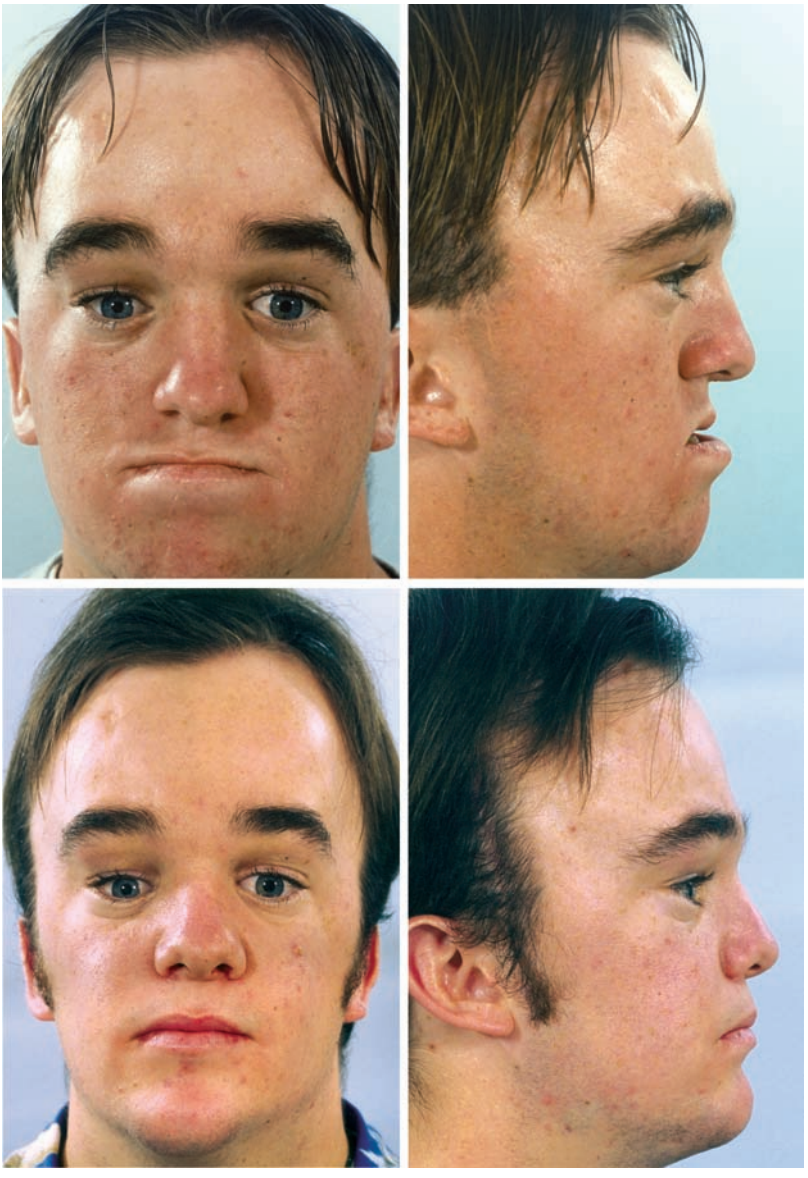


Fig. 18.4 *Above*: Follow-up images at skeletal maturity (16 years) of the same patient as shown in Fig. 18.4, just before Le Fort I advancement to correct class III malocclusion. Forehead and orbital correction are adequate. *Below*: Follow-up images after Le Fort I advancement (H. K. Kawamoto).

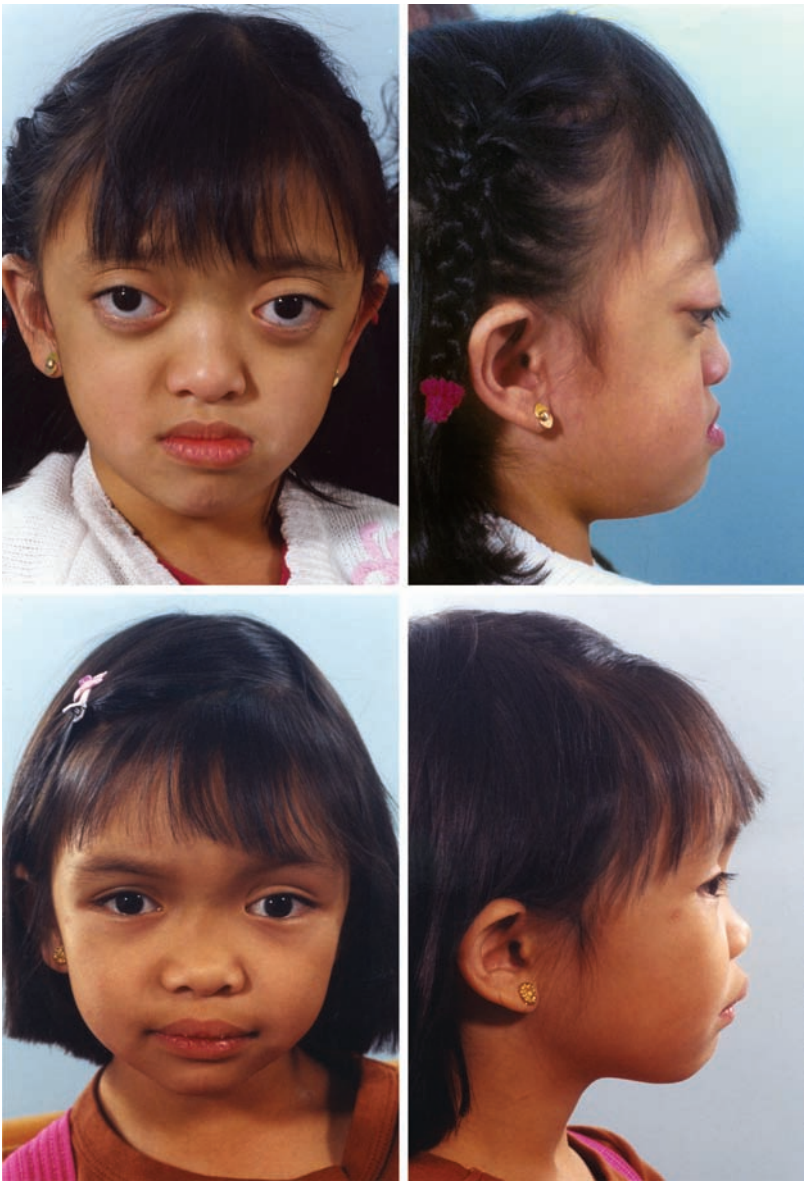


Fig. 18.5 Group 3 (monobloc distraction) patient with Crouzon syndrome. *Above*: Preoperative images before monobloc distraction at eight years of age show forehead and midface retrusion. *Below*: Postoperative images after monobloc distraction (14 mm) show correction of facial deformity (H. K. Kawamoto).

Fig. 18.6 The same patient as shown in Fig. 18.6. Follow-up images one year after monobloc distraction.

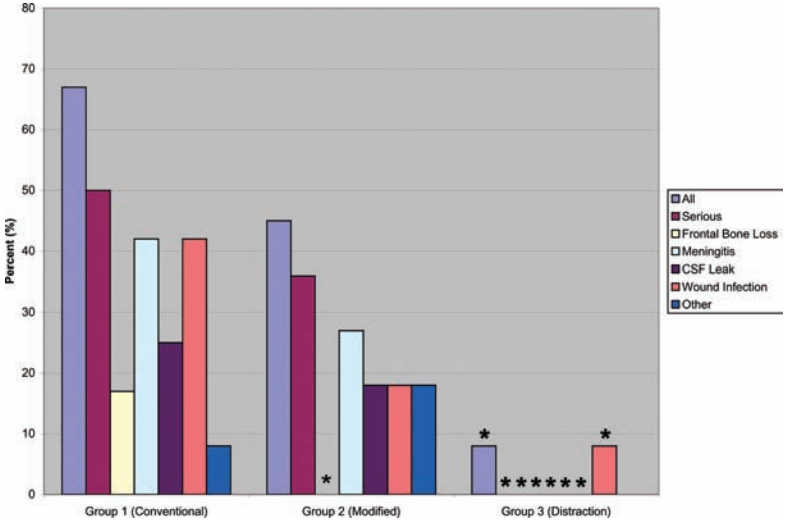


Fig. 18.7 Morbidity was greater in the conventional monobloc procedure group and least in the monobloc distraction group ($^*p = < 0.05$).

Table 18.1 Monobloc Advancement: Cephalometric Changes in the Midface and Mandible in Group 1 (Conventional Monobloc)

	T_1	T_2	T_3	$\Delta T_2 - T_1$ (Advancement)	$\Delta T_3 - T_2$ (Relapse)
Midface					
Maxilla Δx, mm	46	57	52	11	−5
Forehead Δx, mm	63	74	70	11	−4
Midface Δx, mm	73	83	78	10	−5
SNA, degrees	73	75	73	2	−2
Mandible					
Mandible Δx, mm	60	57	58	−3	1
Mandible Δy, mm	77	78	77	1	−1
SNB, degrees	83	76	78	−7	2

Mean values are represented ($n = 12$).

Table 18.2 Monobloc Advancement: Cephalometric Changes in the Midface and Mandible in Group 2 (Modified Monobloc)

	T_1	T_2	T_3	$\Delta T_2 - T_1$ (Advancement)	$\Delta T_3 - T_2$ (Relapse)
Midface					
Maxilla Δx, mm	49	59	54	10	−5
Forehead Δx, mm	65	77	71	12	−6
Midface Δx, mm	74	84	80	10	−5
SNA, degrees	72	73	72	1	−1
Mandible					
Mandible Δx, mm	63	59	61	−4	2
Mandible Δy, mm	75	76	75	1	−1
SNB, degrees	81	77	79	−4	2

Mean values are represented ($n = 11$).

An orthognathic procedure at skeletal maturity is recommended. With proper orthodontic preparation, this offers a stable occlusion in one stage. However, earlier advancement may be required if functional issues like upper airway obstruction must be mitigated. We studied a subset of cleft

Table 18.3 Monobloc Advancement: Cephalometric Changes in the Midface and Mandible in Group 3 (Monobloc Distraction)

	T_1	T_2	T_3	$\Delta T_2 - T_1$ (Advancement)	$\Delta T_3 - T_2$ (Relapse)
Midface					
Maxilla Δx, mm	46	59	58	13	−1
Forehead Δx, mm	62	77	76	15	−1
Midface Δx, mm	72	85	84	13	−1
SNA, degrees	74	79	79	3	−0
Mandible					
Mandible Δx, mm	61	57	60	−4	3
Mandible Δy, mm	77	79	78	2	−1
SNB, degrees	85	77	79	−6	0

Mean values are represented ($n = 24$).

patients with severe maxillary hypoplasia (>10 mm), comparing the traditional technique to distraction osteogenesis.[10]

Le Fort I Distraction

Dentofacial skeletal deformities are common in patients with cleft lip and palate.[11] In 20–25% of patients, orthodontic treatment alone is not sufficient and surgical correction of the class III malocclusion is required with a Le Fort I osteotomy and advancement.[12] A subset of this group of cleft patients has *severe* maxillary deficiency that poses a challenge to the cleft treatment team.[13]

Traditionally, before undergoing a Le Fort I advancement, cleft patients have healed an alveolar bone graft, developed mature dentition, and completed facial skeletal growth. Preoperative orthodontic preparation removes dental compensations. Adequate planning with cephalometric analysis, models, and an occlusal splint allow for good postoperative occlusion in one stage after orthognathic surgery. Although distraction osteogenesis (DO) has been effective in lengthening membranous bone, including the maxilla, in the growing facial skeleton and in the mature

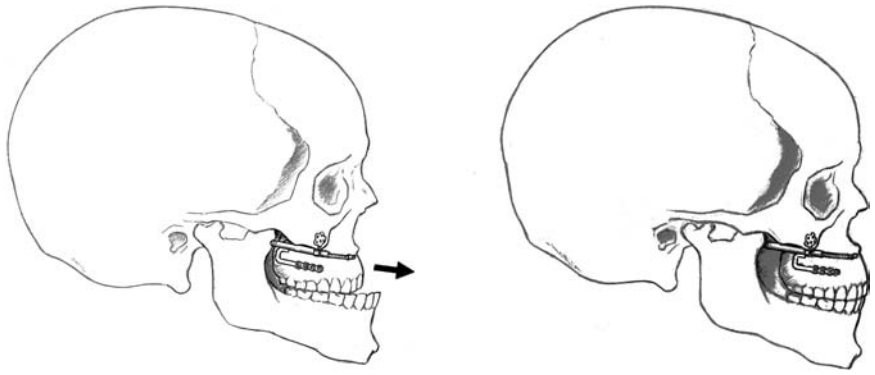


Fig. 18.8 Illustration of a lateral view of the Le Fort I advancement distraction osteogenesis procedure. *Left*: Before distraction, after Le Fort I osteotomy with the internal distraction device in place. *Right*: After distraction, following advancement of the Le Fort I segment.

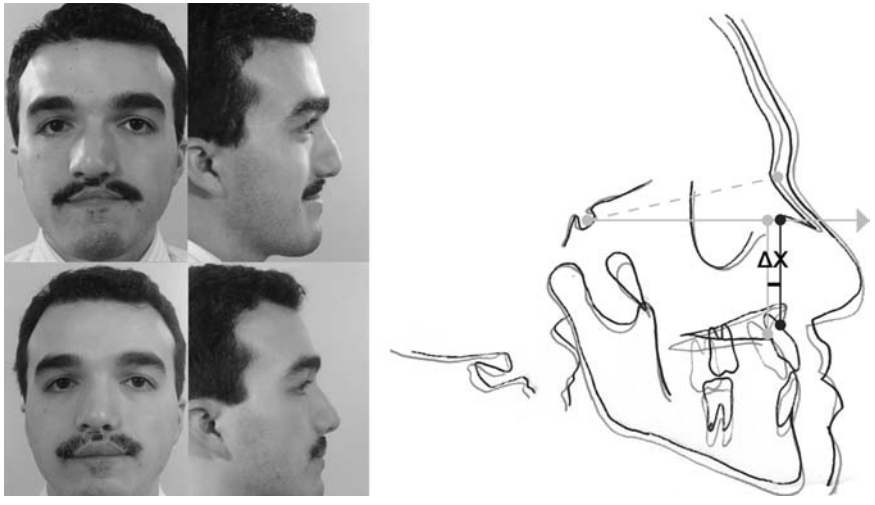


Fig. 18.9 Group 1: Le Fort I advancement for mild-to-moderate deficiency. *Left, above*: Preoperative images (frontal and lateral views). *Left, below*: Postoperative images (frontal and lateral views). *Right*: Comparison of preoperative (gray lines) and postoperative (black lines) cephalograms showing horizontal axis change (Δx).

patient, some difficulties with this technique exist.[14] DO requires multiple stages, and adequate occlusion may be more difficult to achieve.

However, there is a subset of cleft patients with *severe* rather than mild-to-moderate maxillary deficiency, whom we chose to investigate clinically to determine if DO would be beneficial. This subgroup of patients with severe maxillary deficiency is more prone to relapse following one-step Le Fort I advancement. Soft tissue restriction may contribute to the high relapse rates with one-step large advancements and to an increased incidence of velopharyngeal insufficiency (VPI).[15] At times clinicians perform a suboptimal two-jaw procedure with a mandibular setback to compensate for this large maxillary hypoplasia. This compromise results in flatter faces, which may age prematurely because of the lack of hard tissue support for the soft tissue.

To determine if cleft patients with severe maxillary deficiency had less relapse and fewer speech problems with the gradual advancement of Le Fort I internal DO compared to a one-step Le Fort I orthognathic advancement, dentocraniofacial morphology and speech outcomes were analyzed. Clinical examination, cephalometric angular and linear measurements, and quantitative speech scores in preoperative, postoperative, and follow-up patients were used as endpoints of analysis.

We performed a study to test the efficacy of Le Fort I distraction in which patients with cleft lip and palate deformities and maxillary deficiency were divided into three groups treated by Le Fort I advancement: (1) mild-to-moderate deficiency (<10 mm) with the conventional orthognathic procedure, (2) severe deficiency (≥10 mm) with the conventional orthognathic procedure, and (3) distraction procedure for severe deficiency (≥10 mm) ($n = 51$) (Fig. 18.8). Preoperative, postoperative, and follow-up (>1 year) lateral cephalogram measurements were compared including angular (SNA and SNB) and linear (Δx = horizontal and Δy = vertical) changes. In addition, the Pittsburgh Speech Score was used to assess for velopharyngeal insufficiency (score >3 = VPI).

Results from this study showed that Group 1 (mild-to-moderate; conventional Le Fort I) had a mean SNA change from Preop = 78.7 to Postop = 83.8, and a Δx (horizontal) change of 5.0 mm with no relapse. With rigid fixation and proper occlusion this minimum-to-no relapse

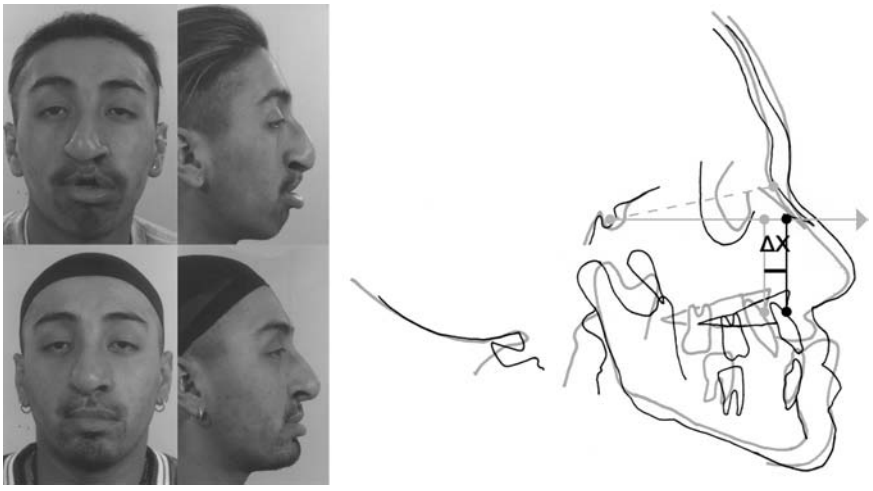


Fig. 18.10 Group 2: Le Fort I advancement for severe deficiency. *Left, above*: Preoperative images (frontal and lateral views). *Left, below*: Postoperative images (frontal and lateral views). *Right*: Comparison of preoperative (gray lines) and postoperative (black lines) cephalograms showing horizontal axis change (Δx).

was expected (Fig. 18.9). Group 2 (severe; conventional Le Fort I) had a mean SNA change from Preop = 76.3 to Postop = 82.0 and a Δx of 7.2 mm with 63% relapse (Fig. 18.10). This significant relapse for a one-stage large maxillary advancement is the reason that often a combined procedure with a mandibular setback is chosen despite suboptimal skeletal positioning. Group 3 (Le Fort I by distraction) had a mean SNA change from Preop = 74.1 to Postop = 84.9 and a Δx of 16.5 mm with 15% relapse (Fig. 18.11). Thus, for severe maxillary deficiency the distraction group had 48% less relapse than the conventional Le Fort I group (Fig. 18.12).

Postoperative speech evaluation showed VPI in the following: Group 1 (mild-to-moderate; conventional Le Fort I) — 4 of 20 patients (15%); Group 2 (severe; conventional Le Fort I) — 9 of 11 patients (82%); Group 3 (Le Fort I by distraction) — 9 of 20 patients (40%).

These data suggested to us that Le Fort I internal distraction for *severe* cleft maxillary deficiency leads to better dental occlusion, less relapse, and better speech results. This distraction technique also allows for more

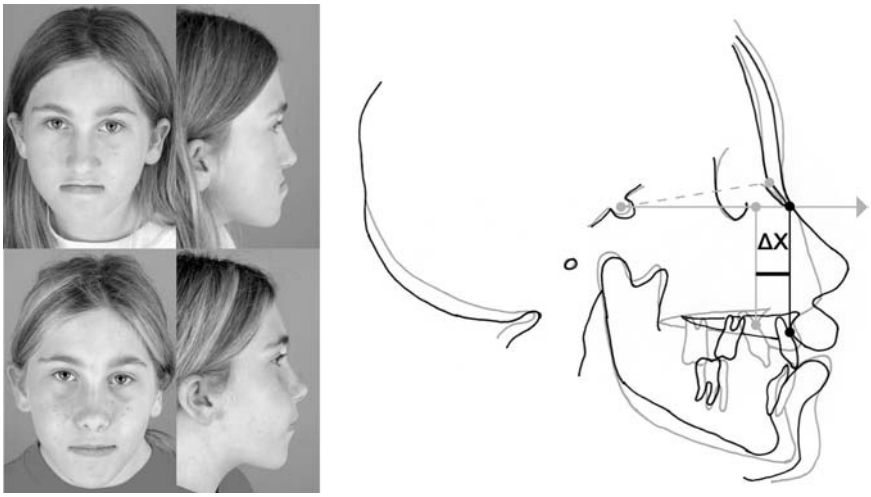


Fig. 18.11 Group 3: Le Fort I distraction osteogenesis for severe deficiency. *Left, above*: Preoperative images (frontal and lateral views). *Left, below*: Postoperative images (frontal and lateral views). *Right*: Comparison of preoperative (gray lines) and postoperative (black lines) cephalograms showing horizontal axis change (Δx).

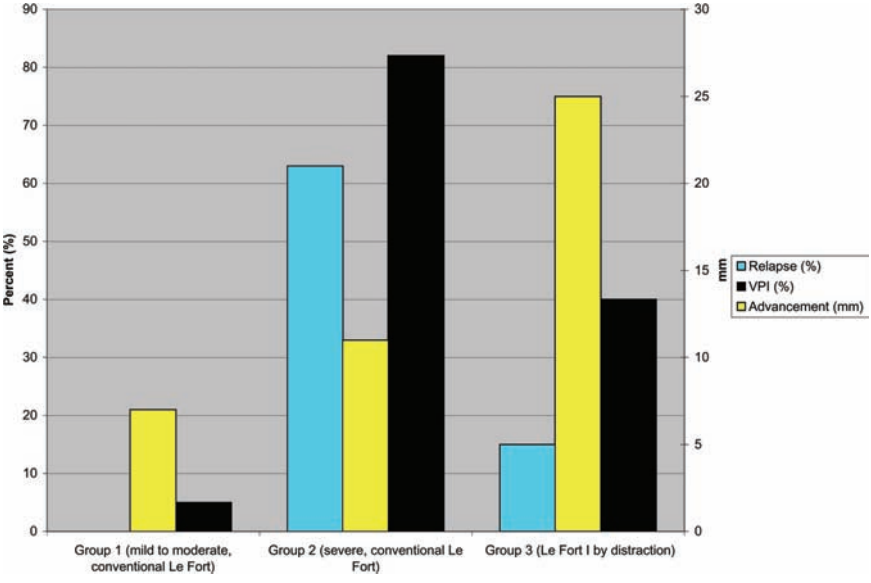


Fig. 18.12 Bar graph of the rate of advancement (millimeters), relapse (percent), and postoperative velopharyngeal insufficiency (percent).

optimal final skeletal balance and cephalometric norms without the compromise of a combined mandibular setback.

Septal Surgery

As a growth center for the nose, the septum should not be operated on until near maturity. Disruption of septal growth from surgery or trauma may result in nasal shortening. Syndromic nasomaxillary growth disturbances like Binder's syndrome also exist. In addition there are teratogens, substances that inhibit normal cartilaginous — and thus normal septal — development and growth. For instance, exposure of a fetus to warfarin (Coumadin©) during the 6–10-week gestation period can result in warfarin embryopathy or fetal warfarin syndrome. This involves respiratory and feeding difficulties in infancy, as well as growth disturbances of the nasomaxillary complex. These septal and nasal growth problems, with warfarin, remain problematic throughout childhood and adolescence.

We reported on a series of UCLA patients with maldevelopment of the nasal pyramid from the teratogenic effects of warfarin (Coumadin nasal deformity) (Figs. 18.13, 18.14).[16] Warfarin is able to cross the placental barrier. The exposed fetus risks warfarin embryopathy of fetal warfarin syndrome, which can result in: (1) CNS disruptive effects secondary to hemorrhage; (2) limb abnormalities, including epiphyseal bony stippling and distal digital hypoplasia; and (3) nasal hypoplasia. The syndrome occurs in approximately 4–6% of fetuses that are exposed during the critical period of 6–10-week gestation. It is during this period that the nasal septum more than doubles in length, from 4 to 10 mm. In a rat model ectopic calcification occurs in the septal cartilage, causing reduction in the longitudinal growth of the nasal septum and associated maxillonasal hypoplasia.

This documentation of clinical cases from birth to adulthood supports the laboratory findings on the importance of the nasal septum as a growth center (Figs. 18.15, 18.16). For corrective surgery with staged nasal lengthening, cranial bone grafts are preferred at our institution. For nasal dorsum augmentation, alloplastic implants may be tolerated, but in a case with previous operations, a traumatized or congenitally abnormal

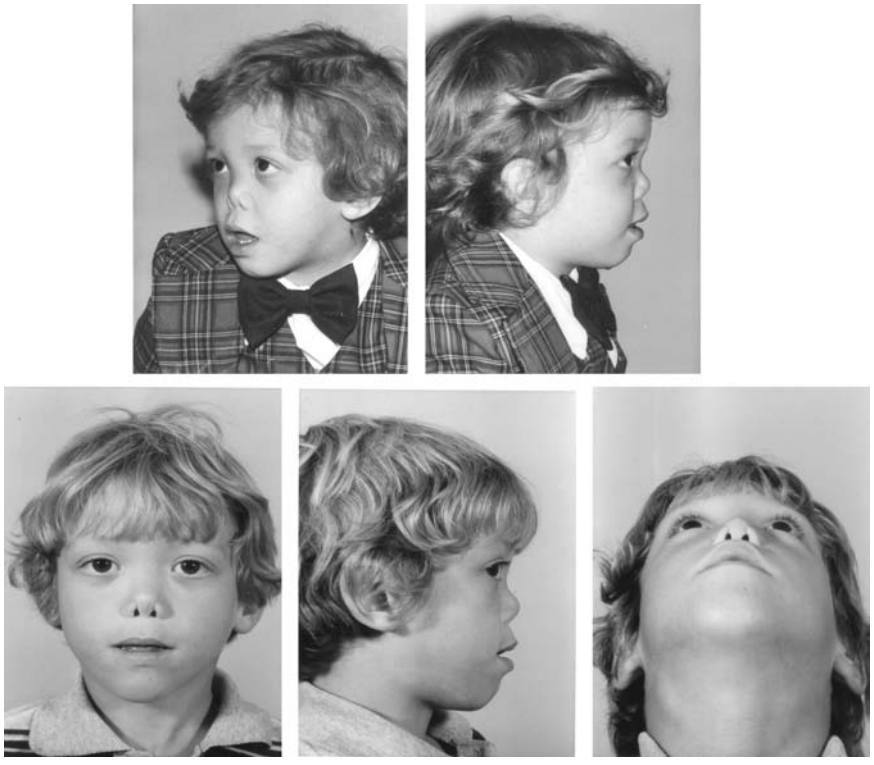


Fig. 18.13 Patient with warfarin-induced nasal hypoplasia. *Above, left* and *right*: Anterior oblique and lateral views of the patient at two years of age, with a foreshortened nose and poor dorsal projection. *Below, left, center*, and *right*: Anterior oblique, lateral, and submental views of the patient at seven years of age, with minimal growth of the nose and a prominent groove between the nasal tip and the ala.

nose, autograft bone or cartilage should be used. However, costal cartilage grafts do not consolidate with the underlying host bone and may occasionally be displaced by traction forces. Also, costocartilage grafts in children are known to warp or twist. We prefer calvarial bone grafting to iliac bone grafting for nasal lengthening because of the hidden donor site, decreased postoperative pain, and ease of harvesting and shaping the grafts (Fig. 18.17). Finally, a staged surgical correction with calvarial grafts is required, since nasal bone grafts fail to keep pace with facial development.

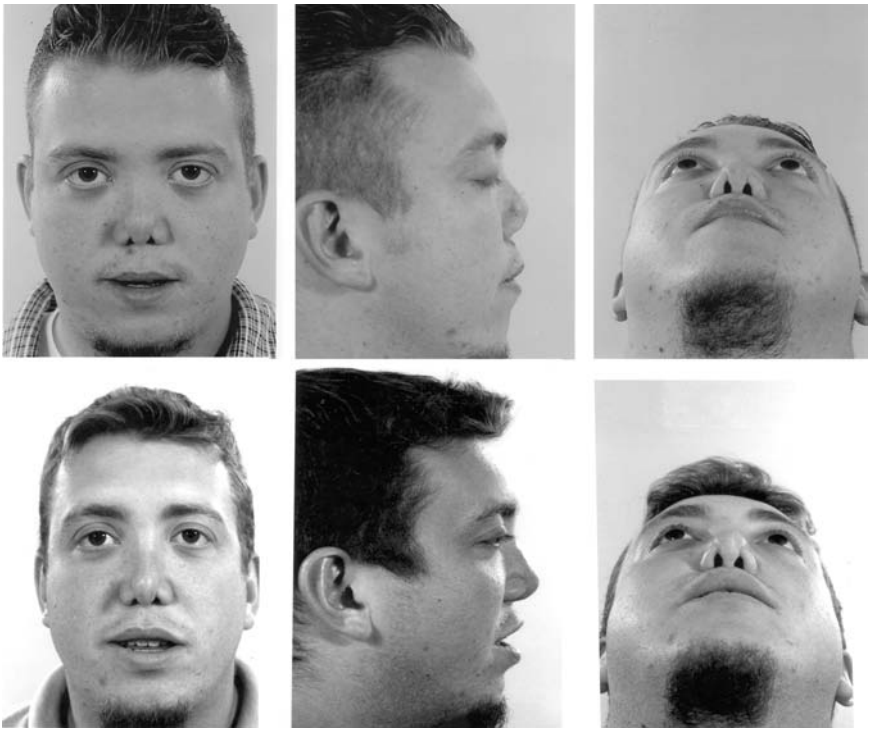


Fig. 18.14 *Above, left, center*, and *right*: Anterior oblique, lateral, and submental views of the same patient in Fig. 18.13 at 23 years of age, after a cranial bone graft at 7 years of age. Growth of the bone graft has not kept pace with facial growth, and recurrence of a foreshortened nose can be observed. *Below, left, center* and *right*: Anterior oblique, lateral, and submental views of the patient at 24 years of age, after cranial bone graft reconstruction. The nose has been lengthened to 5 cm from the radix to the nasal tip.

ALVEOLAR CLEFT

Maxillary hypoplasia in cleft-lip-and-palate patients, as discussed above, is thought to be caused by either surgical scarring from early subperiosteal dissection or an intrinsic growth abnormality, or both. Constriction of the maxilla in the transverse dimension also occurs in these cleft patients. Expansion of the maxilla into a more normal arch form may be accomplished with presurgical nasoalveolar molding in infancy or orthodontic expansion during childhood, typically at 6–8 years of age. However, in

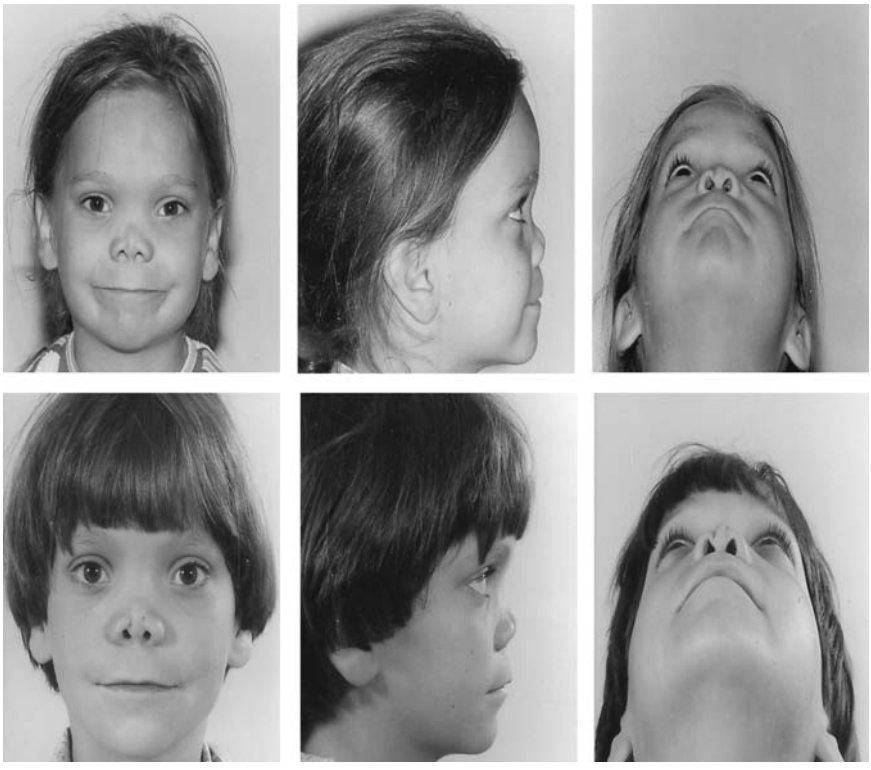


Fig. 18.15 Another patient with warfarin-induced nasal agenesis. *Above, left, center*, and *right*: Anterior, lateral, and submental views of the patient at two years of age, with an upturned nasal tip and a flat nasal dorsum. *Below, left, center*, and *right*: Anterior, lateral, and submental views of the patient at six years of age, exhibiting minimal growth of her foreshortened nose.

older cleft patients with a constricted maxilla, expansion may be more difficult. For this subset of older patients with an alveolar cleft, we conducted a study using a boneborne palatal expansion device.[17]

Boneborne Rapid Expansion

Transverse maxillary hypoplasia is a clinical entity characterized by diminished growth of the maxilla in the transverse dimension, leading to anterior and posterior crowding of the maxillary dentition. This constriction of the

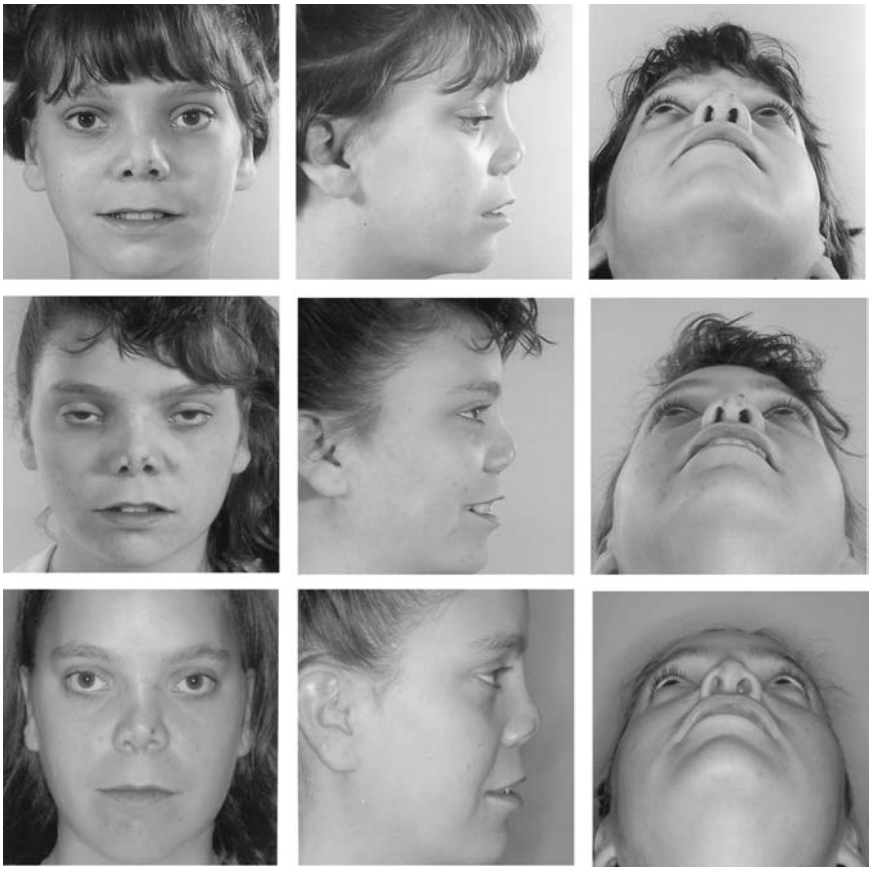


Fig. 18.16 *Above, left, center*, and *right*: Anterior, lateral, and submental views of the same patient in Fig. 18.15 at 11 years of age, after a cranial bone graft to lengthen the nose and provide dorsal protection. *Middle, left, center*, and *right*: Anterior, lateral, and submental views of the patient at 16 years of age, 5 years of bone graft placement and the completion of facial growth. The nasal tip is rotated upward, and the projection of the dorsum is not adequate. *Below, left, center*, and *right*: The patient at 17 years of age, after a final cranial bone graft to optimize the nasal tip position and dorsal projection.

maxillary arch occurs spontaneously or can be associated with cleft-lip-and-palate congenital deformities. Clinical manifestations — unilateral or bilateral palatal crossbite, dental rotation or tilting, and malocclusion — cause significant morbidity. Depending on the specific etiology, the signs and symptoms of transverse maxillary hypoplasia may be progressive.

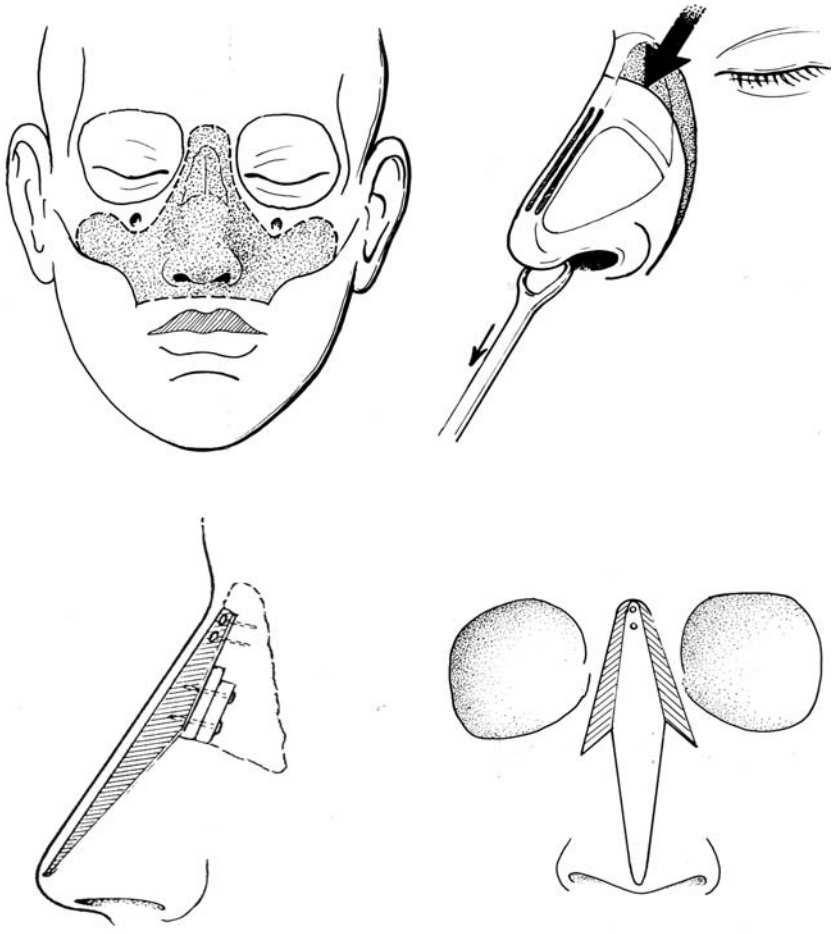


Fig. 18.17 Diagrammatic illustrations of the operative technique for nasal reconstruction of warfarin-induced nasal hypoplasia. *Above, left*: Facial soft tissue elevation. Subperiosteal elevation of the outlined areas is performed through intranasal and intraoral access. *Above, right*: Dissection of the nasal lining. From intercartilaginous incisions, elevation of the upper lateral cartilage attachments and submucous dissection of the septum is performed. Releasing incisions along the nasal bones and nasal sidewalls allow advancement of the nasal lining. *Below, left* and *right*: Stabilization of layered strips of calvarial bone grafts. After shaping of the superficial graft, the middle and lower layers of the fulcrum are secured with miniscrews (0.8 mm). Next, the layered graft is placed within the nasal pocket, with the skin covering at maximal stretch. Fixation is performed just below the radix, to the superior nasal bones. Sidewall grafts are applied as unfixed onlay grafts.

The corrective goal of expanding the dimensions of the palate allows for normal position and function of the dentition, improvement in occlusion and speech, and optimization of esthetic appearance. In patients with clefting of the primary palate, the cleft defect must be expanded to allow for successful bone grafting and accommodation of erupting maxillary teeth.

Orthodontic expansion in the growing patient is generally successful and is often used as a first step to allow space for erupting teeth. However, there remains some controversy regarding how to manage patients who present later in life with severe uncorrected deformities. Even more problematic is the question of how to treat patients who have failed palatal expansion and who have persistent functional and cosmetic deficiencies. This failure of orthodontic expansion may manifest as buccal tipping of molars with no true skeletal expansion. At times, although posterior expansion is successful, transverse expansion of the anterior palate (near the alveolar cleft) is inadequate.

A solution to this problem is rapid palatal expansion (RPE) with a toothborne device. The advantages of this approach include increase in the intercanine, interpremolar, and intermolar distances, lengthening of the alveolar arch perimeter, subsequent amelioration of dental crowding with facilitation of additional orthodontic manipulation, improvement of periodontal health, enhanced nasal air flow, softening of the buccal grooves when the patient is smiling, and improvement of buccal hollowing from lateral repositioning of the lateral maxillary wall.[18] However, the toothborne palatal expander has limitations in this subset of scarred, constricted cleft palate patients. A boneborne palatal distraction device offers an alternative treatment for the two difficult problems of (1) skeletally mature patients with constricted maxillas and (2) patients with collapse of the anterior palate despite previous expansion.

In this study, we describe a series of cleft patients who presented to our craniofacial clinic in adolescence with persistent deformities despite prior attempts at orthodontic expansion, and we document our experience with boneborne RPE after a Le Fort I corticotomy. In addition, we discuss our use of boneborne RPE without surgical corticotomy in several noncleft patients presenting with primary maxillary hypoplasia in early adulthood after failure of prior orthodontic expansion.

We conducted a retrospective study using a cohort of patients with previously repaired unilateral or bilateral cleft-lip-and-palate deformities

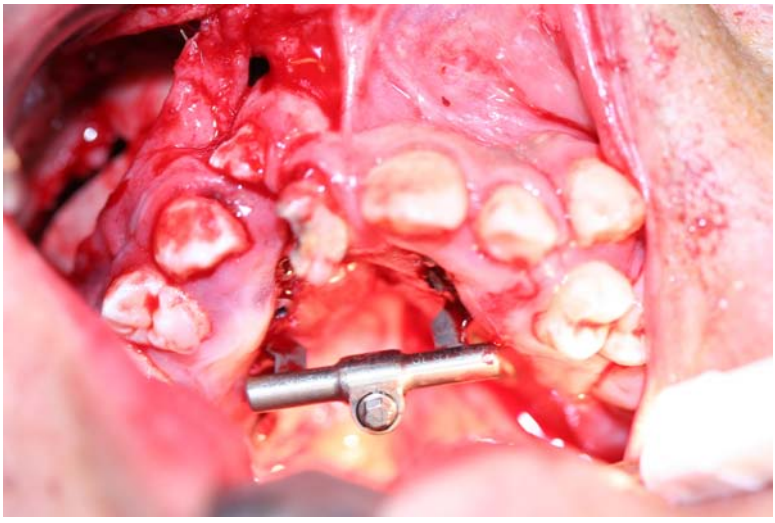


Fig. 18.18 Intraoperative image of a boneborne palatal distraction device placed after corticotomy of the right lesser maxillary segment for a constricted maxilla in a unilateral cleft-lip-and-palate patient.

and who had failed previous orthodontic expansion. Alveolar cleft patients underwent Le Fort I corticotomy with placement of the boneborne distraction device, expansion at a rate of 0.5 mm/day, and, finally, alveolar bone grafting (Fig. 18.18). Preoperative and follow-up maxillary impressions were compared to assess improvements in intermolar distance, intercanine distance, alveolar cleft width, and total palatal area (Fig. 18.19).

Seven patients had bilateral and eight had unilateral cleft deformities. Subsequent to palatal distraction, all patients underwent successful bone grafting of the expanded cleft space. The average follow-up period was 19 months (range 8–30 months). The mean amount of distraction in all patients was 14.1 mm (Table 18.4). The average increase in intermolar distance was 8.4 mm and intercanine distance increased by an average of 9.5 mm. Palate surface areas were increased by a mean of 28.9 mm.[2] There were two minor complications.

Rapid palatal expansion using a boneborne distraction device is a safe and effective approach to treating the challenging patient population comprising older children with transverse maxillary hypoplasia who have

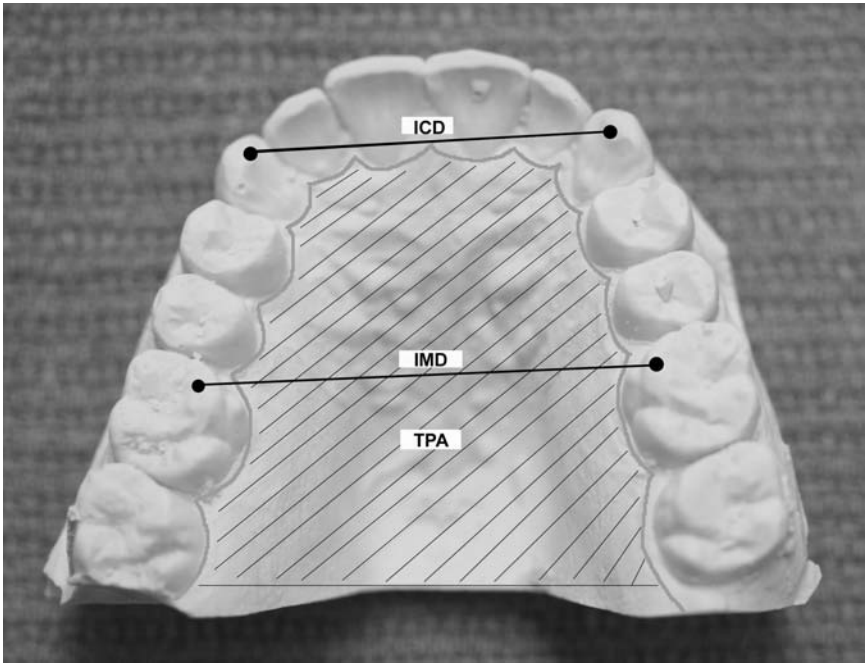


Fig. 18.19 Dental impression model of a maxilla showing standardized measurements for intercanine distance (ICD), intermolar distance (IMD), and total palatal area (TPA).

Table 18.4 Aggregate Data for Patients Without Cleft Deformities Undergoing Expander Placement Only (*n* = 4). Distance and Areas Represent Follow-up Data on All Patients

Noncleft Patient	Age (Yrs)	Diagnosis	Indication	Distraction (mm)	Distance/Area Gained (mm)			TPA (mm^2)	Outcome
					IMD	ICD	Cleft		
1	26	AOP	FOE	10	4	5	4	19	LF1A
2	20	AOP	FOE	13	5	5	5	21	OT
3	19	AOP	FOE	10	5	5	4	20	OT
4	18	AOP	FOE	10	5	5	5	21	OT
			Average	*10.8*	*4.8*	*5.0*	*4.5*	*20.3*	

AOP = adult orthodontic patient; FOE = failed orthodontic expansion; LF1A = Le Fort 1 advancement; OT = orthodontic treatment resumed.

failed nonsurgical orthodontic expansion. The device used allows for distraction through scarred palatal mucosa and precise control of the location of expansion. The procedure provides stable results with minimal complications and facilitates a return to further orthodontic care.

Bone Morphogenetic Protein

Patients with maxillary clefts undergo alveolar bone grafting (ABG) between the ages of 6 and 12 to stabilize the maxilla, close oronasal fistulas, and provide structure for soft tissues. ABG in older patients may be associated with poor wound healing, graft exposure, recurrent fistula, and failure of tooth eruption.[19] We conducted a study in which a new procedure using BMP-2 was compared to traditional iliac grafting to close alveolar defects in older patients.[20] Iliac bone grafting, the gold standard, is known to have donor site morbidity. Our comparison between the new procedure and the traditional procedure consisted of both bone healing and donor site morbidity.

Traditional iliac grafting was compared to a new technique involving stem cells, a resorbable matrix, and BMP-2 (iliac crest aspirate seeded onto a collagen sponge and IN-fuse) (Figs. 18.20, 18.21). Skeletally mature patients with an alveolar cleft defect undergoing alveolar cleft repair were divided into two groups: Group 1 — BMP-2 (experimental) (n = 9); Group 2 — traditional iliac grafting (control) (n = 12). Outcomes for bone healing were analyzed with intraoral examination and NewTom scans (3D, panorex, periapical films). Donor site morbidity was assessed with pain

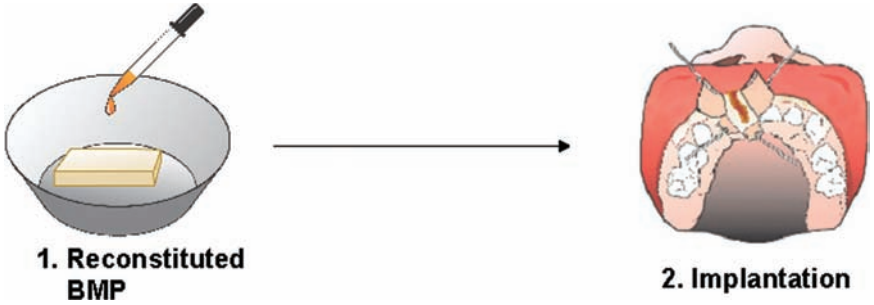


Fig. 18.20 BMP-2 (experimental) procedure. The illustration depicts preparation of the rh-BMP-2 soaked collagen sponge and alveolar cleft defect after surgical exposure.

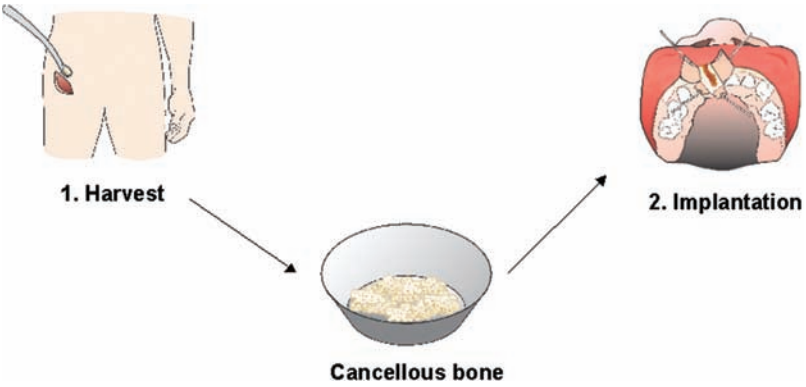


Fig. 18.21 Traditional iliac graft (control) procedure. The illustration shows the iliac crest donor site for cancellous bone and alveolar cleft defect after surgical exposure.

surveys. Overall cost and length of hospital stay were used to examine economic differences.

Results from the intraoral examinations showed that in the preoperative, postoperative (6 weeks), and follow-up (1 year) periods, more complications occurred in Group 2 (traditional iliac grafting) than in Group 1 (BMP-2). Five out of 12 patients in Group 2 experienced partial loss of the bone graft and 1 out of 12 suffered near-complete loss of the bone graft secondary to wound breakdown and problematic healing. Three out of 12 developed an oronasal fistula by 6 weeks postoperatively. By comparison, in Group 1, only 1 of 9 patients experienced prolonged wound healing and granulation, no patients had partial or total loss of the graft, and none developed an oronasal fistula by 6 weeks postoperatively. No patients in either group had signs of ectopic bone formation.

Results from the bone healing analysis showed that Group 1 had higher grades with regard to estimated graft take than Group 2 (2.8 ± 0.2 vs. 1.9 ± 0.4; $p < 0.05$), but the two groups had similar results with regard to alar base support (Table 18.5). Panorex and 3D CT scan readings showed enhanced mineralization in Group 1 (2.9 ± 0.3) compared to Group 2 (2.0 ± 0.4; $p < 0.05$) (Figs. 18.22, 18.23). Volumetric analysis showed that Group 1 had a larger percent alveolar defect filled with new bone (95%) compared to Group 2 (63%) ($p < 0.01$) (Figs. 18.24–18.26).

Table 18.5 Bone Healing Assessment

	Intraoral Examination				
	Alveolar	Alar	Panorex	3D CT Scan	Periapical Film
Group 1: BMP-2	2.8 ± 0.2*	2.2 ± 0.2	2.9 ± 0.3*	2.9 ± 0.3*	3.4 ± 0.3*
Group 2: Iliac bone graft	1.9 ± 0.4	2.0 ± 0.3	2.0 ± 0.8	2.0 ± 0.8	2.8 ± 0.4

For alveolar ridge healing, examiners used a four-point grading system, from 0 to 3 (0 = complete loss of graft to 25% take; 1 = 25–50% graft take; 2 = 50–75% graft take; and 3 = 75–100% graft take). For alar base augmentation, examiners again graded patients from 0 to 3 (0 = minimum or no change from preoperative alar base position; 1 = 25–50% improvement; 2 = 50–75% improvement; and 3 = 75–100% improvement). For the panorex and 3D CT scan, four-point grading from 0 to 3 was used (0 = minimum or no bone mineralization within the alveolar defect; 1 = 25–50% bone mineralization within the defect; 2 = 50–75% bone mineralization within the defect; and 3 = 75–100% bone mineralization within the defect). For the periapical films, bony bridging between the cleft tooth roots was graded from 0 to 4. $^*p < 0.05$.

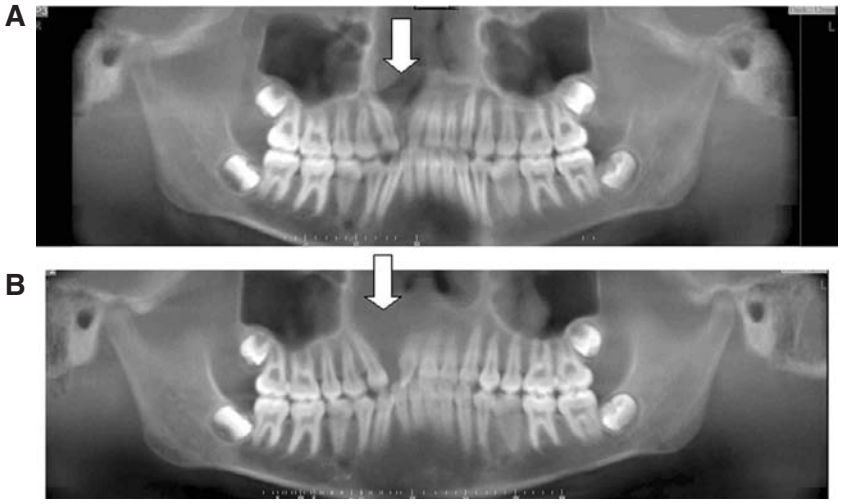


Fig. 18.22 Panorex of a Group 1 (BMP-2) patient. (**A**) A preoperative alveolar cleft defect is seen (⇓). (**B**) A six-month follow-up depicts bone mineralization within the previous alveolar defect site.

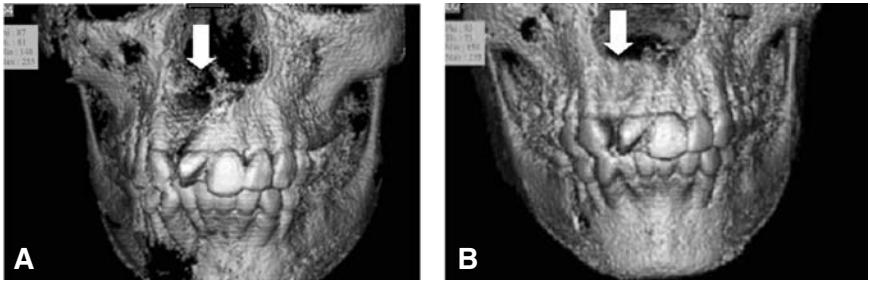


Fig. 18.23 3D reconstruction of a NewTom scan for a Group 1 (BMP-2) patient. (**A**) Preoperative view of an alveolar defect (⇓). (**B**) A six-month follow-up shows subsequent bone repair of the alveolar defect.

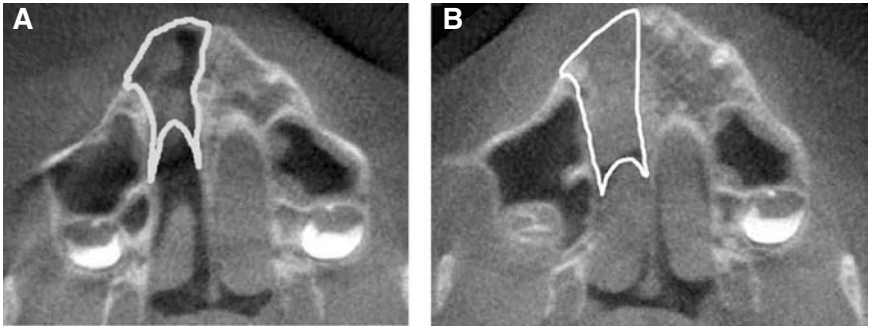


Fig. 18.24 Axial scans of a Group 1 (BMP-2) patient. (**A**) The preoperative alveolar defect is outlined using the NIH ImageJ program. Serial outlined defects were used to obtain the alveolar defect volume. (**B**) Six-month follow-up, with the dotted line showing the healed region of the alveolar defect. Areas of the persistent defect were outlined in other axial cuts and used to calculate the persistent alveolar defect volume.

Morbidity comparisons showed that 100% of patients (12/12) in Group 2 experienced pain on Day 1 postoperatively and the mean pain score was 14/20 (Fig. 18.27). Even at 6 months, 3 of 12 patients in Group 2 still complained of some donor site pain. No patients in Group 1 reported pain on postoperative Day 1 and the mean pain score was 0 at all evaluations. In Group 1, 7/9 patients underwent the procedure as an outpatient. All of the Group 2 patients had their procedures performed as an inpatient (Table 18.6). The mean length of stay was greater for Group 2 patients at 1.8 ± 0.8 days than for Group 1 patients at 0.4 ± 0.4. In addition, the mean

	Group 1: BMP-2 (experimental)	Group 2: Traditional iliac graft (control)
Preoperative	5.6cc ± .3	5.1cc ± .4
Postoperative	.3cc ± .02	1.9cc ± .2

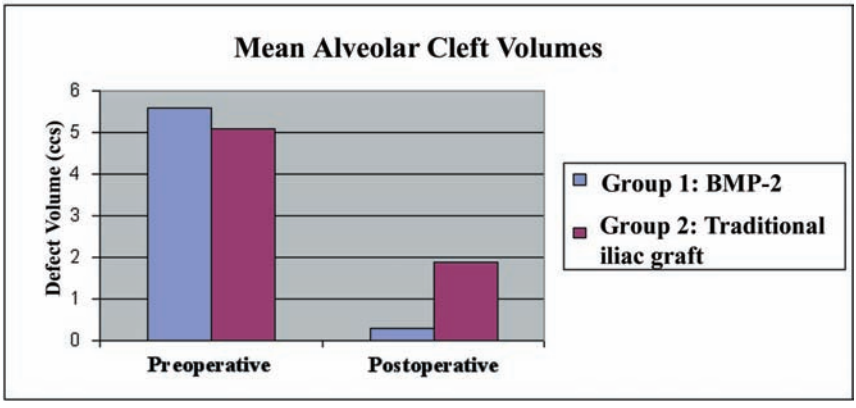


Fig. 18.25 Table and graph of the mean alveolar cleft volumes. Although preoperative alveolar cleft volumes were similar between groups, Group 1 (BMP-2) had a smaller residual volume defect, 0.3 cc, than Group 2 (traditional iliac graft), with a 1.9 cc residual volume defect.

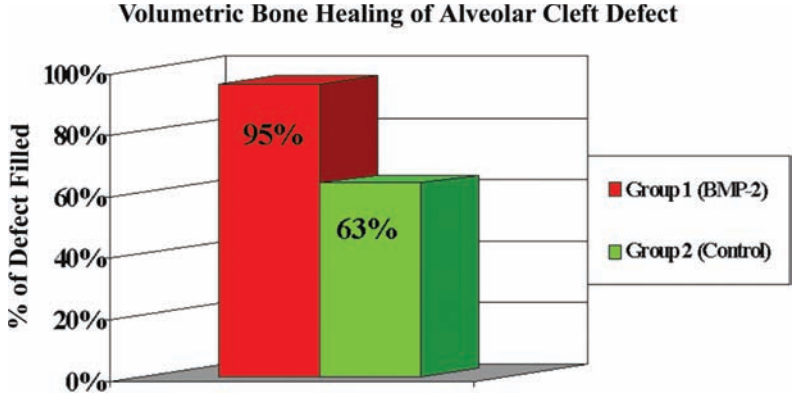


Fig. 18.26 Graph representing volumetric bone healing of the alveolar cleft defect in older patients studied. Group 1 (BMP-2) had 95% new bone fill, compared to 65% in Group 2 (traditional iliac crest graft) ($p < 0.05$).

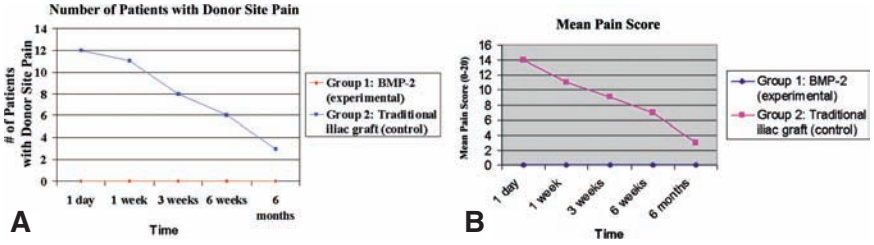


Fig. 18.27 Donor site pain. (A) Number of patients with donor site pain. Note: One-half of the patients with the traditional procedure still had some donor site pain at six weeks, and some even at six months. Of course, the BMP-2 patients had no donor site pain. (B) Mean pain score (0–20) = duration and intensity of pain.

Table 18.6 Length of Stay and Cost of Surgery

	Outpatient Status	Length of Stay (Days)	Cost
Group 1: BMP-2	78% (7/9)	0.4 ± 0.4	US$11,100
Group 2: Iliac bone graft	0% (0/12)	1.8 ± 0.8	US$21,800

Outpatient status — percentage of patients discharged on the same day as surgery; length of stay — mean length of days; cost — mean cost based on surgeon, facility, and anesthesia fees.

overall cost of the procedure — including surgeon, facility, equipment, and anesthesia fees — was greater for Group 2 at US$21,800 than for Group 1 at US$11,100 (this total cost included the cost of the BMP-2 and matrix).

From our data we concluded that for this select group of late-presenting alveolar cleft patients the BMP-2 procedure results in improved bone healing and reduced morbidity compared to traditional iliac grafting. Also, the procedure is significantly more cost-effective. A larger controlled series is necessary for investigating this procedure further.

CLEFT PALATE

Cleft palate and cleft lip are the most common congenital craniofacial defects. Isolated cleft palate occurs once every 1,000 births and is distinct from cleft lip with or without cleft palate, which has a higher incidence

(1:700).[21] Cleft palate is commonly associated with other syndromes of craniofacial maldevelopment and, in fact, cleft palate associated with a syndrome accounts for 55% of cases.[22] The etiology of these midfacial malformations is multifactorial and may involve molecular defects, genetic causes, environmental exposure to drugs and teratogens, and other, *in utero* insults. Any disturbance in the complex events of palatogenesis can cause inadequate fusion of the palatal shelves resulting in cleft palate.

Fibroblast Growth Factor

Fibroblast growth factors (FGFs) are a family of cytokines that are involved in vertebrate development and differentiation. More specifically, FGF-2 has been implicated in the control of skeletal and neural differentiation, angiogenesis, wound healing, and tissue repair.[23] *In vitro* studies show that FGF-2 is stored in extracellular matrix and stimulates osteoblastic proliferation. Several syndromic conditions that may involve cleft palate, such as Apert's syndrome and skeletal dysplasias, are correlated with defects in the FGF-R receptors.[24]

Further strengthening the association between FGFs and cleft palate formation, FGF-R1 and -R2 are expressed specifically in the epithelium of the developing palatal shelves from the time of the outgrowth from the maxillary process through completion of fusion.[25] In addition, FGF-1 and -2 have been found to influence collagen synthesis and extracellular matrix proteins at the time of palatal fusion.[26] Finally, a mouse model (CreloxP) with FGF-R2-IIIb knockout was developed that results in the cleft palate phenotype.[27]

Our laboratory performed a study with the following three purposes: (1) to establish whether FGF signaling is essential for normal palate development, (2) to improve the understanding of the biology of palatal fusion, and (3) to create a new, *in vitro* cleft palate model.[28] For our study an established mouse organ culture system was used. A replication-deficient recombinant adenovirus encoding a truncated chicken FGF-R1 gene was used to transfect palatal cells and produce a dominant negative knockout, thus terminating signal transduction by FGF-R1, -R2, and -R3. Tissue sectioning and staining was used to assess palatal continuity, and immunohistochemistry was used to localize expression of the truncated receptors.

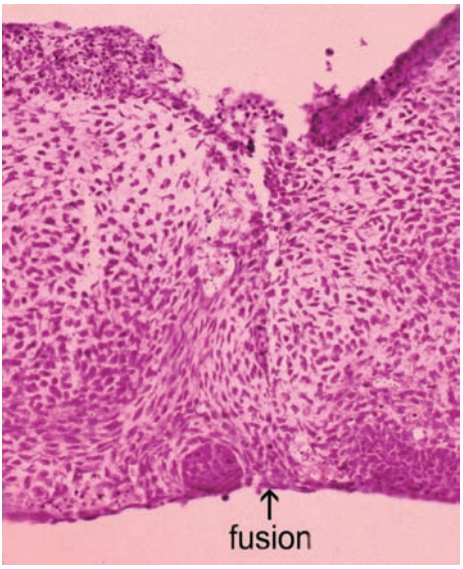


Fig. 18.28 Group 1, control vehicle: H&E. Normal fusion of palatal shelves with resolution of medial edge epithelium (↑), mesenchymal continuity, and formation of epithelial lining on both the oral and nasal sides.

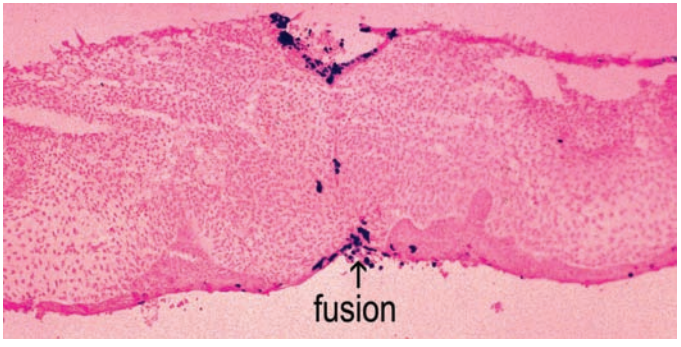
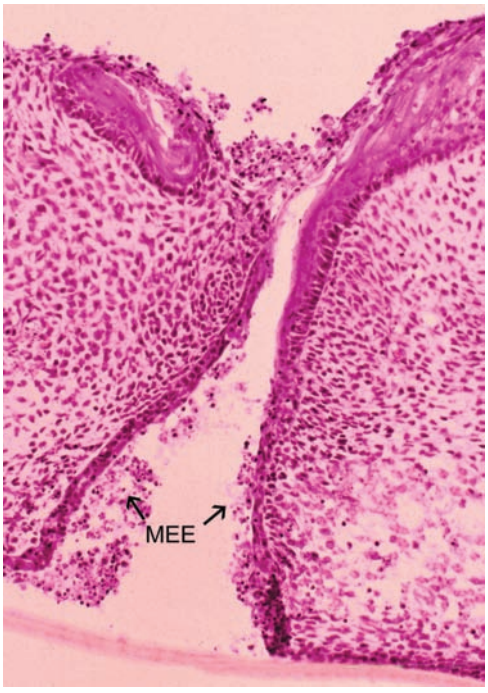
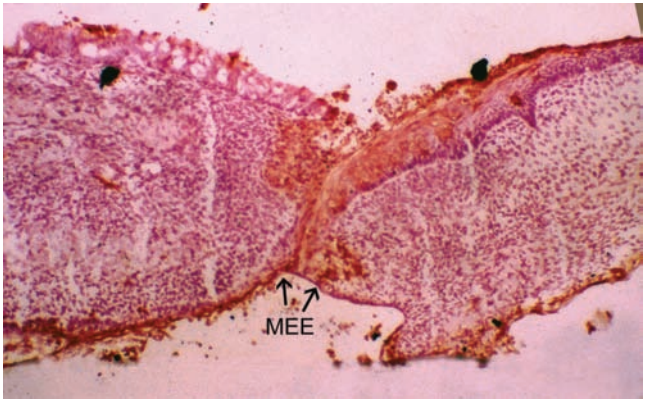


Fig. 18.29 Group 2, LacZ: β-galactosidase staining. Viral infection within the epithelial cells is seen specifically in the area of fusion (↑).

Palatal pairs excised from embryonic day 13.5 mouse palatal shelves were divided into three groups of six ($n = 18$) and cultured on Millipore filters (Corning, New York) with the nasal side down and their medial edge epithelia in close apposition. Control groups received the vehicle only or



(A)



(B)

Fig. 18.30 Group 3, experimental FGF-R1. (**A**) H&E: no signs of fusion, including no resolution of the medial epithelial cells, are seen. (**B**) Immunohistochemistry for the HA epitope tag: red stain indicates infection by the AdCAFGF-TR virus throughout the epithelium and mesenchyme of the palatal shelf.

LacZ recombinant virus (1×10^9 PFU). The experimental group received truncated FGF-R1 recombinant virus with hemagglutinin epitope tag (1×10^9 PFU), producing a dominant negative knockout. Tissue sectioning and staining was used to assess palatal continuity at 96 h and immunohistochemistry was used to localize expression of the truncated receptors.

Both the negative controls (6/6), which received the viral vehicle alone, and the LacZ controls (6/6) showed histological resolution of the medial edge epithelia by 96 h (Figs. 18.28, 18.29). β-galactosidase staining indicated infection of nearly all the cells in the palatal shelves of the LacZ controls, indicating effective delivery of the virus to target cells. None of the specimens (0/6) in the experimental group (truncated FGF-R1) showed histological resolution of the medial edge epithelia seam (Fig. 18.30a). Immunohistochemistry for the hemagglutinin epitope tag indicated infection by the truncated FGF-R1 virus throughout the epithelium and mesenchyme of the epithelium (Fig. 18.30b).

Through terminating signal transduction by FGF-R1, -R2, and -R3, we demonstrated that such signaling is essential for normal mammalian palate development. Biomechanical forces may too play a role but the epithelial–mesenchymal interactions and their signaling pathways are in and of themselves sufficient for cleft formation. This organ system mirrors *in vivo* palate development and avoids the epiphenomenon of transgenics. It provides a clean system to begin investigating interactions of FGFs with other implicated signaling pathways. Future studies will be directed at sequencing the steps involved in cleft formation via blocking analysis.

Delayed Cleft Palate Repair

Ten to 40% of cleft-lip-and-palate patients who undergo appropriate surgical repair, with respect to timing and technique, develop maxillary hypoplasia requiring orthognathic correction.[29] Observations of skeletally mature *unoperated-on* patients with cleft palate have noted normal maxillary growth.[30] The Schweckendiek procedure offers delayed hard palate closure to avoid early subperiosteal dissection and to reduce palatal scarring.[31]

Reports of good results from the Schweckendiek method led the University of Pittsburgh Cleft Palate Craniofacial Center (CPCC) to develop a protocol of delayed hard palate closure with a speech appliance.[31] This protocol

involved closure of the soft palate at one year of age and the use of a pinned–retained speech prosthesis until closure of the hard palate at approximately seven years of age. By contrast, there have also been reports critical to delayed hard palate repair suggesting negative speech outcomes.[32] Variations in the timing of hard palate repair, the method of obturation, the technique of surgery, and speech analysis have led to difficulty in comparison of data.[33]

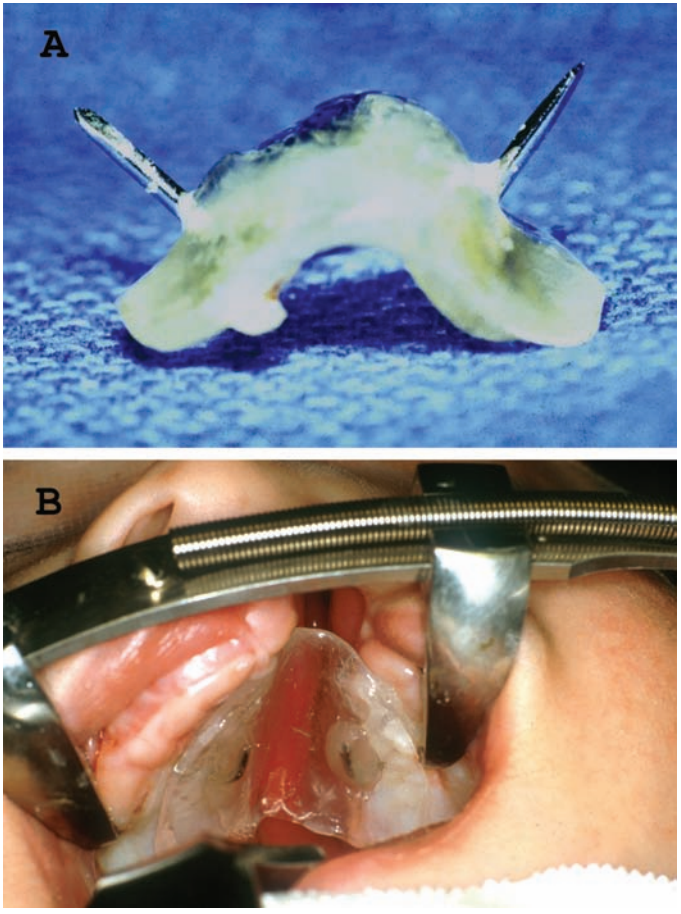


Fig. 18.31 Pinned–retained speech prothesis. (A) An infant impression is used to make this acrylic obturator. Pins are for permanent placement into the hard palate. (B) Intraoral operative view of the pinned–retained speech prothesis. Soft palate repair was done at one year of age, prior to hard palate closure at seven years of age.

We conducted a study in which the efficacy of the delayed hard palate closure technique was compared to that of the single-staged repair (with immediate hard palate closure at one year of age) by speech assessments using the Pittsburgh Speech Score and by analysis of maxillary growth using cephalometric measurements.[6] A retrospective outcome study on unilateral cleft-lip-and-palate patients with either delayed hard palate repair with a pinned–retained speech prosthesis (Schweckendiek repair) [Group 1 (delayed hard palate repair); 1978–1983] or single-staged cleft palate repair [Group 2 (single-staged repair); 1983–1988] was performed (Figs. 18.31–18.33). Patients with complete records to maturity at the CPCC ($n = 82$; 2 equal groups of 41 patients) were studied. Comparative

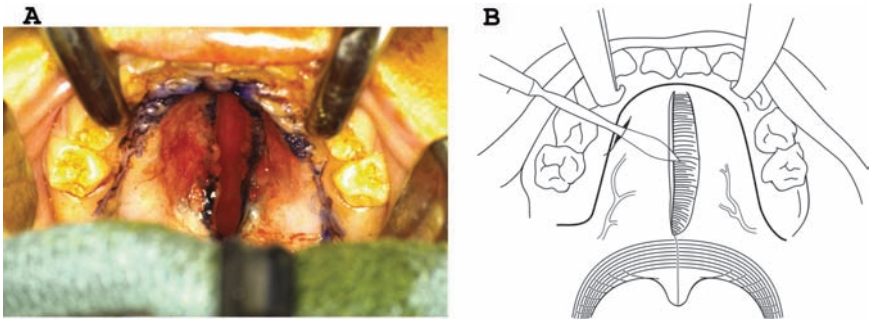


Fig. 18.32 Intraoral operative view of hard palate closure markings. (A) Modified Von Langenbeck repair is planned with markings for unipedicled mucoperiosteal flaps. (B) Illustration of hard palate closure markings and healed soft palate repair.

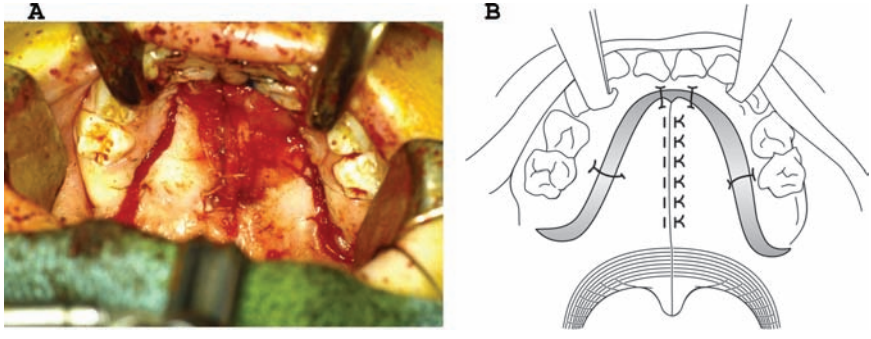


Fig. 18.33 Intraoral operative view of closure. (A) Midline closure with lateral release. (B) Illustration of completed hard palate closure.

Table 18.7 Comparison of Average, Weighted Values for Speech Symptoms: Single-staged Repair versus Delayed Hard Palate Repair

	Group 1 (Delayed Hard Palate Repair) ($n = 41$)			Group 2 (Single-staged Repair) ($n = 41$)		
	Pre-op	Follow-up	Final (Maturity)	Pre-op	Follow-up	Final (Maturity)
Nasal emissions	2.8	2.1*	0.8†	2.9	0.8*	0.2†
Grimace	1.6	1.1*	0.4†	1.5	0.5*	0.2†
Nasality	3.2	1.8*	0.9†	3.4	1.0*	0.1†
Phonation	2.2	1.1*	0.6†	2.1	0.5*	0.1†
Articulation	3.1	1.8*	1.0†	3.2	1.0*	0.2†
Total speech scores	*12.9*	*7.9**	*3.7†*	*13.1*	*3.8**	*0.8†*

* = $p < 0.05$ between groups.

† = $p < 0.05$ between groups.

Numbers represent average values of all patients within a group ($n = 41$).

Table 18.8 Comparison of Speech Outcomes: Single-staged Repair versus Delayed Hard Palate Repair

	Group 1 (Delayed Hard Palate Repair) ($n = 41$)	Group 2 (Single-staged Repair) ($n = 41$)	*p* Value
Velopharyngeal insufficiency (VPI)*	66% (27/41)	20% (8/41)	<0.05
Failed nasoendoscopy or video fluoroscopy†	52% (11/21)	17% (2/9)	>0.05
Secondary procedures for speech‡	63% (26/41)	20% (8/41)	<0.05

*VPI = speech score >3 without fistula after palate closure.

†VP dysfunction based on assessment of nasoendoscopy or video fluoroscopy.

(Note: Not all patients had studies done.)

‡Patients requiring at least one secondary procedure after palate closure.

data were collected from multidisciplinary evaluations, perceptual speech scores, speech tests, and cephalometric analysis.

Single-staged cleft palate repair had a lower fistulization rate (11%) than delayed hard palate repair (58%). Single-staged repair had better

Table 18.9 Comparison of Maxillary Growth with Regard to Occlusion, Cephalometric SNA, Need for Le Fort I, and Amount of Advancement Required: Single-staged Repair versus Delayed Hard Palate Repair

	Group 1 (Delayed Hard Palate Repair) ($n = 41$)	Group 2 (Single-staged Repair) ($n = 41$)	*p* Value
Class III malocclusion*	66%	31%	<0.05
Cephalometric SNA† (± standard deviation)	74.8° ± 2.8	78.2° ± 2.5	<0.05
Le Fort I advancement‡	42%	24%	<0.05
Advancement required§ (mm) (± standard deviation)	9.0 ± 2.8	6.0 ± 1.8	>0.05

*Percentage of patients within group with Class III malocclusion at maturity.

† SNA = sella–nasion–A point (recorded from presurgical lateral cephalograms).

speech outcomes than delayed hard palate repair: mean speech score (3.1 vs. 7.8), final speech score (0.9 vs. 2.9), velopharyngeal incompetency (21% vs. 66%), failed videofluoroscopy or nasoendoscopy (18% vs. 52%), and need for secondary speech procedure (20% vs. 63%) (Tables 18.7, 18.8). Single-staged repair showed less maxillary growth disturbance, including: class III malocclusion (31% vs. 66%), cephalometric SNA (78.2 vs. 74.8), need for Le Fort I advancement (24% vs. 42%), and amount of maxillary advancement required (6 mm vs. 9 mm) (Table 18.9).

The delayed cleft palate repair led to worse speech outcomes (more oronasal fistulization, more VPI, and a greater need for secondary surgeries for speech); thus, our center abandoned this technique in favor of single-staged repair. In addition, our data showed that the delayed cleft palate repair led to deleterious maxillary growth.

SUMMARY

Midface surgical techniques have evolved to address syndromic midface hypoplasia, as well as the more common cleft palate maxillary growth disturbances. With the use of distraction osteogenesis and bone tissue engineering techniques, improved outcomes with decreased morbidity are

becoming possible. Sarnat's midface growth studies have allowed surgeons to optimize the timing and techniques for their midface procedures.

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PART III

THE ORBIT AND EYE

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Osteology of the Orbit*

The orbits of the rabbit separate the cranial from the facial portions of the skull (Davis 1929, Craigie 1960, Prince 1964). They are situated laterally, with the plane of the external opening at an angle of 80° to the transverse plane of the head. The vertical diameter of the orbital rim makes an angle of about 30° with the sagittal plane of the head.

The orbit is incomplete and is formed by the frontal, lacrimal, maxillary, palatine, pterygoid, sphenoid, temporal and zygomatic bones (Figs. 19.1, 19.2). A small portion of the ethmoid bone may reach the medial orbital wall. The orbit can be divided into six walls. Four walls are bony — inner, superior, anterior, and posterior. Two walls are not bony; the inferior one is muscular and the external side is the orbital orifice or entrance.

Inner wall. The inner wall, which is concave and saucer-shaped, is formed by the inferior portion of the orbital process of the frontal bone, the wing of the sphenoid, and the maxilla below. The inner walls of the orbits fuse to form a single bony partition — the interorbital septum. It is perforated by the optic foramen, which joins its fellow foramen into a single canal.

Inferior wall. The inferior wall is largely made up of the muscles of mastication. In the anterior portion there is a bony projection of the maxilla

*Excerpted from: Sarnat BG. (1981) The orbit and eye: experiments on volume in young and adult rabbits. *Acta Ophthalmol*, *Suppl* **147**: 1–44.

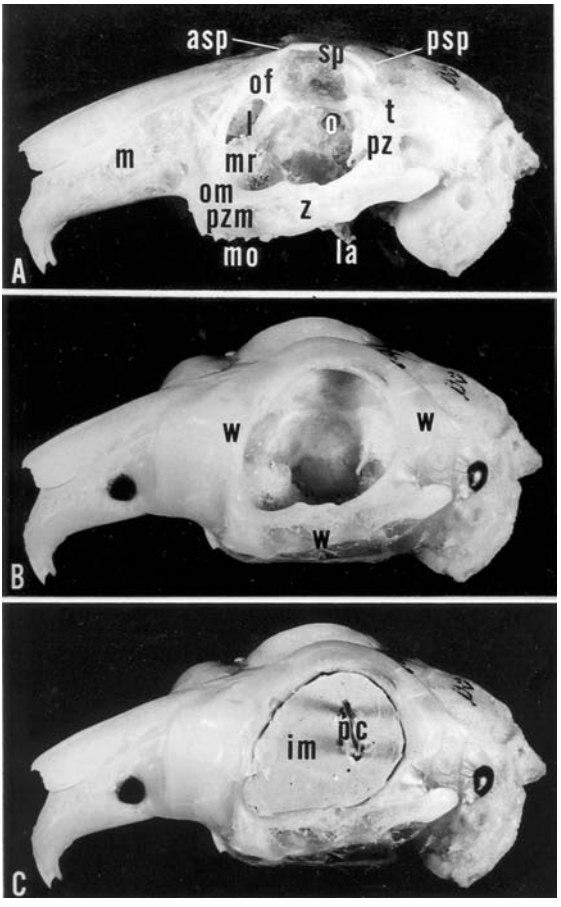

Fig. 19.1 Lateral view photographs of a 180-day-old rabbit skull. (**A**) Prepared skull; asp and psp — anterior and posterior supraorbital processes of the frontal bone; 1 — lacrimal bone; la — lateral lamina of the pterygoid bone; m — maxilla; mo — premolars and molars; mr — molar root region; o — optic foramen; of — orbital process of the frontal bone; om — orbital process of the maxilla; pz — zygomatic process of the squamosal; pzm — zygomatic process of the maxilla; sp — supraorbital process of the frontal bone; t — temporal fossa; z — zygomatic arch. (**B**) Openings of the orbital rim and walls sealed with wax and the periorbital region reinforced with wax, preparatory to the making of the orbital imprint; w — waxed areas. (**C**) Elastic rubber base orbital imprint (im) in place. The paper clip (pc) facilitates removal of the imprint (im). Note the slight separation along the posterior and superior margins between wax and imprint which was prepared more than three years previously. [From: Prechter TK, Sarnat BG. (1973) Comparison of direct and indirect determinations of rabbit orbital volume. *Acta Morphol Neerl Scand* **11**: 151–160.]

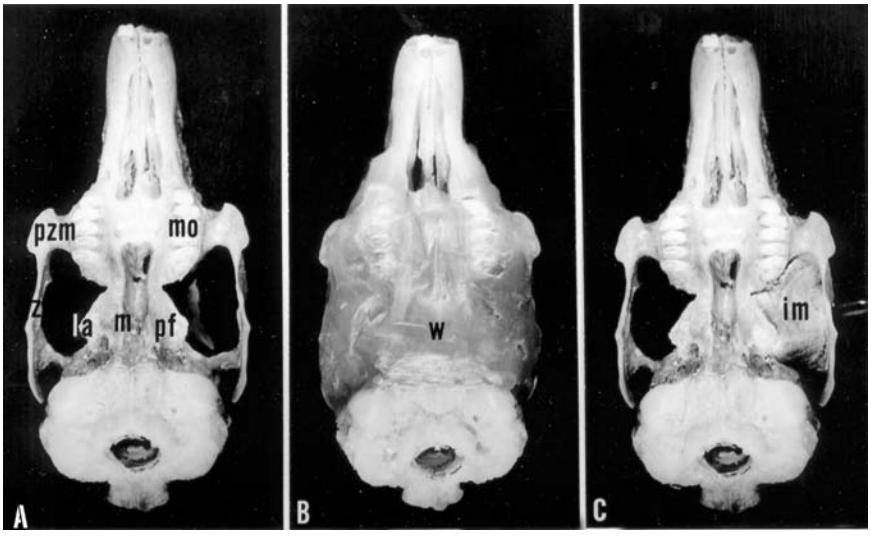

Fig. 19.2 Ventral view photographs of the rabbit skull in Fig. 19.1. (**A**) Prepared skull; la and m — lateral and medial laminae of the pterygoid bone; mo — premolars and molars; pf — pterygoid fossa; pzm — zygomatic process of the maxilla; z — zygomatic arch. (**B**) Periorbital region waxed preparatory to the making of the orbital imprint; w — wax. (**C**) Elastic rubber base orbital imprint (im) in place after wax has been removed. [From: Prechter TK, Sarnat BG. (1973) Comparison of direct and indirect determinations of rabbit orbital volume. *Acta Morphol Neerl Scand* **11**: 151–160.]

which supports the three molars (Fig. 19.2). The upper surface of the pterygoid process of the sphenoid furnishes a small bony shelf.

Superior wall. The superior wall consists principally of the frontal bone, which curves over to form a crest known as the supraorbital process. This has two projections from its body — anterior and posterior. Between these and the body of the frontal bone are located the anterior and posterior supraorbital incisures, which are transformed by ligaments into foramina.

Anterior wall. The anterior wall is formed by the lacrimal bone, the ethmoidal portion of the orbitosphenoid, and the supraorbital process of the sphenoid.

Posterior wall. The posterior wall consists of the temporal bone, the greater wing of the alisphenoid, and the posterior wing of the orbitosphenoid.

External side. The external side, bordered by the bony rim, is the orbital orifice or entrance. The adult orbit is oval. The margin is incomplete at the temporal fossa and at the anterior root of the zygomatic arch. The horizontal dimension, measured from the lacrimal bone to the posterior projection of the supraorbital process, is about 30 mm, and the vertical dimension, measured from the supraorbital process to the dorsal border of the zygomatic arch to the center of the optic foramen, is about 25 mm. Fibrous projections from the orbital rim augment the depth.

Deceleration of Growth of the Orbit*

INTRODUCTION AND PURPOSE

The size and shape of the skull are dependent in part upon the size and shape of the orbit and eye. A variety of factors may influence the orbit and eye. Studies of normal and abnormal orbital and eye growth include the embryonic and postembryonic stages. A wide variety of animals — ranging from the ambystoma, frog, chick, mouse, rabbit, dog, cat, and pig to the primate — have been studied.

Several articles on embryonic growth of the orbit are of interest. Hale,[23] by keeping pregnant sows on a vitamin-A-deficient diet, produced microphthalmia in the offspring. Washburn and Detwiler[63] removed the optic vesicle from an *Amblstoma punctatum* embryo and replaced it with the corresponding region from a donor *A. tigrinum* embryo (which develops a larger eye). After 50–60 days this orbit was larger than on the unoperated-on side. Steinitz[58] reported experiments by Schaper, who removed the eyes bilaterally of 22-day-old frog larvae. From 50 to 95 days later the orbital length was a fifth to a third less than that of the unoperated-on frogs. The cranial length was lessened only by the amount by which the orbital length was lessened. Coulombre and Crelin[9] produced unilateral and bilateral microphthalmia by allowing vitreous humor to escape at the end of the fourth day of incubation in chicks and killed them 14 days later.

*Excerpted from: Sarnat BG. (1981) The orbit and eye: experiments on volume in young and adult rabbits. *Acta Ophthalmol* **59**(Suppl 147): 9–44.

They found that with retardation of eye growth not only was the orbit smaller but also the effects extended to the skull and a cross beak. Tonneyck-Miiller[60] removed the primordium of the lens in chick embryos on the third day of incubation and killed them at the ages of 5, 7, and 9 days. The anterior part of the skull was depressed, not as long and asymmetrical on the operated-on side.

The postnatal relationship of the eye to the orbit in growing mammals was reported as early as 1876 (Gudden in Ref. 30). Popow (quoted in Ref. 30) extracted the eyeball of the dog, cat, and pig 2–3 weeks after birth and killed the animals 2 months later. Not only was the orbit significantly smaller on the operated-on side but also the distance from the midline of the face to the outer border of the orbit was less, the cranium was asymmetric, and the curvature of the cranium was greater on the operated-on side. With decreased orbital contents in young rabbits,[59] kittens,[27] and lambs,[3] orbital growth was less than normal. Wessely[64] aspirated the lens in 18 newborn rabbits and noted 2–8 months later that both the eye and the orbit were not as large as the unoperated-on ones. Conversely, he produced buphthalmos in 16 newborn rabbits and observed 2–8 months later that the eye and orbit were larger than on the unoperated-on side.

There have been other studies of the eye and orbit.[34] Schultz,[54] in his report on several hundred primates of all major groups and widely differing ages, concluded that the relative capacity of the orbit and the size of the eye diminish with increase in body weight.

A series of surgical experiments on both young and adult rabbits[2,21,33,36,42,43,45–53] was conceived, designed, and carried out to determine essentially:

(1) Orbital and eye volume methods;
(2) Orbital and eye volume in the young and adult;
(3) Orbital volume in the young and adult after decrease or increase of orbital contents;
(4) Eye volume in the young and adult after periodic intrabulbar injections of silicone;
(5) Relationship of orbital and eye volume to each other and to age, weight, and sex.

This is a review, analysis, and summary of selected information obtained over the past several years about basic concepts of gross postnatal changes — both normal and abnormal — of the orbit, eye, and facial skeleton. For specific details the reader is referred to the original work.

MATERIALS AND METHODS

New Zealand albino and Dutch rabbits, both young and adult, were used as experimental and control animals. Rabbits were selected because of their rapid growth, the increase in volume of the orbit and eye, and the ease of obtaining littermates. The disadvantage in the use of rabbits was that the orbit had a smaller bony enclosure and differed considerably from the human one.

The Orbit

Most orbital size determinations have been based solely on linear measurements.[27,59] Since the orbit is an irregular, polymorphic, ellipsoidal concavity, volumetric rather than linear determinations should be more accurate. Various methods are available for determining orbital volume.[1,25,36,54]

Volumetric Determination

An elastic rubber base impression material was selected, because of its many advantages.[42] The openings of the orbital walls and rims of cleaned skulls were sealed with a semisoft wax to simulate the intact orbit in the living rabbit. Undercut areas in the depth of the orbit were not modified. Templates made of double thickness hard base plate wax were warmed and pressed into place to create an imprint of the orbital borders. A paper clip was then inserted through the template, with the portion of the clip in the orbital cavity bent to a right angle.

The elastic rubber base material, used to make imprints of the orbit, had the following advantages: it produced good detail accurately, was easily handled and set at room temperature, was elastic for a long period of time, was dimensionally and heat-stable, resisted weathering and oxidation, was radiopaque, and could be readily inserted and removed without damage to either the imprint or the anatomical specimen.

The light-bodied elastic rubber base imprint material was poured into the orbital cavity. The template was then positioned. After the material had set, the wax template was freed from the imprint and paper clip. The orbital imprint was then removed by gripping the protruding paper clip with pliers. From the net weight and specific gravity of the imprints, the orbital volumes were calculated.

Comparison of Direct and Indirect Orbital Volumetric Determinations

With a sliding Helios dial-reading, needlepoint caliper, the greatest anteroposterior, superoinferior, and lateromedial dimensions were measured to the nearest 0.1 mm of the orbit, the orbital imprint, and the roentgenographic imprint image.

The anteroposterior (width, horizontal) orbital distance was taken anteriorly from the region of the inner orbital rim of the maxillary orbital process to the most posterior part of the orbital rim at the zygomatic process of the squamosal bone. The superoinferior (height, vertical) measurement was taken from the region of the anterior supraorbital process of the frontal bone to the orbital rim on the zygomatic arch. The lateromedial (depth) dimension was measured from the region of the midportion of the external lower orbital rim on the zygomatic arch to the most medial point of the orbital rim on the posterior sphenoid bone.

Direct measurements were made with the orbital imprint oriented with its horizontal axis parallel to, and its flat lateral surface perpendicular to, a flat table. The anteroposterior measurement was the linear distance between the parallel anterior and posterior planes. The superoinferior measurement was the linear distance between the parallel superior and inferior planes. The lateromedial measurement was the linear distance between the parallel flat lateral surface and the most medial plane of the imprint.

All roentgenographs were taken with the imprint positioned in the orbit. Standard dental occlusal film was used with a dental X-ray unit at a constant source-to-target/film distance of 28 cm, operated at 75 kVp, 15 mA, and 0.5 s exposure. The lateral view was taken with the flat outer surface of the imprint perpendicular to the line of exposure. The superoinferior and posteroanterior views were taken with the flat outer surface

of the imprint parallel to the line of exposure. The roentgenographic imprint image was about 10% larger than the imprint. Measurements from the superoinferior and posteroanterior roentgenographs were made parallel and perpendicular to the flat surface of the roentgenographic imprint image. The measurements from the lateral view were the greatest distances on the roentgenographic imprint image parallel to the vertical and horizontal planes of the orbit.

The greatest measurements in the approximate anteroposterior, superoinferior, and lateromedial planes were used of the orbit, orbital imprint, and roentgenographic imprint images. Formulae from which the estimated volumes were to be calculated were fitted to these average linear measurements. The estimated volumes were compared with the observed volumes.

Surgical Experimentation

Orbital volume after reduction of orbital contents

Young rabbit orbital volume after evisceration, enucleation, or exenteration

New Zealand albino rabbits from 7 to 42 days postpartum were operated on. In the 7–21-day-old animals, two drops of 0.5% tetracaine HCl were instilled into the conjunctival sac. Then about 0.25 ml of a solution of 1% procaine HC1 was injected into the upper and lower eyelids and retrobulbarly for local anesthesia. In addition, in the 42-day-old animals an injection was given into the marginal ear vein of a 1% aqueous solution of pentobarbital sodium (40 mg/kg). Each rabbit was secured on an operating board, with the side of the face exposed. This was cleansed with an antiseptic solution and the area draped. After injection of the local anesthetic agent, the eyelids were separated manually.

In one group, an evisceration of the globe was done. A keratome incison was made at the limbus into the anterior chamber at the 9 o'clock meridian. One 6-0 plain catgut suture was inserted through the anterior and posterior margins of the incision. The incision was then enlarged circumferentially about 6 mm with corneal scissors. The intraocular contents were completely evacuated. The limbal incision was then closed with interrupted 6-0 plain catgut sutures and the eyelids approximated with interrupted 6-0 black silk sutures.

In a second group, an enucleation of the eye was done. Black silk traction sutures were placed near each margin of the upper and lower eyelids and sometimes through the nictitating membrane. After a complete conjunctival peritomy was performed, the recti muscles were isolated and cut free of the scleral insertions. The bulb was delivered and the remaining muscles and extraocular structures were cut and the bulb enucleated. Bleeding was controlled with local pressure. The capsule and conjunctiva were closed with mattress sutures of 6-0 plain catgut. Interrupted 6-0 plain catgut sutures were used to reinforce the first row of sutures. The eyelids were approximated with 6-0 black silk sutures.

In a third group, an exenteration of the orbit was performed (Fig. 20.1). The orbit was then packed with petrolatum-impregnated gauze strips and the eyelids sutured with 6-0 black silk. The gauze pack was removed one week later. In each animal the opposite orbit was used as a paired control for the operated-on side.

During the postoperative period, the animals were observed periodically. They were weaned at 6–8 weeks of age postpartum. The postoperative survival ranged from 1 to 283 days. Immediately after euthanization, the head was severed from the body and a portion of the soft tissues was resected. In several instances, the contents of orbits that had been previously operated on were removed and fixed in 10% formalin for histologic study. The heads were then fixed in 70% ethyl alcohol. Subsequently, the skulls were cleaned by boiling in water to which a detergent had been added.

Lateral, frontal, and dorsal view photographs of the heads were taken prior to death and lateral, anterior, posterior, dorsal, and ventral views were taken of the skulls, the waxed orbits, and the orbits (Fig. 20.2). Dorsoventral and posteroanterior roentgenographic views were taken of representative skulls. The elastic rubber base material was used to make imprints of the orbit. The orbital volume was determined from the net weight and specific gravity of the imprint.

Orbital volume after evisceration or enucleation with an implant[52]

Dutch rabbits from 15 to 19 days after birth were operated on. The anesthetic and surgical procedure was as previously described. In one group of rabbits, an evisceration of the right globe was done and the

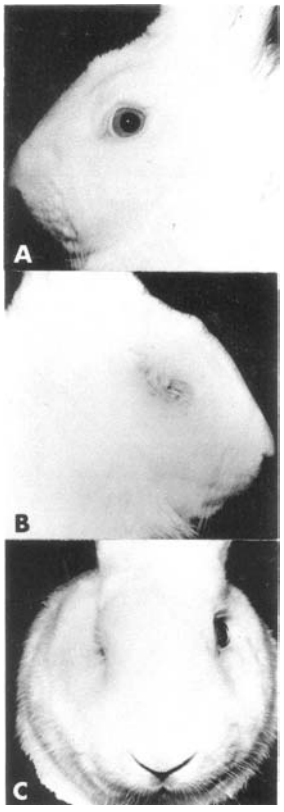

Fig. 20.1 Antemortem photographs of the face of a rabbit euthanized after exenteration of the right orbit at 42 days of age and a postoperative survival of 246 days. (**A**) The unoperated-on left orbit had a postmortem volume of 6.0 ml. (**B**) The exenterated right orbit had a postmortem volume of 3.9 ml. (**C**) Frontal view. Note the lesser fullness of the right orbital and periorbital regions as compared with the unoperated-on left side. [From: Sarnat BG, Shanedling PD. (1970) Orbital volume following evisceration, enucleation and extenteration in rabbits. *Am J Ophthalmol* **70**: 787–799.]

largest possible implant that would be retained (6-mm-in-diameter acrylic sphere) was inserted into the scleral shell (Fig. 20.2). In a second group, an enucleation of the right eye was done and a 6-mm-in-diameter acrylic sphere, similar to the one placed after evisceration, was inserted into Tenon's capsule. The same-size spheres were implanted to keep this factor constant after both evisceration and enucleation.

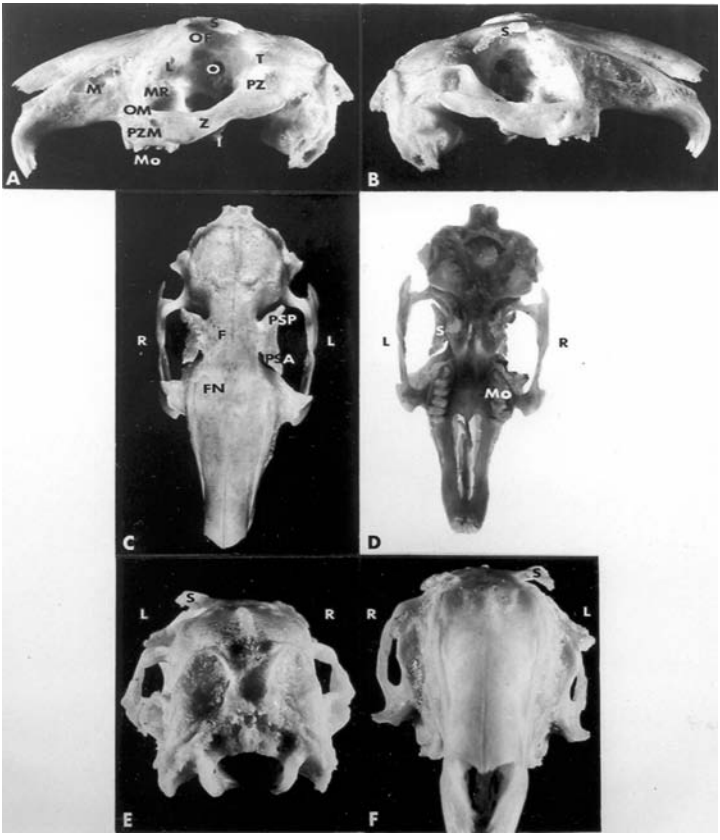

Fig. 20.2 Photographs of the skull of a rabbit which was killed after a postoperative survival of 266 days. (**A**) Left lateral view. The unoperated-on left orbit had a volume of 8.0 ml. (**B**) Right lateral view. The right orbit from which the eye was enucleated at 21 days of age had a volume of 6.4 ml. Note, in comparing the unoperated-on left orbit and the operated-on right orbit, that the former was larger, the circumference of the orbital rim was greater, the supraorbital process was larger and higher, and the zygomatic arch was longer. (**C, D**) Dorsal and ventral views, respectively. The snout deviated toward the operated-on right side. (**E, F**) Posterior and anterior views, respectively. F — frontal bone; FN — frontonasal suture; L — lacrimal bone; l — lateral lamina of the pterygoid bone; M — maxilla; Mo — premolars and molars; MR — molar root area; O — optic foramen; OF — orbital part of the frontal bone; OM — orbital process of the maxilla; PSA and PSP — anterior and posterior supraorbital processes of the frontal bone, respectively; PZ — zygomatic process of the squamosal; PZM — zygomatic process of the maxilla; S — supraorbital process of the frontal bone; T — temporal fossa; Z — zygomatic arch. [From Sarnat BG, Shanedling PD. (1970) Orbital volume following evisceration, enucleation and extenteration in rabbits. *Am J Ophthalmol* **70**: 787–799.]

In each animal the unoperated-on orbit was used as a paired control for the operated-on side.

The rabbits were weaned at 6–8 weeks of age. They were observed periodically for 161–165 days postoperatively. After euthanization the skulls were cleaned and prepared, and orbital volumes were determined as previously described. In some animals, photographs of the dissected skulls and of the imprints were taken before and after death.

Adult rabbit orbital volume after enucleation[45]

Dutch rabbits were raised from weaning to 10 months of age (adulthood), under standard laboratory conditions, before an enucleation was done. The anesthetic and surgical procedures and orbital volume determinations were as previously described.

RESULTS

Orbital Volume in Young and Adult Rabbits

In the New Zealand albino rabbits, the orbital volume ranged from about 0.7 ml at 14 days of age to 7.8 ml at 302 days of age. It about doubled from 14 to 31 days of age and about tripled by 42 days of age. Within the same age group there was variation in the orbital volume. By about 180 days of age the orbital volume had reached about 6.5 ml, or near its maximum, and was about 9 times the size at 14 days of age. In the Dutch rabbits the orbital volume ranged from about 3.6 ml at 98 days of age to about 5.6 ml at 540 days of age. By about 180 days of age the Dutch rabbit orbital volume had reached its maximum of about 5 ml and was about 25% larger than at 100 days of age. The New Zealand rabbit orbital volume was larger than the Dutch rabbit orbital volume. The younger animals had a more rapid rate of orbital growth.

Comparison of Direct and Indirect Orbital Volumetric Determinations

Generally, with change in the orbital volume, there was a corresponding change of each orbital linear dimension. The largest roentgenographic

measurements in each dimension were larger than the direct orbit and orbital imprint measurements. Orbit, orbital imprint, and roentgenographic measurements were evaluated separately with three types of formulae which view the orbit as ellipsoidal. The estimated volumes with the least range for each of the three types of formulae were obtained with the equations for the roentgenographs. The smallest range of deviations between the observed and estimated volumes was +8.3 to −9.8%, with two-thirds of the estimated volumes within a ±4% deviation of the observed volumes.

Surgical Experimentation

Orbital volume after reduction of orbital contents

Young rabbit orbital volume after evisceration, enucleation, or exenteration

In the living young rabbit, immediately after evisceration, enucleation, or exenteration the eye region on the operated-on side was noted to be flatter than the intact side (Fig. 20.1). The findings on the dissected skull were more apparent than those on the living animal and were limited to the orbital and periorbital regions. Generally, the orbit (evisceration, enucleation, exenteration) was not as large, the supraorbital process was less developed and not as high, and the zygomatic arch was not as long as on the unoperated-on orbital side (Fig. 20.2). In several animals there was a deviation of the snout toward the side of the operated-on orbit but this was not a consistent finding (Figs. 20.2C, D).

Microscopic examination showed that tissue removed from the exenterated orbit was composed principally of fibrous and fatty tissue, as well as of lesser amounts of muscle, lacrimal gland, and lymphoid tissue. The tissues in the orbits in which an enucleation had been done were similar to those from the exenterated orbits except for the presence of extraocular muscle and a considerable hyperplasia of the lacrimal glands. The tissues in the orbit in which an evisceration had been done showed the cornea and sclera with mural fibrosis and a thin lining of degenerated tissue, no intraocular tissue, an atrophic optic nerve, slightly atrophic and fibrotic extraocular muscles, minimal chronic conjunctivitis, and foci of chronic interstitial inflammation of the lacrimal glands.

The volumes of the orbits after evisceration of the eyes ranged from about 0.8 ml at 22 days of age with a 15-day postoperative survival to 7.5 ml at 287 days of age with a 266-day postoperative survival. The volumes of the orbits of the intact eye ranged from 1.0 ml at 22 days of age to 7.8 ml at 287 days of age. Of greater interest was that the volume of the orbit after evisceration was always not as great as that of the unoperated-on orbit. Generally, the difference in orbital volumes was greater in the animals with a longer postoperative survival.

The volumes of the orbits after enucleation ranged from about 0.7 ml at 14 days of age with a 7-day postoperative survival to 6.9 ml at 302 days of age with a 283-day postoperative survival. The volumes of the orbits of the intact eyes ranged from 0.8 ml at 14 days of age to 8.0 ml at 287 days of age. Of greater interest was that the volume of the orbit after enucleation was always not as great as the orbit with no surgical procedure. Generally, the difference in orbital volumes was greater in the animals with a longer postoperative survival.

The volumes of the orbits after exenteration ranged from about 3.9 ml at 288 days of age with a 246-day postoperative survival to 4.6 ml at 316 days of age with a 274-day postoperative survival. The volumes of the orbits in which the contents had not been disturbed ranged from 5.1 ml at 219 days of age to 6.0 ml at 288 days of age. The difference in orbital volumes between the intact and operated-on sides was greatest at 288 days of age.

In addition, the data on orbital volume after evisceration, enucleation, and exenteration were analyzed according to four age groups with a progressively longer postoperative survival. The mean orbital volumes after evisceration, enucleation, or exenteration all increased with age. There was a more rapid deceleration of orbital growth after 250 days of age. The 251–350-day postoperative survival group was operated on at an average age of 20–42 days. Their mean orbital volumes would probably have been less had they been operated on at an earlier average age, such as 7–19 days, as were the animals with a shorter average postoperative survival of 1–250 days. Removal of orbital mass at an earlier age would have a greater decelerating effect upon orbital growth.

In a similar analysis, the mean orbital volumes of the unoperated-on side increased directly with age and were always larger than the mean

orbital volumes of the operated-on sides. The mean of the differences of orbital volumes between the unoperated and operated-on sides after evisceration, enucleation, or exenteration was also determined according to postoperative survival. The findings were comparable to those above.

Orbital volume after evisceration or enucleation with an implant

For the dissected skulls, in every instance where an implant had been inserted, it was recovered after death. After evisceration the implant was found encapsulated within the scleral shell, and after enucleation it was found deep in the orbit, in the superior posterolateral region. The implant was small in relation to the orbit and its contents.

The volumes of the orbits after evisceration of the eyes at 15 days of age postpartum and a postoperative survival of 165 days ranged from 4.5 to 5.0 ml, with a mean of 4.8 ml. The volumes of the orbits with intact eyes ranged from 4.8 to 5.6 ml, with a mean of 5.2 ml. In each animal the volume of the orbit with the eye eviscerated was less than that of the orbit with no surgical procedure.

The volumes of the orbits after evisceration of the eye and implantation of a 6 mm acrylic sphere at 15 or 19 days of age and a postoperative survival of 161 or 165 days ranged from 3.9 to 5.0 ml, with a mean of 4.5 ml (Fig. 20.3). The volumes of the orbits with intact eyes ranged from 4.3 to 5.3 ml, with a mean of 5.0 ml. In each animal the volume of the orbit with the eye eviscerated, plus a 6 mm implant, was less than that of the orbit with no surgical procedure.

The volumes of the orbits after enucleation of the eyes at 15 days of age and a postoperative survival of 165 days ranged from 4.1 to 4.7 ml, with a mean of 4.3 ml. The volumes of the orbits with intact eyes ranged from 4.6 to 5.4 ml. In each animal the volume of the orbit with the eye enucleated was less than that of the orbit with no surgical procedure.

The volumes of the orbits after enucleation of the eyes and implantation of a 6 mm acrylic sphere at 15 days of age and a postoperative survival of 165 days ranged from 3.7 to 4.3 ml, with a mean of 4.1 ml. The volumes of the orbits with intact eyes ranged from 4.7 to 5.6 ml, with a mean of 5.1 ml. In each animal the volume of the orbit with the eye enucleated

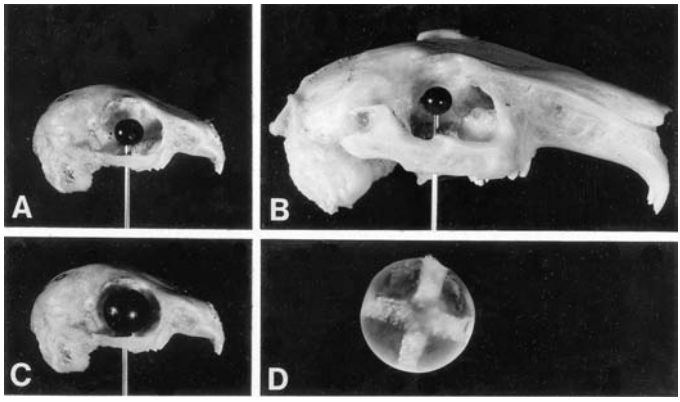

Fig. 20.3 Right lateral views of Dutch rabbit skulls. (**A**) Animal 19 days old, with a black (for illustrative purposes) sphere, 6 mm in diameter, in the orbit. (**B**) Animal 180 days old, with a black sphere, 6 mm in diameter, in the orbit. (**C**) Animal 19 days old, with a black sphere, 9 mm in diameter, in the orbit. Note that the 9 mm sphere is not contained within the orbit. (**D**) Acrylic sphere, 9 mm in diameter, with channels in the horizontal and vertical axes. This type of implant was inserted into the orbits of young rabbits after enucleation of the eyes. Although fibrous tissue grew into channels, the implant was extruded prior to termination of the experiment. [From: Sarnat BG, Shanedling PD. (1972) Orbital growth after evisceration or enucleation without and with implants. *Acta Acta* **82**: 497.]

followed by insertion of a 6 mm implant was less than that of the orbit with no surgical procedure.

Adult rabbit orbital volume after enucleation

A flatness of the eye region was conspicuous immediately after enucleation, in contrast with the unoperated-on side. During this postoperative period, little difference was noted in the orbital region of the operated-on side as compared with the unoperated-on side. No gross differences on the dissected skulls were noted. Generally the orbits, after enucleation, appeared to be equal, the supraorbital process was equally developed and as high, and the zygomatic arch was equal to the unoperated-on side.

The volumes of the orbits at 18 months of age after enucleation at 10 months of age ranged from 4.4 to 5.4 ml. The volumes of the orbits with the intact eye at 18 months of age ranged from 4.7 to 5.4 ml.

The volumes of the orbits in the unoperated-on control animals at 10 months of age ranged from 4.1 to 5.0 ml. The volumes of the orbits in the unoperated-on control animals at 18 months of age ranged from 4.5 to 5.9 ml.

The mean orbital volume at 18 months of age in the males after enucleation at 10 months of age was 5.09 ± 0.29 ml on the enucleated side, while the opposite orbit without enucleation was 5.05 ± 0.24 ml. At 18 months of age in the females the mean orbital volume, after enucleation at 10 months of age was 4.82 ± 0.27 ml, while the opposite orbit without enucleation was 5.05 ± 0.32 ml. The mean difference in mean orbital volumes for males, –0.04 ± 0.19 ml, was not significantly different from zero, but that for females, 0.23 ± 0.16 ml, was at the 0.05 level of significance.

DISCUSSION

Methods of Determining Orbital Volume

Various methods of determining orbital volume have been reported.[36,51,54,59] Any direct method requires the sealing of openings and immediately introduces a possible source of error. An accurate determination is precluded in the use of rape seeds, sand, or liquid substances, because the orbital entrance is not represented by a single plane.[54] Low-fusing metal has been used to determine the volume of the maxillary sinus[41] and could be used to develop permanent orbital imprints. The orbit would be altered, however, in removal of the imprints because of undercut surfaces and rigidity of the metal. Indirect methods, such as roentgenographic assessment, are less accurate. Alexander *et al.*[1] determined the orbital volume of human skulls by the use of sand. Lead markers were then placed in selected parts of the orbit and measurements made on the roentgenographs. The estimated orbital volume determined from these measurements by the use of three formulae did not correlate with results obtained by the use of sand. Other roentgenographic methods,[24] stereoroentgenography, and tomograms, for determining orbital volume, could be of use in the live animal. Radiopaque dyes for outlining the orbital walls,[6] might serve as a substitute for our

use of the roentgenographic imprint method. Haack and Meihoff[22] reported a method for estimation of human cranial capacity from cephalometric roentgenographs.

The method of a direct imprint with an elastic rubber base material seemed to offer the most advantages. But it was not without disadvantages. The same person waxed the orbital openings and made the orbital imprints. He had no knowledge of the history of the animal. If any errors were made in sealing the orbital openings at varying levels, they should have been fairly constant. The possibility of error is lessened when there are fewer orbital openings to be sealed, as in the primate.

The rubber base material has the advantages of being easily handled and setting at room temperature, producing good detail accurately including undercuts, being elastic for a long period of time, being dimensionally and heat-stable, resisting weathering and oxidation, being readily inserted and removed without destruction of the anatomical specimen, and being roentgenopaque. The imprint method with an elastic rubber base material is of value in determining orbital volume under normal and abnormal conditions.

Orbital Volume of Young and Adult Rabbits

Most rabbits attain maturity by 210 days after birth. The female, when mature, is heavier than the male.[11] Maximum development of the skull occurs between 4 and 6 months of age in the rabbit,[14] with full orbital growth in the Dutch rabbit at about 5 months of age.[38] The findings in this report support the above personal communications. The orbital volumes in the New Zealand albino rabbits ranged from about 0.7 ml at 14 days of age to 7.8 ml at 302 days of age. By about 180 days of age the orbital volume had reached about 6.5 ml, near its maximum, and was about 9 times the size at 14 days of age. The orbital volumes in the Dutch rabbits ranged from 3.6 ml at 98 days of age to 5.8 ml at 540 days of age and were not as large as the New Zealand rabbit orbital volumes. By about 180 days of age the Dutch rabbit orbital volume had reached its maximum of about 5 ml and was about 25% larger than at 100 days of age.

Comparison of Linear Measurements and Estimated Volumes of Orbital, Imprint, and Roentgenographic Imprint Images

Previous investigators have relied principally upon specific anatomical landmarks to determine linear dimensions of the approximate anteroposterior, superoinferior, and lateromedial planes of the rabbit orbit. Thomson[59] measured the height, width, and depth of three rabbit skulls and in every instance found all of the dimensions to be less on the operated-on enucleated side. Kennedy[27] confirmed these findings for horizontal and vertical measurements, while the depth measurements were equal or less. In unilateral anophthalmos in the human, although the orbit was smaller, Koch and Brunetti[28] found that the depth measurement was the same for the affected and unaffected orbits. Kennedy[27] also found that after enucleation the usually nearly circular orbital rim was oval, with its long axis in a horizontal direction, and that the difference for the vertical measurements averaged 17.4% (compared with the 14% seen by Petrula and Sarnat[33]), and for measurements of the horizontal distance, 8.2% (compared with the 4.5% seen by Petrula and Sarnat[33]).

The rabbit orbit is an irregular, polymorphic, ellipsoidal concavity. Because the greatest diameter of the lateral part of the orbit is medial to the rim, measurement of the orbital rim will be less. In addition, the rabbit orbit has many openings of the rim and walls. This precludes an accurate determination of orbital size. To lessen variations of both the anatomical landmark positions and the inclination of the planes, we chose instead to measure the greatest linear dimension of the approximate anteroposterior, superoinferior, and lateromedial planes. There were some inconsistencies in obtaining the greatest orbital linear measurements. When the anteroposterior orbital dimension was measured, one could not always be certain of the exact beginning of the inner border. Since the greatest diameter of the lateral part of the orbit is medial to the rim, any measurement of the orbital rim will be too low. Thus, linear measurements of the orbital imprint were greater than those of the orbit.[33] Consequently, the thought was that the greatest direct linear orbital dimensions, regardless of anatomical position, would correlate better with observed orbital volumetric determinations by the imprint method.

In general, the anteroposterior, superoinferior, and lateromedial dimensions were smallest in the direct orbital measurements. Measurements of the imprint were similar to the direct orbital dimensions in the lateromedial but larger in the anteroposterior and superoinferior dimensions. Variability in the measurements due to the smaller orbital rim circumference with respect to the inner regions of the orbit accounted for the larger anteroposterior and superoinferior measurements of the imprint. The measurements of the imprint image of the roentgenograph were the largest in all dimensions, because of overlap of various layers of the imprint as well as an about 10% magnification.

The observed orbital volumes, moreover, were obtained from the imprint and were used as a base to which formulae were fitted in developing equations. Undercuts and irregularities in the orbit, reflected in the imprint, probably accounted in part for the difference.

Surgical Experimentation

Orbital volume after reduction of orbital contents

Young rabbit orbital volume after evisceration, enucleation, or exenteration

In the rabbit, the bony orbit does not cover a considerable portion of the superior surface of the eyeball, which projects about 12 mm beyond the rim of the supraorbital crest.[37] The middle of the cornea, however, projects only 5 mm beyond the edge of the zygomatic arch. Postoperatively after evisceration, enucleation, or exenteration, the eye region was flatter than that of the unoperated-on side. We could not differentiate with any degree of accuracy the type of surgical procedure on the basis of the flatness.

A comparison of the data of the orbital volumes after evisceration, enucleation, and exenteration suggested a direct relationship between the lack of orbital mass and the subsequent retardation of development of the orbit. There were, however, individual exceptions and a certain amount of overlap among the groups.

In this experiment, postnatal increase in the volume of the orbit was decelerated after removal of different amounts of the contents. Other local changes noted were a smaller and less elevated supraorbital process and a less long zygoma. Deviation of the facial skeleton toward the side

of the operated-on orbit contents was noted in several animals. Pfeiffer[35] stated that "… removal of the eye arrests the development of the orbit, and indeed leads to a contraction of it, or to a reduction of its capacity." Our findings were to the contrary. The orbital size, although not as large as on the unoperated-on side, became progressively larger in growing animals, with a longer postoperative survival period. In other words, the orbit was not smaller, actually, but was smaller relative to the unoperated-on orbital side.

Orbital volume after evisceration or enucleation with an implant

Postoperatively after evisceration or enucleation with orbital implants, the eye region was flatter than the unoperated-on side. On the basis of the relative flatness, we could not determine the surgical procedure that was done.

In one group of rabbits, a 6 mm sphere was inserted into the scleral shell immediately after evisceration to help offset the loss of volume after evisceration. After a postoperative survival of about 165 days, the average volume of the orbits with unoperated-on eyes was 5.0 ml, or 11% greater than the mean volume of the orbits in which the eyes had been eviscerated and implants inserted (4.5 ml).

In a group of animals after enucleation, and enucleation followed by insertion of an implant, the mean orbital volume of the unoperated-on side (5.1 ml) was 18% greater than that of the enucleated eye side (4.3 ml). In a second group of rabbits, a 6 mm sphere was inserted into Tenon's capsule immediately after enucleation. After a postoperative survival of 165 days, the mean volume of the orbits with unoperated-on eyes was 5.1 ml, or 24% greater than the mean volume of the orbits in which the eyes had been enucleated and implants inserted (4.1 ml).

The mean orbital volumes of the unoperated-on sides were 5.1 ml. The mean orbital volume after enucleation alone was 4.3 ml, and after enucleation followed by insertion of an implant, 4.1 ml. Contrary to expectations, the difference in orbital volumes was greater, rather than less, in those rabbits in which an implant had been inserted. After evisceration of the eye, the 6 mm implant did not increase orbital size over those without an implant.

In a study of Dutch rabbits, the volume of the bulb in 7 of 9 instances at 15 days of age ranged from 0.5 to 0.7 ml.[52] The 6-mm-in-diameter acrylic sphere implanted at 15 days of age had a volume of 0.133 ml. This represented a volume of about one-fifth that removed by evisceration or enucleation. The volume of the bulb in 8 of 11 instances at 180 days of age ranged from 2.1 to 2.4 ml. Thus, by 180 days of age the implant represented a volume of about one-sixteenth that of the globe.

The 6-mm-in-diameter acrylic sphere was the largest implant that was retained consistently. Larger implants were rejected. The presence of a bore did not aid retention (Fig. 20.3). The largest sphere that Kennedy[27] used in 2 kittens (9 and 12 days of age) was 8 mm. These were retained for about 1 month. Orbital volume might be enhanced by periodic increase in the volume of the implant by substitution of a larger sphere, by adding multiple small beads, or by inflating a sphere.[26,56]

Adult rabbit orbital volume after enucleation

After unilateral enucleation of the eye in 14 adult rabbits at 10 months of age, there was not a meaningful clinical difference in orbital volume between 10 and 18 months of age.

These studies demonstrated that in young rabbits an increase in bulbar volume resulted in an increase in orbital volume,[53] and conversely a decrease in the volume of the orbital contents decelerated growth of the orbit.[51,52] This suggests that orbital dimensions in the young rabbit are dependent at least in part upon its contents. Repetition of these experiments in adult rabbits did not produce changes in orbital dimensions.[45,46] Growth of the orbit at the frontomaxillary and frontozygomatic sutures has been studied in a limited way by the use of radiopaque implants and serial roentgenography.[20] Growth at the sutures bounding the medial wall of the orbit is regulated by growth of the cartilaginous nasal septum.[55] It would be of interest to inject animals with alizarine red S, or some other vital dye that marks calcifying tissues, to determine the relative amounts and sites of bone growth of the orbit under varying conditions. Is there a key factor or are there many factors in orbital growth? Is there a correlation between orbital size and intraorbital mass? If so, what role is played by the muscles and other extraocular

structures, the globe (and sclera), the vitreous and aqueous humor, and the lens?

Since increase in the size of the cranial and orbital cavities is partially explained on the basis of increase in the volume of the contents, what are the factors related to the increase in the volume of air-filled cavities such as the sphenoid, ethmoid, frontal, and maxillary sinuses? As pertains to the maxillary sinus, it has been reported to be larger when the adjacent teeth were absent.[41]

SUMMARY AND CONCLUSIONS

New methods of producing permanent models were developed to determine the volume of the orbit and the volume of the eye. This approach was preferred to the calculation of volume from linear measurements.

The orbital volumes in the New Zealand albino rabbits ranged from 0.7 ml at 14 days of age to 7.8 ml at 302 days of age. By about 180 days of age the orbital volume had reached about 6.5 ml, near its maximum, and was about 9 times the size at 14 days of age. The orbital volumes in the Dutch rabbits ranged from 3.6 ml at 98 days of age to 5.8 ml at 540 days of age and were smaller than the New Zealand rabbit orbital volumes. By about 180 days of age the Dutch rabbit orbital volume had about reached its maximum of 5 ml and was 25% larger than at 100 days of age. The mean orbital volume was less at 540 than at 450 days of age.

The BV/OV (bulb volume/orbit volume) in young (98 days) male Dutch rabbits had little or no relationship to weight, while in females there was a striking decrease of BV/OV with weight. The BV/OV mean was slightly larger for females. In adult (450–550 days) male rabbits there was a striking decrease of BV/OV with weight, and in females only a slight decrease. Adult rabbits of both sexes showed decreases of BV/OV with increase in weight. For fixed age both bulb and orbital volume increased with weight, although the ratio decreased with increase in weight.

After evisceration, enucleation, or exenteration the orbit continued to increase in size. There was a direct relationship between the lack of intraorbital mass and the subsequent lack of development of the orbit. The orbit continued to increase in volume after removal of the orbital contents but at a decelerated rate. In young rabbits the addition of a constant-sized

implant after evisceration or enucleation of the eye did not enhance orbital growth either by its small volume in relation to orbital volume or as a foreign body. Periodic increase in the size of the implant may be essential to increased orbital growth. In adult rabbits enucleation of the eye did not subsequently alter orbital volume.

Growth of the orbit, a three-dimensional mosaic bony cavity, is a result of the synchronous coordination of the differential activities of the eye, various bony growth sites, and other factors. The dynamics of the growth and change of the orbit are a fascinating, complex, incomplete chapter of craniofacial biology.

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Orbital Volume After Increase of Orbital Contents*

YOUNG RABBIT ORBITAL VOLUME AFTER PERIODIC INTRABULBAR INJECTIONS OF SILICONE[53]

Four-week-old Dutch rabbits were divided into two groups. Silicone was injected into only the right or left eye in the first group. Nothing was injected into the eyes of the untreated second group.

Dow Corning No. 360 medical grade fluid silicone (2000 centistokes) was injected under pressure into the anterior chamber of the eye with a tuberculin syringe, and a 24-gauge needle inserted at the limbus and parallel to the iris plane. There was a 2-week period between the first and second injections. Thereafter, the injections were on a weekly basis. In most instances a total of 10 injections were given over a 10-week period. The first 3 injections were 0.1 ml and the remaining were usually 0.2 ml. The total amount of silicone injected into each eye ranged from 1.2 to 1.6 ml. The majority of rabbits received the latter amount (Fig. 21.1).

They were euthanized by an intracardiac injection of pentobarbital sodium 1 week after the last injection. The skulls were prepared and the orbital volumes determined as previously described. Serial photographs were taken of certain animals while alive and photographs were made at

*Excerpted from: Sarnat BG. (1981) The orbit and eye: experiments on volume in young and adult rabbits. *Acta Ophthalmol* **59**(Suppl 147): 9–44. (See Chap. 20 for references.)

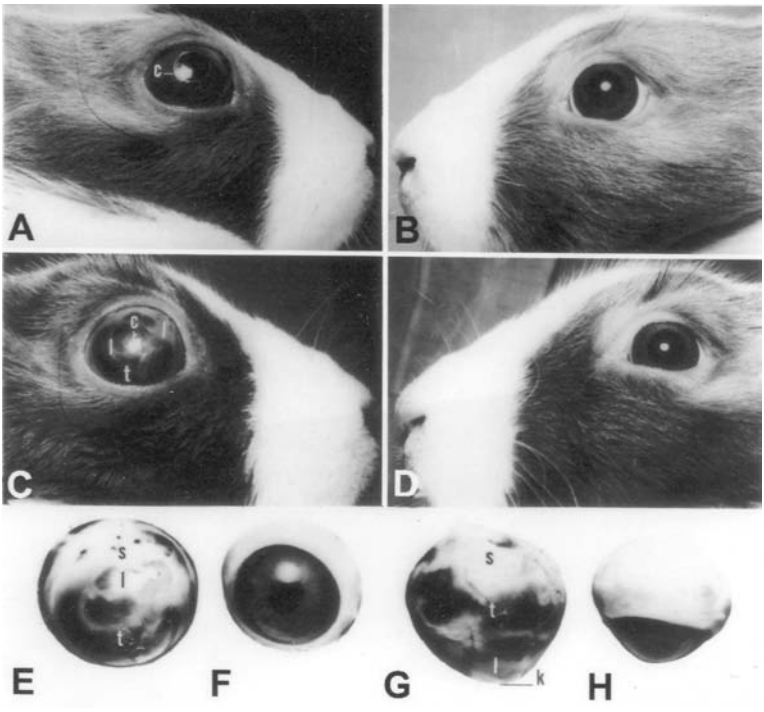

Fig. 21.1 (**A**) Dutch rabbit, 6 weeks of age. After 2 injections, 2 weeks apart, a total of 0.2 ml of silicone had been instilled into the anterior chamber of the right eye. Note the bulging of the eye compared with (**B**) The left noninjected eye. (**C**) Same rabbit at 15 weeks of age. Note the megalocornea with widening of the interpalpebral fissure and distortion of the corneal light reflex, c, as a result of corneal aberration and the presence of a globule of silicone in the anterior chamber. After 10 injections at about weekly intervals, a total of 1.6 ml of silicone had been instilled into the anterior chamber of the right eye. Note the increased bulging of the eye in C, compared with **A**, 9 weeks earlier, and **D**, left noninjected eye; increased megalocornea; geographically distributed corneal leukomata, l; distortion of the corneal light reflex, c; scleral thinning, t, with choroidal pigment visible as a dark area; and widened interpalpebral fissure. (**D**) Left noninjected eye. (**E**) Anterior view of the enucleated injected eye in **C**. Note the enlarged bulbus; megalocornea; corneal leukoma, l; distortion of the corneal surface, sclera, s; and choroidal pigment visible through thin sclera, t. (**F**) Anterior view of the enucleated noninjected eye in **D**. Compare with **E**. (**G**) Superior view of the enucleated injected eye in **C**. Note the keratoconus, k, with megalocornea; corneal leukoma, l; sclera, s; and equatorial scleral thinning, t, with dark, diffusely distributed choroidal pigment visible. (**H**) Superior view of the enucleated noninjected eye in D. Compare with **G** [From: Sarnat BG, Shanedling PD. (1974) Increased orbital volume after periodic intrabular injections of silicone in growing rabbits. *Am J Anat* **140**: 523–532.]

death of selected enucleated eyes (Fig. 21.1). Photographs and dorsoventral and posteroanterior roentgenographs were taken of some dissected skulls, and imprints were made of the orbits.

ADULT RABBIT ORBITAL VOLUME AFTER PERIODIC INTRABULBAR INJECTIONS OF SILICONE

Nineteen adult Dutch rabbits, raised in our laboratories since weaning, were used. They were divided into two groups. Silicone was injected into only the right or left eye in the first group. Nothing was injected into the eyes of rabbits of the untreated second group.

Dow Corning No. 360 medical grade fluid silicone (2000 centistokes) was injected under pressure initially into the posterior and later into the anterior chamber of the eye with a Luer-lok syringe and a 22 gauge, 3.8 cm (1½ in.) needle. In most instances a total of 10 injections, at 1-week intervals, were given over a 9-week period. The first 4 injections, about 1 ml each, were into the posterior chamber; the remaining, about 0.5–0.8 ml, were into the anterior chamber. The total amount of silicone injected into each eye ranged from 5.7 to 7.6 ml. The majority of rabbits received the latter amount.

The animals were euthanized by an intracardiac injection of pentobarbital sodium 1 week after the last injection. Impressions were made of the freshly enucleated eyes. Volume was determined from the weight and specific gravity of the model. The skulls were prepared and orbital volumes were determined as previously described.

RESULTS

Orbital Volume After Increase of Orbital Contents

Young rabbit orbital volume after periodic intrabulbar injections of silicone

The antemortem findings, generally after an intraocular injection of silicone, were that the bulb bulged, was conspicuous and felt hard (Fig. 21.1). In the anterior chamber a gray globule of the injected silicone could frequently be seen. With subsequent injections of silicone the eye appeared increasingly larger than the noninjected opposite eye.

In the postmortem findings after the eyes were enucleated, the injected ones were usually larger in all dimensions than the uninjected eyes. The remaining soft tissue and orbit appeared to accommodate to the increased size of the eye. The cornea was gray, with a dull, nonglistening surface and a distorted light reflex. There were irregularly distributed corneal leukomata. Some specimens had megalocornea, while others in addition had keratoconus. Choroidal pigment was visible through the irregularly thinned sclera. The sclera posterior to the equator did not appear grossly to be thinner.

The findings on the dissected skulls were limited to the orbital and periorbltal regions. Generally the orbit that had contained the eye injected with silicone was larger and the supraorbital process was larger, more developed, and higher than that of the orbit that had contained the uninjected eye (Fig. 36.3).

In the 6 untreated animals, the differences between the right and left orbital volumes ranged from –0.1 to 0.2 ml (–2.4–4.7%). The mean orbital volumes were 4.17 ml and 4.13 ml for the right and left sides. The standard errors of these means were 0.15 ml and 0.14 ml. The mean of the differences was 0.03 ml, which is not significant at the 0.05 level using a t-test with 5 degrees of freedom. In the 12 animals in which the eye had been injected with silicone, the differences between the injected and noninjected orbital volumes ranged from 0.6 to 0 ml (14.6–0%). The mean orbital volumes were 4.32 ml (the standard error was 0.12 ml) for the injected eyes and 3.98 ml (the standard error was 0.08 ml) for the noninjected eyes. The mean of the differences was 0.34 ml, which is significantly different at the 0.001 level using a t-test with 11 degrees of freedom. The standard error of the mean difference was 0.050 ml.

The differences of the right from the left lateromedial (depth) dimensions of the orbits in 6 untreated animals ranged from –0.01 to 0.05 mm. The mean of the differences was 0.02 mm. In rabbits in which the eye was injected with silicone, the differences between the orbital depths of the injected and noninjected sides ranged from –0.30 to 0.20 mm. The mean of the differences was 0.08 mm. The greater depth of the orbit that had formerly contained the silicone-injected eye could be seen grossly in some of the rabbits.

Adult rabbit orbital volume after periodic intrabulbar injections of silicone

The antemortem findings, generally after the initial intraocular injection of silicone into the posterior chamber, were that the bulb bulged slightly if at all. Because after the subsequent three injections of silicone the eye did not appear larger than the noinjected opposite eye, the remaining injections were into the anterior chamber, as in the young rabbits. Nevertheless, no gross differences in size between the injected and noninjected eyes were noted at the end of the experiment.

In the postmortem findings after the eyes were enucleated, the injected ones were usually equal in all dimensions to the noninjected ones. During the dissection, extraocular pockets of silicone were noted. The gross orbital findings on the dissected skulls did not suggest any difference in orbital volumes between the injected eye side and the noninjected eye side. A t-test was performed on the mean differences of the eye and orbital volumes of the injected and noninjected sides for each group. No significant difference was found.

DISCUSSION

Orbital Volume After Increase of Orbital Contents

Young rabbit orbital volume after periodic intrabulbar injections of silicone

The primary purpose of injecting silicone into the young rabbit eye was to observe the effect on both the eye and the orbital volumes. After injection of silicone, the visible periocular region was more pronounced than that of the noninjected side.

The highest viscosity silicone, which could be injected through the smallest bore needle, was used. The amount injected was limited so as not to rupture the expanding bulb. Occasionally, after withdrawal of the needle, a small amount of aqueous humor and/or silicone (despite its high viscosity) leaked through the injection site. This procedure should not be compared with replacement of the aqueous and vitreous humor with an equal volume of silicone.[4,8] Generally, with each injection the bulb appeared more prominent. With the increased intraocular pressure it is

possible that (1) some of the silicone was absorbed, (2) a secondary glaucoma was produced, thus further increasing the intraocular pressure, and (3) the normal growth potential of the bulb was affected. After multiple injections of silicone into the eye, the orbital volume was greater, and the supraorbital process was larger, thicker, and higher on that side than on the side of the noninjected eye.

Orbital volume might be enhanced in other ways — by periodic substitution of an increasingly large implant, by adding multiple small beads,[7] by implanting a hydrogel which swells,[12] or by periodically inflating a sphere.[25,26] In these instances the increase in bulk must be adequate in order to produce increase in orbital size. The problem is for the orbit to retain the increase in bulk so as to obtain the result. No reference is made to orbital change in reports on the effects of genetically determined buphthalmia in rabbits.[18,31] Proptosis was produced in dogs by intraorbital injection of silastic but no mention was made of orbital size.[19]

Adult rabbit orbital volume after periodic intrabulbar injection of silicone

The purpose of injecting silicone into the adult rabbit eye was to observe the effect on both the eye and the orbital volumes. After injection of silicone the visible periocular region was not more pronounced than that of the noninjected side.

The highest viscosity silicone which could be injected through the smallest bore neddle was used. The amount injected was limited so as to lessen the possibility of rupturing the bulb. After withdrawal of the needle, at times a small amount of the aqueous humor and/or silicone (despite its high viscosity) leaked through the injection site. Initially, the posterior chamber was selected because of not only the greater ease of injection than into the anterior chamber but also the possibility of less loss of silicone. Postinjection increase in intraocular pressure was postulated as a result of the increase in intraocular volume. Because no gross increase in eye size was noted after four injections of silicone into the posterior chamber, the remaining injections were into the anterior chamber. Still, no increase in eye size was noted. This was in contrast to the increase in eye size in the young rabbit after only a few injections of silicone into the anterior

chamber. The total amount of silicone injected into the eyes of young rabbits ranged from 1.2 to 1.6 ml, whereas in the adult rabbits (with a larger eye) it ranged from 5.7 to 7.6 ml.

The injected adult rabbit eye did not present buphthalmos as did the injected young eye, possibly because of the rigidity of the sclera and cornea in the adult eye as contrasted with the thinner, more elastic young bulb. Conjecture must also be made as to the fate of the injected silicone. Since silicone leakage at the site of the insertion of the needle occurred in both the adult and young rabbits, this would not explain the failure of enlargement of the bulb during injection. The frequent finding of subconjunctival swelling could be accounted for by escape of the silicone through the injection site. The upper lid edema could be either inflammatory or, less likely, infiltration of extravasated silicone. Aqueous production may have been impeded because of injury to the ciliary body or inflammation.

Without increase in bulbar volume there was no opportunity to test the ability of the adult orbit to react. This might be accomplished in adult animals by increasing the volume of the orbital contents other than the eye.

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The Eye*

INTRODUCTION

Most eye size determinations have been based solely on linear measurements[29,43] and by the gravimetric method.[62] Despite minimal handling and keeping the eye moist at all times, changes in shape were noted during the period of linear measurements. These measurements could not be repeated with accuracy. Live rather than dead animals were used to avoid softening of the globe prior to study. Because of the above limitations, an alternate method of immediate permanent duplication of the freshly enucleated rabbit eye was developed and described by Gault and Sarnat.[21]

VOLUMETRIC DETERMINATION

In brief, two different paste impression materials were used to enclose the eye with minimal distortion. After setting, they could be separated readily, because the surfaces did not adhere, and the eye was removed. A mixture of stone was poured into the cavity and a model of the eye was obtained. Eye volume was determined from the specific gravity and weight of the model.

*Excerpted from: Sarnat BG. (1981) The orbit and eye: experiments on volume in young and adult rabbits. *Acta Ophthalmol* **59**(Suppl 147): 9–44. (See Chap. 20 for references.)

COMPARISON OF LINEAR AND VOLUMETRIC EYE DETERMINATIONS

The duplicated stone models of 40 enucleated eyes from 15–540-day-old Dutch rabbits were used in this study. The volume of each eye was determined from the net weight and the specific gravity of the model. The same models were used to measure the greatest anteroposterior, superoinferior, and lateromedial dimensions with a sliding Helios dial-reading, needlepoint caliper to the nearest 0.1 mm, and the volume was calculated. Linear regression and t-statistic evaluation tests were employed to analyze the data.

RESULTS

Eye Volume in Young and Adult Rabbits

In Dutch rabbits the eye volume ranged from about 0.6 ml at 15 days of age to a maximum of 3.2 ml at 540 days of age. By about 300 days of age the increase in the eye volume had leveled. The volumes of the eyes at 10 months of age ranged from about 2.5 to 3.1 ml. The volumes of the eyes at 18 months of age ranged from 2.7 to 3.3 ml. There was a positive correlation between increase in eye volume and increase in age. Within the same age group there was variation in eye volume. There was also an overlap of eye volume size between adjacent age groups. The younger animals had a more rapid rate of eye growth. The volume of the eye increased 3–4 times from 15 to 180 days of age and about 5 times by 300 days of age, when increase in the volume ceased.

Comparison of Linear and Volumetric Eye Determinations

The volume as measured by the linear methods was consistently greater than that obtained by the gravimetric method.[2] The difference varied from 0.1 to 0.4 ml (mean 0.14 ml). There was a good correlation between the results from the two methods. A t-statistic evaluation test between the data from the two methods showed no significant deviation.

Relationship of Eye and Orbital Volume to Each Other and to Age, Weight, and Sex

The eye volume ranged from about 1.9 ml at 98 days postpartum to a maximum of about 3.3 ml at 540 days of age. By about 300 days of age the

increase in the eye volume had leveled. There was a positive correlation between eye volume and age. Within the same age group there was variation in eye volume. There was also an overlap of eye volumes between adjacent age groups. The younger animals had a more rapid rate of eye growth.

In 98-day-old male rabbits, there was little or no relationship of BV/OV to weight. In the 98-day-old females, there was a striking but not statistically significant decrease of BV/OV with weight. The BV/OV mean for females was slightly larger than for males, but not significantly.

For both male and female rabbits, the bulb and orbital volumes had smaller means for the 540-day-old than for the 450-day-old animals. The BV/OV ratio was slightly larger for the older animals, 450 and 540 days of age. All correlation coefficients for these two age groups of bulb volume versus weight and orbital volume versus weight were positive. Correlation coefficients of BV/OV with weight were negative. All correlation coefficients for orbital volume versus bulb volume were positive.

In the combined 450–540-day-old male rabbits, there was a striking but not significant decrease of BV/OV with weight, while in the females of corresponding age there was only a slight decrease with weight. The BV/OV mean for females was slightly and significantly larger than the mean for males. Adult rabbits of both sexes showed decreases of BV/OV with increases in weight, although not significantly so. Although the evidence is not conclusive, it suggests a negative relationship of BV/OV to weight for mature animals. For fixed age both bulb and orbital volume correlated positively with weight, although the ratio correlated negatively with increase in weight.

DISCUSSION

Methods of Determining Eye Volume

Comparison of the linear and gravimetric methods of determining eye volume

If the shape of the eye in rabbits is assumed to be ellipsoidal, the linear method gives higher volumetric results.[2] In the gravimetric method for

measuring the volume of the duplicated eye, the eye model can be weighed accurately and the specific gravity remains the same. This method can be used for an accurate estimate of eye volume. Since the results of the two methods are highly correlated, the linear method could be used for comparison purposes when a true eye volume is not necessary.

Eye Volume of Young and Adult Rabbits

The size of the rabbit eye varies considerably with the age of the animal. Although the bulb is only about 6 mm in diameter at birth, growth is rapid. At 20 days postnatally the globe is about two-thirds, and at 60 days about 90% of the adult size, which may be reached by 98–140 days. Land[29] stated that growth of the albino rabbit eye is virtually complete by about 160 days. The adult volume is 15 times that of the newborn.[63] From the data in this report on the Dutch rabbit, at 15 days of age the eye volume is about 20% of the adult size, at 100 days of age it is about two-thirds of the adult size, and at 180 days of age it is about 85% of the adult size, which is reached at about 300 days of age. One of the conclusions in these studies is that there is no meaningful clinical difference in eye volume between 300 and 540 days of age.

In the human, the eye attains its adult size at a much earlier age than the body as a whole.[16] Compared with the rest of the body except for the brain, the eyeball grows relatively little after birth. While the body increases in volume 21 times from birth to maturity, the eye increases 3 times (from 2.4 ml to 6.9 ml) and 70% of this is attained by 4 years of age. Thus, this is divisible into 2 stages: a period of relatively rapid growth up to the age of 3 years, a process particularly evident in the first year of life, followed by a slower phase between the ages of 3 and 14 years, when the adult size is substantially attained. The eyeball fills about 75% of the orbital cavity in late fetal life but only about 32% at maturity.[54]

Relationship of Eye and Orbital Volume to Each Other and to Age, Weight, and Sex

In young rabbits an increase in bulbar volume resulted in an increase in orbital volume[53] and conversely a decrease in the volume of orbital

contents decelerated growth of the orbit.[51,52] This suggests that, in the young rabbit, orbital dimensions are dependent at least in part upon its contents. These same experiments repeated in adult rabbits resulted in no change in either bulbar or orbital volume.[45,46]

After reviewing and correlating previous work, Washburn and Detwiler[63] divided the relationship of the eye to the orbit into three periods: (1) in the embryo, the rapidly developing eye appears as a force exerting an influence on all surrounding parts that is sufficient to change the proportions of the whole chondrocranium; (2) in the infant, the eye is still rapidly growing but the effects are limited for the most part to the orbit; and (3) in a comparative study of adults, the eye appears inert, growing slowly if at all, and bearing a close relation to the size of the orbit. The orbit may continue to grow independently of the eye. Coulombre and Crelin[9] hypothesized that "…the extent to which the developing eye influences the skull depends upon the relationship between the intrinsic growth rates of the orbit and the eye." Tonneyck–Miiller and Van Limborgh[61] reported that although the eye is an important factor in the control of orbital growth, there are also other factors. The role of the eyeball in relation to the growth of the orbit and face will depend upon and vary not only with the experiment employed but also with the age and the type of animal studied.

In addition, there have been studies of the eye and orbit in unoperated-on postmortem material. Schultz,[54] in his report on several hundred primates of all major groups and widely differing ages, concluded that the relative capacity of the orbit and the size of the eye diminish with increase in body weight. In fetuses and newborns the eyeball is so large in relation to the socket that it projects beyond the orbital rim so that a normal fetal exophthalmus exists. In infants the eyes are not only larger in proportion to body weight than in the adult but also in proportion to the size of the orbit. Schultz further concluded that the size of the orbit is dependent upon the size of the eyeball in only the most general way and the two structures can vary in size independently to a surprising extent.

SUMMARY AND CONCLUSIONS

In the Dutch rabbit, at 15 days of age the eye volume was about 20% of the adult size, at 100 days of age it was about two-thirds of the adult size, and

at 180 days of age it was about 85% of the adult size, which was reached at about 300 days of age. There was no meaningful clinical difference in the eye volume between 300 and 540 days of age. The mean bulb volume was less at 540 than at 450 days of age.

These studies demonstrated that in young rabbits an increase in bulbar volume resulted in an increase in orbital volume[53] and conversely a decrease in the volume of the orbital contents decelerated growth of the orbit.[51,52] This suggests that orbital dimensions in the young rabbit are dependent at least in part upon its contents. Repetition of these experiments in adult rabbits did not produce changes in orbital dimensions.[45,46]

Growth of the orbit at the frontomaxillary and frontozygomatic sutures has been studied in a limited way by the use of radiopaque implants and serial roentgenography.[20] Growth at the sutures bounding the medial wall of the orbit is regulated by growth of the cartilaginous nasal septum.[55] It would be of interest to inject animals with alizarin red S, or some other vital dye that marks calcifying tissues, to determine the relative amounts and sites of bone growth of the orbit under varying conditions. Is there a key factor or are there many factors in orbital growth? Is there a correlation between orbital size and intraorbital mass? If so, what role is played by the muscles and other extraocular structures, the globe (and sclera), the vitreous and aqueous humor, and the lens?

Since increase in the size of the cranial and orbital cavities is partially explained on the basis of increase in the volume of the contents, what are the factors related to increase in the volume of air-filled cavities such as the sphenoid, ethmoid, frontal, and maxillary sinuses? As pertains to the maxillary sinus, it has been reported to be larger when the adjacent teeth were absent.[41]

CHAPTER 23

The Upper Face and Orbit: Clinical Considerations

SARNAT'S GROWTH STUDIES OF THE ORBIT AND UPPER FACE

Bony orbital growth is related to orbital contents and their growth. Sarnat showed that a reduction of orbital contents in rabbits with exenteration led to a deceleration but continuation of orbital growth.[1] This potential is lost when a patient is skeletally mature. In his animal investigations Sarnat also found that increasing the volume of the normal eye with liquid silicone injections led to increasing orbital bony volumes.[1]

MICROPHTHALMIA

The complete absence of orbital contents in true congenital anophthalmia is rare; however, the more common microphthalmia represents the underdevelopment of the globe. The causes of congenital anophthalmia and microphthalmia include intrauterine infections (such as rubella and cytomegalovirus), exposure to chemicals (such as thalidomide and lysergic acid diethyl amine), vitamin A deficiency, radiation, and trauma.[2] Bilateral involvement is rare and is usually associated with other systemic problems. Recently, a mutation in the SOX2 gene has been shown to result in bilateral anophthalmia.[3]

An anophthalmic or severely microphthalmic eye can lead to severely underdeveloped bony orbital growth and overall face maldevelopment. The normal infant eye is approximately 70% of its adult size and grows most

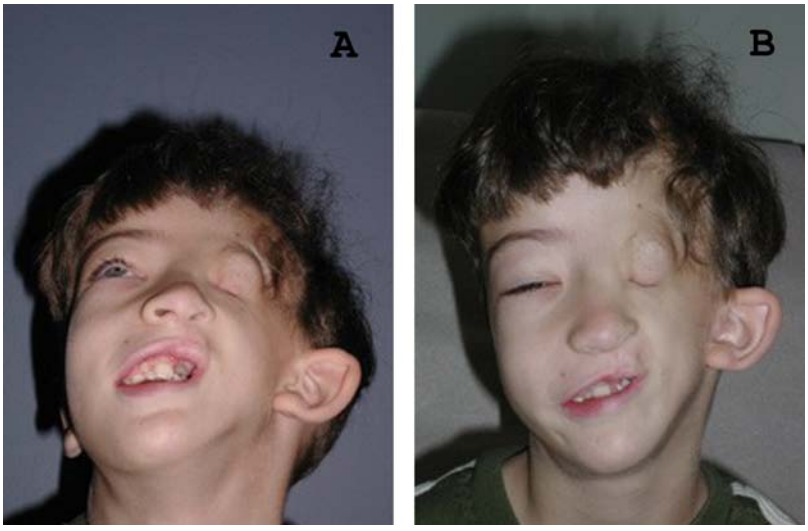

Fig. 23.1 Image of a patient with left-sided facial hypoplasia and severe microphthalmia. Note the reduced palpebral length.

rapidly in the first 12 months of age. The face is only about 40% of the adult size at 3 months of age, but by 5½ years of age it is about 90% of the adult size.[4] The physiology of ocular and orbital development, characterized by Sarnat in his studies, is important to understand for the management of an anophthalmic or microphthalmic socket (Fig. 23.1). A child less than 5 years of age needs an implant that can be increased in size. This implant can be: (1) a dermal fat graft that will grow with the child or (2) an orbital tissue expander. An experienced ocularist using monthly progressive conformer expansion can achieve growth of the orbital soft tissue and bone. In a child older than 5 years of age a large, fixed-size implant may be used.

Orbital implants can be porous like hydroxyapatite or polyethylene (Medpor) for fibrous ingrowth. However, these implants can extrude. To reduce this extrusion risk, surgeons have wrapped the implants using temporoparietal fascia or a substitute like alloderm (cadaveric dermis).[2] Solid, smooth implants are the alternative. Pegs may be placed in the orbital implant to improve mobility.

The goals of the management of both congenital anophthalmia and microphthalmia are to enlarge the conjunctival cul-de-sac, increase the

fissure length, promote the growth of the lid, and expand the orbit. If orbital expansion is not done in the first 5–6 years of life, older children or skeletally mature patients may require surgical expansion of the bony orbit. At the same setting of bony orbital expansion, soft tissue reconstruction with a local flap, like transposition of the temporalis muscle, may be performed. In the more common unilateral case, a template may be made using the contralateral orbit. However, for the best results the affected orbit should be made slightly smaller than the template from the contralateral "normal" orbit. Secondary surgical procedures to the eyelids may involve expansion of the palpebral fissure, canthoplasty, soft tissue flap transfer to the socket, and ptosis correction. Early surgery is not recommended, as it can lead to scarring and inhibition of much-needed growth.

CONGENITAL ORBITAL DYSTOPIA

Orbital dystopia is any type of abnormal displacement of the entire orbital cone and its contents that can occur in a three-dimensional plane. Horizontal orbital dystopia or hypertelorbitism (a term first used by Dr. Paul Tessier) is a separation of the bony orbit in the transverse plane (Fig. 23.2). The orbital separation or bony interorbital distance may be measured with a CT scan as the interdacyron (the most medial region of the orbit) distance. Excessive interdacyron distance or hypertelorbitism may be mild (30–34 mm), moderate (35–39 mm), or severe (> 40 mm). In the growing child, excessive distance may be considered anything over 25 mm.

Vertical orbital dystopia is an asymmetry of the orbits from displacement of the entire bony orbit and cone in a vertical dimension (Fig. 23.3). Cases of vertical orbital dystopia are among the most challenging to correct because of the asymmetric displacement in various directions along three dimensions (i.e. anterior/posterior, cephalad/caudad, or even rotated).

Both hypertelorbitism and vertical orbital dystopia were initially considered a congenital condition; subsequently other etiologies have been described, including facial trauma, muscular torticollis, facial skeletal tumors and with iatrogenic and idiopatic causes.[5] Nevertheless, most traumatic, acute displacement of the orbital walls does not accompany

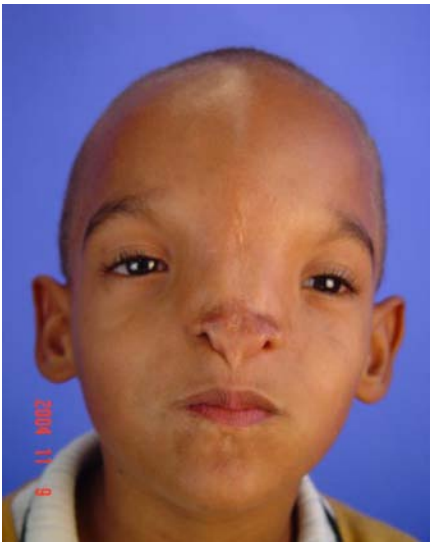

Fig. 23.2 Horizontal orbital dystopia or hypertelorbitism. Note the wide separation of the bony orbit in the transverse plane.

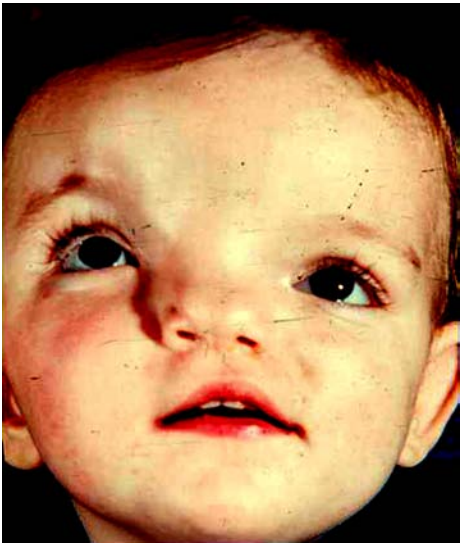

Fig. 23.3 Vertical orbital dystopia. Note the asymmetry of the orbits from displacement of the entire bony orbit and cone in a vertical dimension.

displacement of the bony orbital rims and should not be referred to as hypertelorbitism or vertical orbital dystopia. Thus, low impact traumatic force does not lead to orbital dystopia, mainly because there is not enough energy to mobilize the entire orbital cone.

Horizontal Dystopia

As mentioned above, the dacryon is the most medial osseous part of the orbit and is identifiable on a CT scan (Fig. 23.4). The measurement between the two dacryons or lacrimal crests is an objective manner of determining orbital distance. If the interdacryon distance (distance between the medial bony orbits) is greater than 40 mm in adults or approximately 28 mm in children, then orbital hypertelorism (or hypertelorbitism) exists. This objective measurement distinguishes candidates for orbital correction from others with telecanthus (wider soft tissue around the medial canthus) and abnormal ocular movements (interpupillary distance may also be abnormal) (Fig. 23.5).[6,7]

Facial bipartition surgery and orbital box osteotomies have been shown to be effective methods for the correction of hypertelorbitism.[6] The

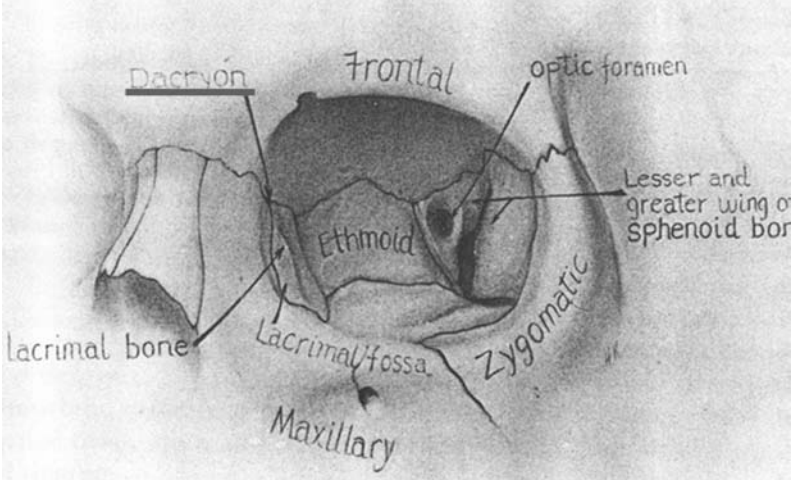

Fig. 23.4 As depicted in this illustration, the dacryon is the most medial osseous part of the orbit and is identifiable on a CT scan.

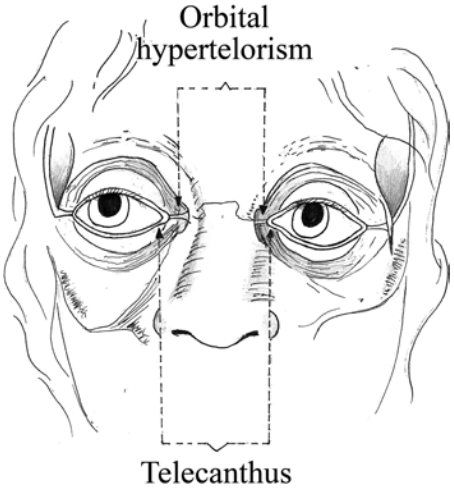

Fig. 23.5 Illustration demonstrating the difference between telecanthus (wider soft tissue around the medial canthus) and orbital hypertelorism (increased orbital bony separation).

removal of a wedge of bone from the internasal area and lower forehead region allows the rotation of the orbits medially, thereby making the midface conform to more standard norms (Fig. 23.6). With this bony reduction centrally, correction of the excess soft tissue in the intercanthal area and glabellar region (interbrow region) must also be performed.

We reviewed a series of syndromic and nonsyndromic patients at UCLA who underwent correction of hypertelorbitism. We prefer the facial bipartition technique to an orbital box osteotomy technique for reduction of intradacyron distance and correction of horizontal orbital dystopia. In this study we highlight a suture technique for reducing the widely spaced eyebrows in these patients. The "K stitch" technique corrects the excess glabellar soft tissue without the use of external incisions, which would otherwise result in unsightly scarring (Fig. 23.7).

Correction of Hypertelobitism; K Stitch Reconstruction

For the 12 patients in the series reviewed, the diagnoses consisted of Crouzon ($n = 4$), Apert ($n = 3$), Pfeiffer ($n = 2$), frontonasal encephalocele

Fig. 23.6 Removal of a wedge of bone from the internasal area and lower forehead region to allow the rotation of the orbits medially, thereby making the midface conform to more standard norms.

($n = 2$), and craniofacial cleft ($n = 1$). The mean patient age was 11.3 years (range = 8–20). Facial bipartition was performed in 11 of the 12 cases and 8 had simultaneous advancement (6 of which were done with distraction osteogenesis) (Fig. 23.8).

The mean preoperative interdacryon distance was 38 mm and the range was 34–45 mm. The mean postoperative distance was 16.8 mm; this was a 55.4% decrease in the interdacryon distance after orbital narrowing with facial bipartition as measured directly by intraoperative calipers. The mean intercanthal distance decreased from 48.8 mm to 29.8 mm, a decrease of 39.2%. The change in the medial canthus width was 39%. Interbrow distance decreased from a mean of 45.7 mm to 27.8 mm; this was a decrease of 38.8%. Two patients had revisions to the K stitch at the time of secondary surgery. The final interbrow position was used when calculating the mean postoperative values and percent decrease.

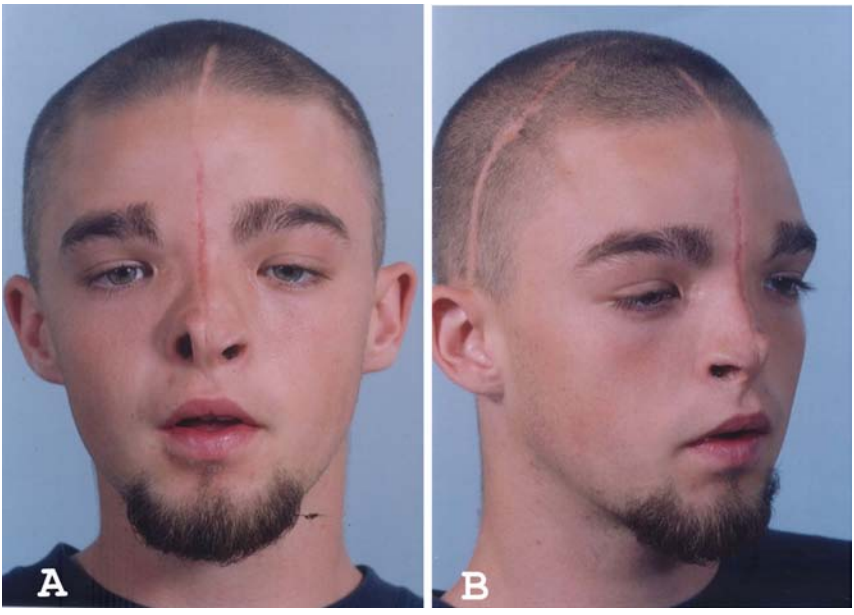

Fig. 23.7 A 16-year-old boy 1 year after facial bipartition to reduce interorbital distance. The presence of an unsightly midline forehead and nasal scar is evident. (**A**) Frontal view. (**B**) Oblique view.

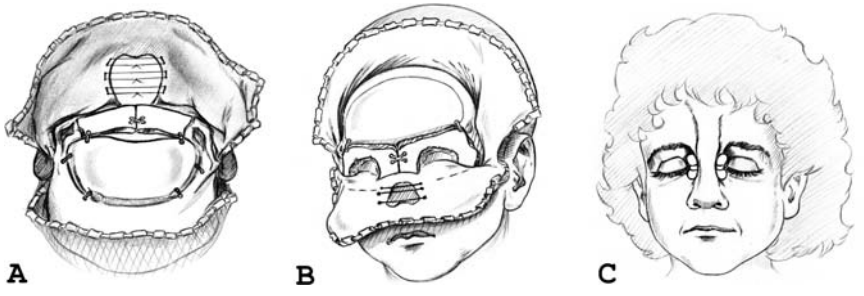

Fig. 23.8 Intraoperative illustration of the K stitch technique. (**A**) With the coronal flap reflected anteriorly, bony fixation after facial bipartition is seen. After excision of subcutaneous soft tissue in the medial region between the brows, multiple horizontal mattress sutures are placed, as shown. (**B**) From a frontal view, bone fixation and placement of K stitches are seen. (**C**) After closure of the coronal incision, soft tissue medial canthal wires are secured over bolsters. The interbrow width has been removed by the K stitch, and redundant skin is seen in the midline.

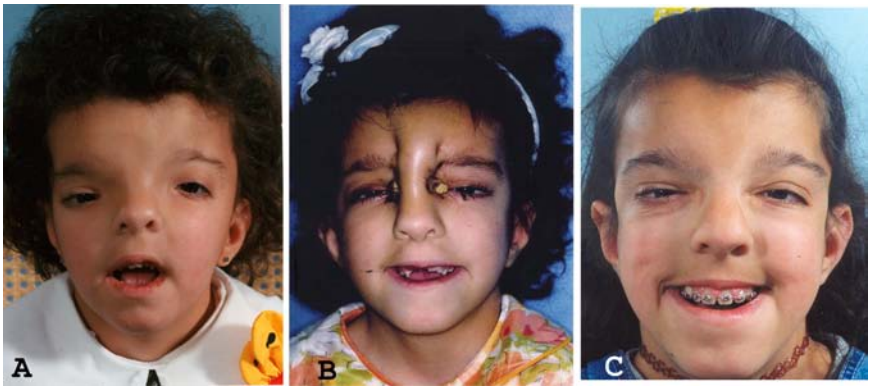

Fig. 23.9 A nine-year-old girl with asymmetric hypertelorbitism. (**A**) Preoperative frontal view. (**B**) The photograph one week after surgery shows the soft tissue medial canthi bolster and K stitch in place. (**C**) Three-year follow-up photograph. The frontal view shows reduced intercanthal and interbrow distances with minimal scarring after the K stitch procedure.

The excess "bunched" skin in the central forehead and between the brows resolved in 6–8 weeks in all patients. In some patients, suture indentations were seen initially but also resolved. The two revisions mentioned above were offered to create additional brow narrowing. Patients and families expressed *initial* concerns about appearance of the brow region. However, all patients and families reported high satisfaction with the brow appearance after 6 weeks (Fig. 23.9).

Evaluations showed normal or unchanged postoperative visual acuity and extraocular movements. Two patients developed unilateral ptosis, which improved over 6 months and did not require correction. A proper relationship of the globe to the orbit had been maintained.

Vertical Dystopia

Vertical dystopia involves displacement of the entire orbit along the vertical plane (cephalad or caudad), but displacement may also occur in other directions, like anterior–posterior or rotation away from the center. This creates asymmetries, which are difficult to correct. As previously mentioned, it should not be considered true vertical dystopia if only one, two,

or even three orbital walls are displaced (as in orbital trauma). A study of UCLA patients with craniofrontonasal dysplasia documented before led to an algorithm for treating these patients known to have vertical orbital dystopia.

Craniofrontonasal Dysplasia

Craniofrontonasal dysplasia is a rare, familial X-linked syndrome with coronal synostosis (brachycephaly or plagiocephaly), hypertelorbitism (frequently asymmetric), and extracranial anomalies. One of the most striking features is the asymmetric vertical orbital dystopia (Figs. 23.10 and 23.11). At UCLA we reviewed a series of patients ($n = 21$) whom a multidisciplinary team had diagnosed with craniofrontonasal dysplasia (the largest cohort to date).[8] Data were used to create a surgical treatment algorithm. This algorithm, for the treatment of patients with craniofrontonasal

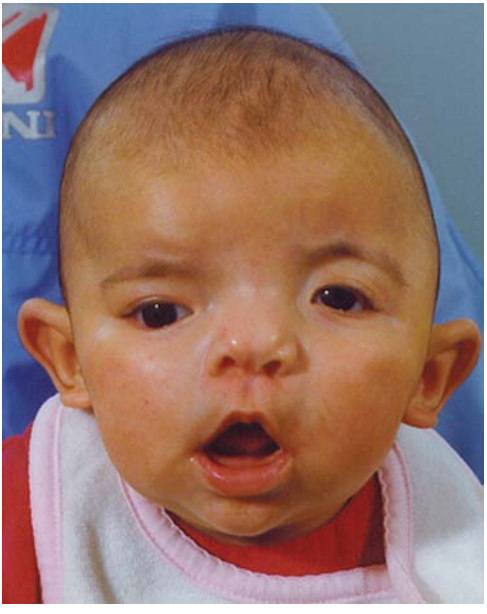

Fig. 23.10 Example of craniofrontonasal dysplasia phenotypes: left unicoronal synostosis in a five-month-old girl, also with asymmetric hypertelorbitism, high-arched palate, mildly bifid nasal tip, and protruding ears.

Fig. 23.11 Another patient displaying craniofrontonasal dysplasia phenotypes: bilateral coronal synostosis in a three-month-old girl, with symmetric hypertelorbitism, mildly bifid nasal tip, and low-set ears.

dysplasia, focused on surgical timing, technique, and outcomes. Office, hospital and operative records, photographs, lateral cephalograms, and 3D CT scans. Based on surgical outcomes, a treatment algorithm was created.

Fourteen patients were female and 7 patients male, and 5 patients had a family history of craniofrontonasal dysplasia (24%). Eight patients had unilateral coronal synostosis (plagiocephaly) and 13 had bilateral coronal synostosis (brachycephaly). Patients also had a cleft lip and palate (10%) (Fig. 23.12), ear deformities (19%), strabismus or esotropia (81%), dry frizzy hair (100%), syndactyly (14%), nail abnormalies (100%), or other abnormalies. Eleven patients had asymmetric hyperorbitism and 10 had symmetric hyperorbitism (Figs. 23.13 and 23.14).

The phenotypic expression of craniofrontonasal dysplasia is described to recognize patients early. In addition, a treatment algorithm for craniofrontonasal dysplasia patients based on timing and technique is offered to decrease the need for revision and improve the outcomes (Fig. 23.15).

Fig. 23.12 Craniofrontonasal dyplasia patient with left cleft-lip-and-palate deformity in a five-month-old boy with left coronal synostosis and asymmetric hypertelorbitism.

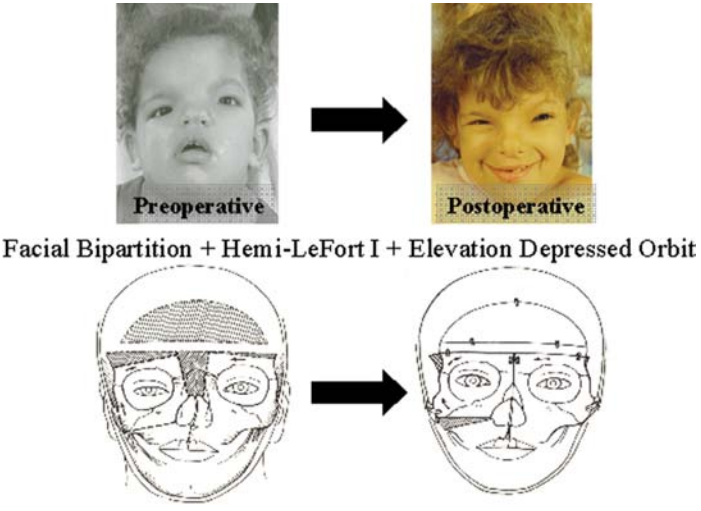

Fig. 23.13 Asymmetrical facial dysmorphology: facial bipartition is modified for asymmetry such that an asymmetrical midline wedge osteotomy is made favoring the depressed orbits side (*left*). The half with the depressed orbit is then elevated so as to achieve ocular alignment (*right*). If, however, permanent dentition is present, a hemi–LeFort I to the depressed orbits side or a complete LeFort I may be performed so as to maintain the occlusal relationship.

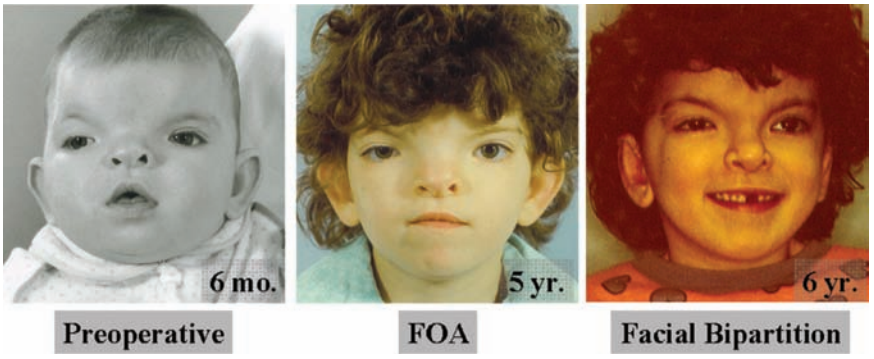

Fig. 23.14 Symmetrical facial dysmorphology: a female patient with bilateral coronal synostosis and hypertelorbitism who presented at six months of age (*left*) and underwent immediate frontal orbital advancement (FOA) and remodeling (*middle*), and after permanent maxillary incisor eruption, with mixed dentition present, a facial bipartition with nasal correction was performed (*right*).

Craniofacial Cleft

Congenital craniofacial clefts are anatomic distortions of the face and cranium with deficiencies or excesses of tissue along a linear region.[9] They are among the most disfiguring of all facial anomalies. Tessier developed a classification of rare craniofacial clefts numbered from 0 to 14 (Fig. 23.16). The eyelids and orbits define the primary axis of this functional system, dividing the face into upper and lower hemispheres. Tessier used these landmarks because the orbit belongs to both the cranium and the face. The orbit separates facial clefts 0–7 with cranial clefts 8–14 (Fig. 23.17). In addition, the following cleft combinations are clinically observed: 0 and 14, 1 and 13, 2 and 12, 3 and 11, 4 and 10, 5 and 9, and 6 and 8.

With cranial clefts 10–14 the distance between the medial canthi may be increased (telecanthus) and the bony interorbital distance may be increased (orbital hypertelorism or hypertelorbitism). The midline cleft 14 may have horizontal or transverse dystopia with the bony orbits displaced laterally (orbital hypertelorism) (Fig. 23.18) or medially (hypotelorism), whereas the lateral clefts 10–13 may have a component of vertical dystopia

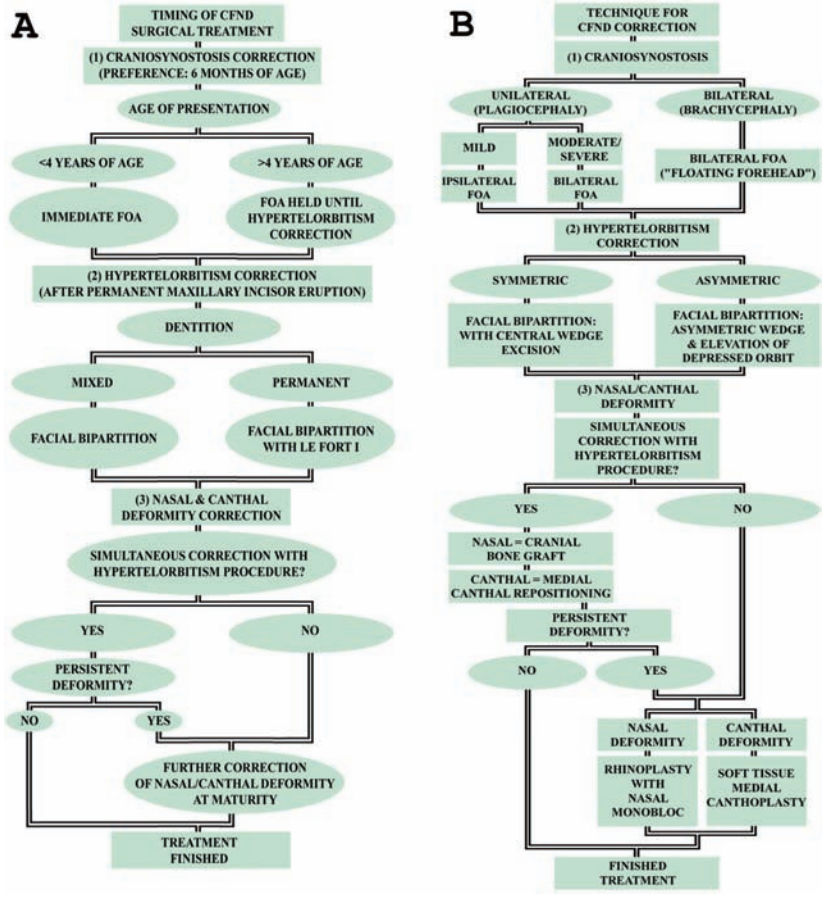

Fig. 23.15 (A) Surgical treatment algorithm for craniofrontonasal dysplasia patients based on timing. Timing of craniosynostotic correction depends on the age of presentation. Hypertelorbitism correction is performed after maxillary central incisors erupt (around 5–6 years of age), and nasal/canthal deformities are addressed at the same time and revised at skeletal maturity (14–17 years of age). (**B**) Surgical treatment algorithm for craniofrontonasal dysplasia patients based on a technique. The technique for craniofrontonasal dysplasia correction is based on: (1) craniosynostotic correction, (2) hypertelorbitism correction, and (3) nasal/canthal deformity correction. An FOA is used to treat craniosynostosis, but the type of FOA is dependent on whether the patient presents unilateral or bilateral craniosynostosis and the severity. Hypertelorbitism is corrected by a facial bipartition procedure, but with varying techniques within the procedure, depending on the symmetry on hypertelorbitism. The nasal or canthal deformity is treated either concurrently with the hypertelorbitism correction or at skeletal maturity.

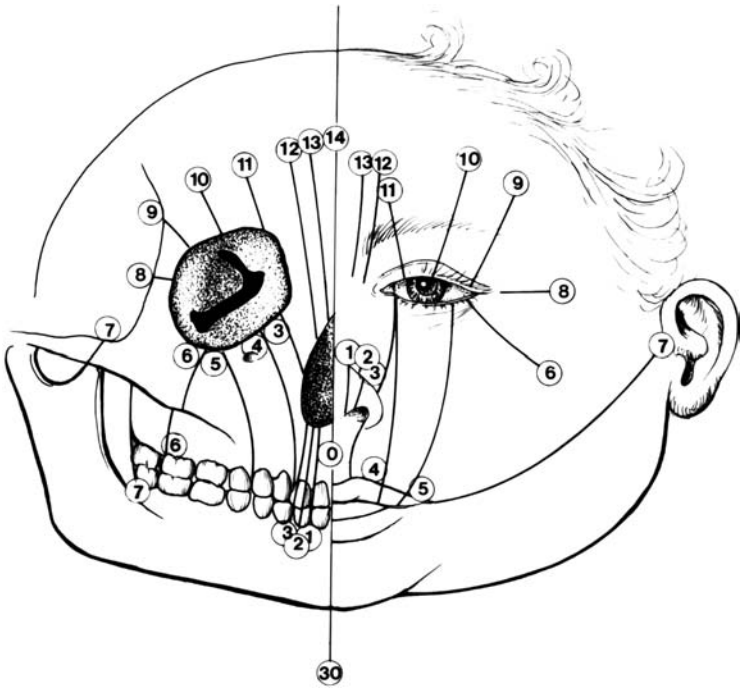

Fig. 23.16 Illustration of the Tessier classifications of rare craniofacial clefts numbered from 0 to 14, with skeletal landmarks on the right face and soft tissue landmarks on the left face.

or asymmetric orbital hypertelorism with the orbits on different horizontal planes (Fig. 23.19).

Correction of hypertelorbitism may be achieved with a facial bipartition or orbital box osteotomy. A facial bipartition involves a coronal and gingivobuccal sulcus incision, a craniotomy for exposure, orbital and midface osteotomies, a central wedge ostectomy (between the orbits), transposition of the orbits to an intradacyron distance less than 17 mm, and rigid fixation. Medial canthi bolsters and correction of excessive glabellar soft tissue are necessary. In addition to narrowing the orbital distance, a facial bipartition procedure will widen a constricted palatal arch. Alternatively, an orbital box osteotomy may be used to narrow the orbital distance or correct vertical dystopia without disrupting the maxilla.

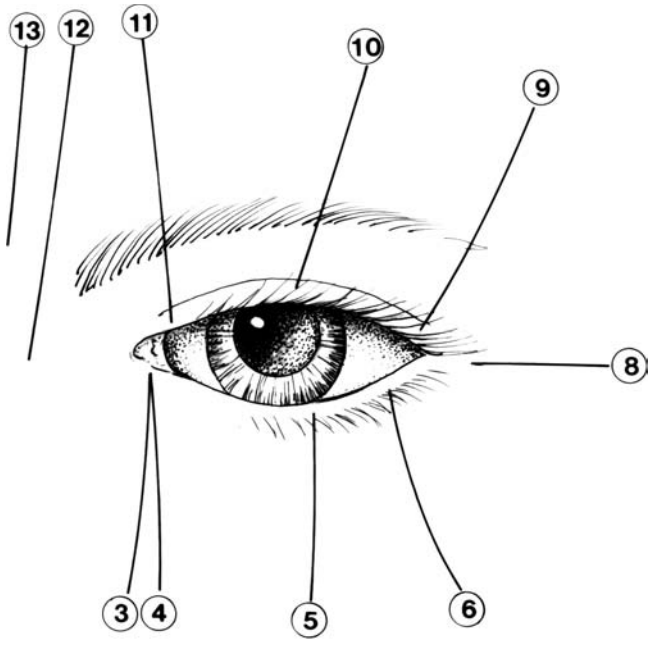

Fig. 23.17 Illustration showing the orbit as the separation of facial clefts 0–7 from cranial clefts 8–14.

However, at UCLA we prefer the versatility of a facial bipartition for the correction.

ORBITAL TRAUMA

As with other bony trauma, treatment of orbital trauma requires reduction of displaced fracture segments, rigid fixation and, at times, bone grafting.[10] Inadequate treatment of orbital fractures can lead to long-term issues like enophthalmos, restriction of eye motility, orbital dystopia or other long-term cosmetic and functional problems (Fig. 23.20). The common regions involved in orbital fractures include the zygomaticomaxillary complex, the orbital floor, and the medial orbital wall (often through the lamina papyracea, thin bones which protect against globe rupture or injury), frontorbital (roof fractures), or nasorbital ethmoid region.

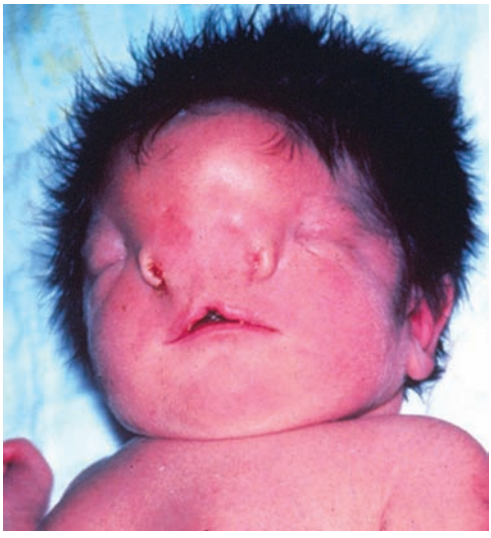

Fig. 23.18 Patient with the midline cranial cleft 14 and the facial cleft 0 resulting in horizontal or transverse dystopia with the bony orbits displaced laterally (orbital hypertelorism).

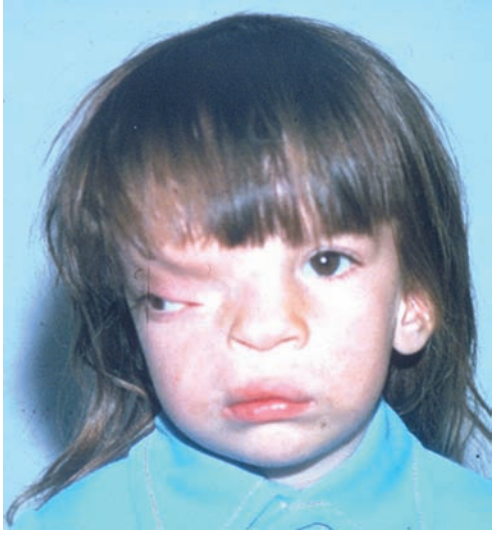

Fig. 23.19 Patient with the right lateral cranial cleft 10 with vertical dystopia or asymmetric orbital hypertelorism with the orbits on different horizontal planes.

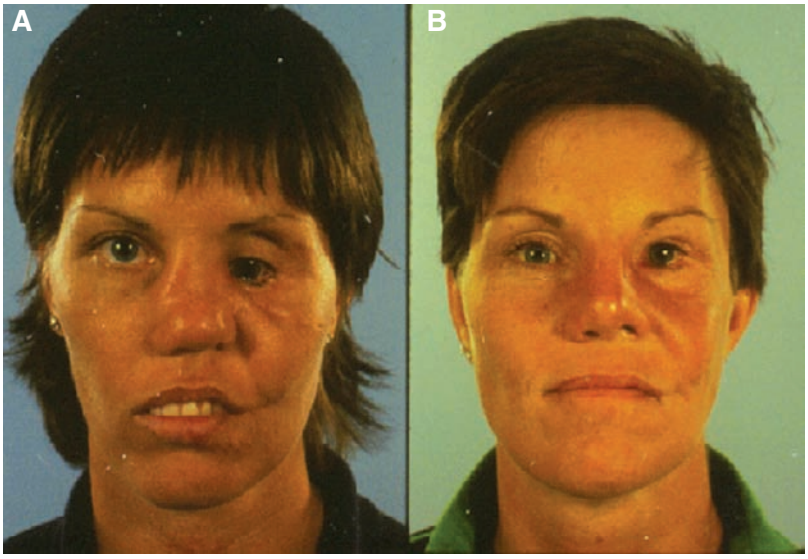

Fig. 23.20 Posttraumatic facial deformity. (A) Preoperatively this patient had inadequate treatment of orbital fractures resulting in long-term problems of enophthalmos, restriction of eye motility, orbital dystopia, and malar depression asymmetry. (B) Postoperatively the patient had improvement in the globe and malar position from zygomatic maxillary repositioning and cranial bone grafts to the orbital floor and medial orbital wall. [From H.K. Kawamoto, MD, DDS.]

The reduction and internal fixation of the orbital rim components currently involves internal titanium plates and wires. The principle of orbital wall reconstruction is to approximate the orbital volume as closely as possible by reconstruction of the pyradimal shape of the orbit. Thin cranial bone grafts shaved off the endocranial surface are the preferred grafts at UCLA. However, other prosthetic implants may provide proper restoration. In this region infectious complications with these foreign body implants are rarer than with implants in other parts of the body.

SUMMARY

In considering optimal treatment of severe microphthalmia, orbital dystopia, or orbital trauma, understanding orbital anatomy and the principles of

orbital growth is paramount. As with other facial reconstruction, a multidisciplinary approach is sometimes necessary with a plastic surgeon, ophthalmologist, ocularist, or head and neck surgeon.

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PART IV

TOOTH DEVELOPMENT AND ASSOCIATED CONDITIONS

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Tooth Development*

The concept that the growing tooth is a biologic recorder of both health and disease has received increasing confirmation from various experimental and clinical studies of the influence of metabolic conditions on tooth development. The growing enamel and dentin yield accurate, prompt, and permanent records of both normal fluctuations and pathologic accentuation of mineral and general metabolism. Fortunately, these records are easily read, by virtue of the orderly and rhythmic growth of these tissues in their daily ringlike succession.

Growing long bones also may serve as recorders of systemic disturbances. Transverse lines of increased density that correspond to the period of altered metabolism can be observed on roentgenographs. However, enamel and dentin have certain distinct advantages over bone: (1) unlike bone, they are not ordinarily subject to resorption, and the record is therefore immutable; (2) the chronology of development is more precise; and (3) this can be more readily studied not only on a roentgenographic but also on a clinical and histologic basis.

A brief review of primate dental histogenesis will facilitate the understanding of some of the differences of dental tissues from each other and from bone, as well as the development and dating of dental aberrations. Tooth development consists of a number of stages, governed by an orderliness in the elaboration of shape, size, position, and function.

*Excerpted from: Sarnat BG. (1984) Differential growth and healing of bones and teeth. *Clin Orthop Relat Res* **183**: 219–237.

Growth involves five basic developmental processes in the elaboration of the various specialized tissues and structures (Fig. 24.1). During each of these periods, various aberrations may develop (Table 24.1). Initiation marks the beginning of the formation of the tooth buds from the oral epithelium. It is characterized by stimulation of particular cells of the oral epithelium to become odontogenic. Lack of initiation of one or more tooth buds results in partial or total anodontia (see Chap. 27). Excessive initiation will be responsible for supernumerary teeth.

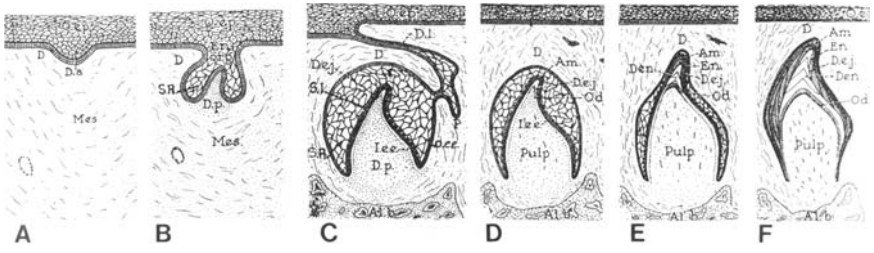

Fig. 24.1 Diagrammatic representation of the embryology and early eruption of the lower human deciduous central incisor: (**A**) initiation, (**B**) proliferation, (**C**) histodifferentiation, (**D**) morphodifferentiation, (**E, F**) apposition and early eruption. Oep — oral epithelium; Da — dental anlage; Dp — dental papilla; En — enamel organ; Oee — outer enamel epithelium; SR — stellate reticulum; SI — stratum intermedium; Iee — inner enamel epithelium; Mes — mesenchyme; Dej — dentinoenamel junction; Dl — dental lamina; Alb — alveolar bone; Am — ameloblasts; Od — odonoblasts; En — enamel; Den — dentin. [Reproduced with permission from Byars LT and Sarnat BG. Surgery of the mandible: the ameloblastoma. *Surg Gynecol Obstet* (1945) **81**: 575–584.]

Table 24.1 Stages in Dental Development Correlated with Dental Aberration

Stages in Growth, Calcification and Eruption	Dental Developmental Aberration
Initiation	Anodontia
Proliferation	Ameloblastoma
Morphodifferentiation	Hutchinson incisor, mulberry molar
Apposition	Enamel hypoplasia
Eruption	Hemifacial atrophy (deficient tooth size and eruption)

Proliferation, the second stage, consists of rapid mitotic multiplication of cells. The tooth germ increases in size, leading to the bud and cap stages of the enamel organ. The connective tissue that underlies the proliferating epithelium soon shows increased activity. It becomes the dental papilla. The connective tissue that surrounds the enamel organ becomes the dental follicle. Proliferation normally ceases with the beginning of the next stage, histodifferentiation. If proliferation continues excessively, the enamel organ enlarges without restraint and an ameloblastoma (preameloblastoma) may result (see Chap. 28).

In the stage of histodifferentiation, the cells of the enamel organ and dental papilla change in size and shape. They cease to multiply, and become specialized in structure and function. The cells of the inner enamel epithelium become ameloblasts and acquire their appositional growth potential to form enamel. This potentially proceeds at a definite rate. The mesenchymal cells subjacent to the ameloblasts and under their influence differentiate into the specialized odontoblasts, and a similarly disciplined program of activity leads to the deposition of dentin.

In the next stage, morphodifferentiation, the basic shape and size of the tooth are established soon after histodifferentiation starts. The inner enamel epithelium assumes an arrangement that outlines the future dentinoenamel junction. Thus, the morphologic pattern of the crown is determined. A disturbance in morphodifferentiation with dwarfing of the dentinoenamel junction may be responsible for the peg tooth, microdontia, the Hutchinson incisor, and the Moon molar (see Chaps. 29 and 38C).

Apposition and mineralization do not begin until the cells have attained full histodifferentiation and reached their particular position along the future dentinoenamel junction. With these two layers of cells (odontoblasts and ameloblasts) in contact at the dentinoenamel junction, a microscopic cusp of dentin is formed, which is soon followed by a corresponding amount of enamel. A synchronous recession of the ameloblasts and odontoblasts from each other then occurs. Incremental layers of enamel are apposed, one on top of another, until the cusp is fully formed. Subsequent layers are apposed at the sides until the crown is complete. For each layer of enamel, a corresponding layer of dentin is apposed, one within another. After enamel formation has ceased, dentin formation continues, for completion of the root. Arrest of enamel apposition due to

either systemic or local factors results in enamel hypoplasia (see Chaps. 30 and 38A). Mineralization of the enamel and dentin follows, for the most part, closely on the deposition of the matrix.

EXPERIMENTS OF NATURE: DENTAL AND FACIAL DEVELOPMENT

A knowledge of the stages of normal dental development gives a better understanding of the development (Table 24.1). The dental developmental process is initiated at definite intervals for the various teeth in both dentitions. The occurrence of a genetic or sufficiently severe systemic disturbance during development of the teeth may affect the particular stage in progress at the time and be expressed clinically at a later date as one of the following dental development dystrophies of number, shape, and size. Four examples are reported here: (1) lack of initiation of dental development, (2) disturbance of proliferation, (3) systemic disturbance of morphodifferentiation, and (4) systemic disturbance of apposition (Table 24.1 and Chaps. 27–30).

Effects of Hibernation on Tooth Development*

INTRODUCTION

The marked depression of general metabolism during the hibernating state has been well known. General metabolic changes are recorded accurately and chronologically in the teeth. We have undertaken to demonstrate quantitatively the effects of hibernation on tooth development. Intravital staining by means of alizarin red S was done to assess the rate of dentin growth.

The effects of hibernation on tooth development in the 13-lined ground squirrel were studied in 28 animals. Nine animals were used as controls. The animals were subjected to intravital staining with alizarin red S to determine the rates of dentin apposition. The changes in body weight were observed during these experiments.

The essential findings were:

(1) No changes were found in the roentgenographs and gross examination of the skulls, incisors, molars, and femurs of animals subjected to hibernation.
(2) The weight loss was inversely proportional to the time the animal hibernated. The average weight loss was: Group I (86–100% hibernation) — 1.4 g per day; Group II (24–71% hibernation) — 2.7 g per day; and Group III (0–20% hibernation) — 5.8 g per day.

*Excerpted from: Sarnat BG, Hook WE. (1942) Effects of hibernation on tooth development. *Anat Rec* **83**: 471–493.

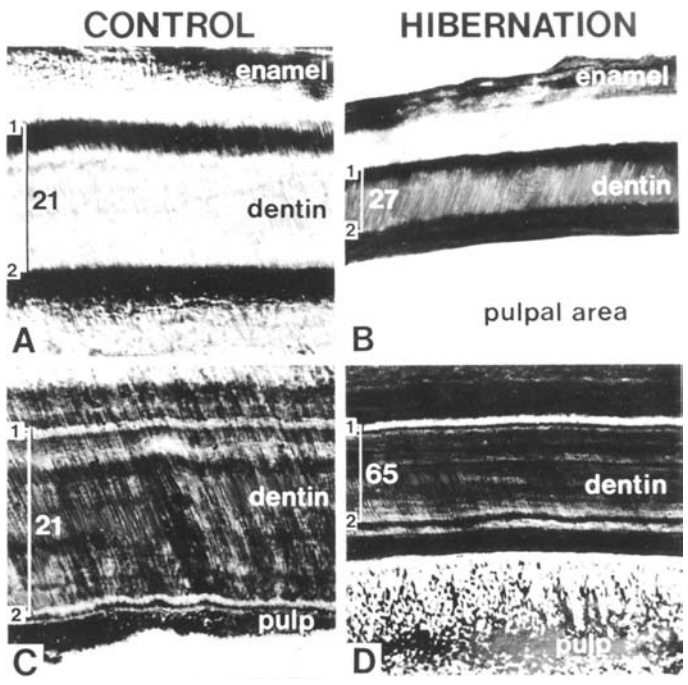

Fig. 25.1 (**A**) Photomicrograph of a longitudinal ground section of the upper left incisor of control 13-lined ground squirrel No. 44. 1 and 2: Effects on dentin of the first and second intraperitoneal injections of alizarin red S administered 21 days apart. The distance between the two lines (measured at the incisal third) was 232 μm. The daily rate of apposition was 11.0 μm. (**B**) Photomicrograph of a longitudinal ground section of the upper left incisor of experimental animal No. 29. 1 and 2: Effects on dentin of the first and second intraperitoneal injections of alizarin red S administered 27 days apart. The distance between the two lines (measured at the incisal third) was 109 μm. The first injection was given 4 days before the animal was placed in the constant temperature room at 2°–5°. The second injection was given 2 days after return to laboratory temperature. The calculated rate of daily dentin apposition was 1.5 μm. (**C, D**) Photomicrographs of longitudinal demineralized hematoxylin and eosin-stained sections of the upper right incisors of animals No. 33 and No. 58. 1 and 2: Calciotraumatic lines (dark hematoxylin-stained stripe preceded by light eosin-stained stripe); effects of the first and second intraperitoneal injections of alizarin red S. (**C**) Animal No. 33 was maintained at the standard laboratory temperature, and the time between the first and second injections of alizarin red S was 21 days. (**D**) Animal No. 58 was maintained at 2°–5° for 59 days. The injections of alizarin red S were administered 65 days apart, 4 days before and 2 days after the animal was at 2°–5°. The animal was euthanized 7 days after the second injection of alizarin red S (original modification, ×125). [Modified from: Sarnat BG, Hook WE. (1942) *Anat Rec* **83**: 493.]

(3) The rate of dentin apposition of the incisor was likewise retarded in approximate proportion to the time the animal hibernated. The average rate in the control animals was 12.8 μ per day. The calculated rate in the experimental group was: Group I (86–100% hibernation) — 1.5 μ per day; Group II (24–71% hibernation) — 2.5 μ per day; and Group III (0–20% hibernation) — 6.6 μ per day (Fig. 25.1).

This report shows that all of the stages of tooth development, namely growth, calcification, eruption, and attrition, are severely retarded during hibernation. This is in accord with the extreme depression of general metabolism in hibernation.

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Yellow Phosphorus and Teeth*

INTRODUCTION

The purpose of this investigation was to study and compare the effects of prolonged administration of yellow phosphorus on growing bones and growing teeth and to determine, if possible, the mechanisms of these effects. Reports on the effects of yellow phosphorus on growing teeth have not been found (see Chapter 31).

GROWING TOOTH

In the rat, the incisor grows and erupts continuously, whereas the molar is of limited growth and eruption. For this reason, the dentin of the incisor is renewed about every 35 days, but the molar is permanent. The dentin is laid down from the pulpal surface, one layer within the other, and is like a kymographic record. Once dentin is formed and calcified, it is, unlike bone, not subject to mineral exchange. The record will last for the life of the dentin. Changes in the general condition of an animal may cause abnormal formation and calcification of dentin, which is demonstrable histologically. Yellow phosphorus has a general deleterious effect on the animal, and consequently the calcification of the dentin produced while the animal is receiving the drug is abnormal. The deeply hematoxylin-stained narrow stripe in the dentin which corresponds to the time of

*Excerpted from: Adams CO, Sarnat BG. (1940) Effects of yellow phosphorous and arsenic trioxide on growing bones and growing teeth. *Arch Pathol* **30**: 1192–1202.

dietary change has been observed also after parathyroidectomy, hypophysectomy, and in fluorosis. It has been termed "the calciotraumatic line."

The effect of yellow phosphorus on growing bones is dependent on diminished resorption of bone and cartilage matrix. A similar change in the tooth is not expected, because dentin resorption is not physiologic. Comparison of our findings on teeth and bones show that yellow phosphorus has similar effects on teeth and dissimilar effects on bones. It can be concluded, therefore, that yellow phosphorus has a nonspecific effect on dentin (Table 26.1).

Since the rate of long bone growth is diminished, one might also expect the rate of dentin apposition to be diminished. This could be studied by injecting sodium alizarin red S and examining ground sections of the growing teeth. By means of the phosphorus bands, the rate of growth of long bones has been studied roentgenographically. From our observations, similar studies on roentgenographs of growing teeth would not be possible.

No changes were found on the roentgenographs of the growing teeth. Histologically, zones of disturbed mineralization were found in the

Table 26.1 Differences Between Endochondral Bone and Dentin*

Endochondral Bone (Normal)	Dentin (Normal)
1. Subject to resorption (record not permanent)	1. Not subject to resorption (record permanent)
2. Bone preformed in cartilage	2. Single process of formation and calcification
3. Cellular	3. Acellular
4. Vascular	4. Avascular
Affected by administration of yellow phosphorus	
1. Specific effect (resorption of bone diminished)	1. Nonspecific effect (no resorption possible, but calcification disturbed)
2. Evident roentgenographically	2. Not evident roentgenographically
3. Variation in dosage not readily recognizable histologically	3. Variation in dosage recognizable histologically

*Reprinted from: Adams CO, Sarnat BG. (1940) Effects of yellow phosphorus and arsenic trioxide on growing bones and growing teeth. *Arch Pathol* **30**: 1192–1202.

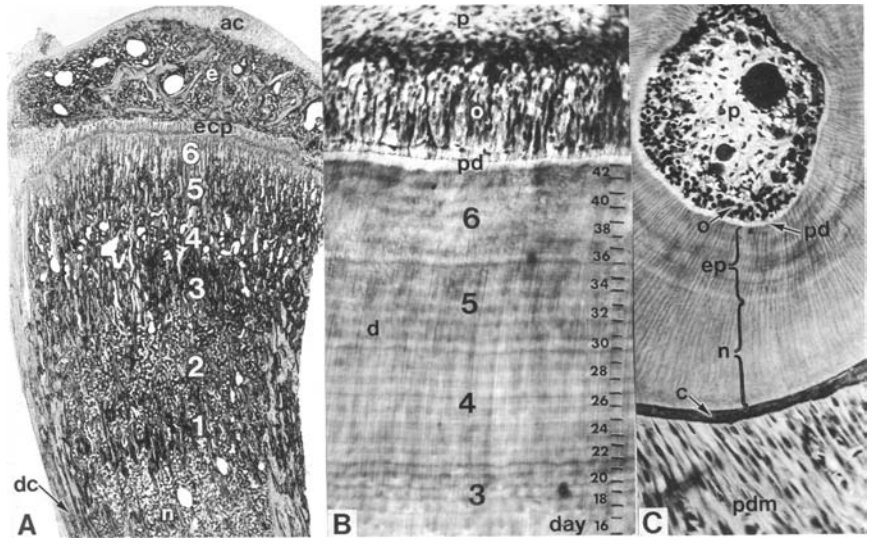

Fig. 26.1 Photomicrographs of demineralized sections in the rat of (**A**) the proximal end of a tibia; (**B**) the labial dentin of an incisor; and (**C**) a molar; for which 0.01% yellow phosphorus was added to the cod liver oil of the diet during the first, third, and fifth weeks of the experiment and which was killed at the end of the sixth week. (**A**) ac — articular cartilage; e — epiphysis; ecp — epiphyseal cartilage plate; dc — diaphyseal cortex; n — pre-experimental period. (**A**, **B**) 1, 3, and 5 — the effects of yellow phosphorus administered during the first, third, and fifth weeks; 2, 4, and 6 — the periods of the second, fourth, and sixth weeks, during which no yellow phosphorus was administered. (**B**) d — dentin. (**B**, **C**) p — pulp; o — odontoblasts; pd — predentin. (**C**) pdm — periodontal membrane; c — cementum; n — pre-experimental period; ep — experimental period. Because the rat incisor (**B**) is a tooth of continuous growth and eruption, the record of only the last four weeks remains. The rat molar (**C**), a tooth of limited growth and eruption, will retain the record permanently. In the rat that received yellow phosphorus, the rate of apposition of dentin of the molar was about 10% of that of the incisor and about 0.02% of that of apposition of tibial bone [hematoxylin and eosin; original magnifications: (**A**) ×20, (**B**) ×221, (**C**) ×315].

dentin of the rat incisors and molars that corresponded to the period of the ingestion of the drug (Fig. 26.1). By the use of roentgenographs, yellow phosphorus could be employed to measure the rate of growth between the phosphorus bands of selected bones but not of teeth. This difference is attributed to the dual capacity of bone for deposition and resorption whereas teeth usually have the capacity for only deposition.

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Anodontia*

INTRODUCTION

The importance of the deciduous and permanent teeth in the development of the face and jaws has been a much-debated question for a long time. A child aged one year and nine months was referred to us, because no teeth had appeared in the oral cavity. Roentgenographic examination revealed the complete absence of teeth and tooth buds. Study of serial cephalometric roentgenographs taken up to the age of five years and four months showed that craniofacial development was within the lower limits of normal and proceeding at a normal rate.[1]

The previous report (2–5 years of age) was concerned with the period of growth and eruption of the deciduous dentition and craniofacial development. This report is concerned in addition with a 10-year follow-up (6–16 years of age) of craniofacial development in the same patient with complete anodontia during the period normally covering eruption of the permanent dentition. Serial cephalometric roentgenographs and photographs were taken at periodic intervals. Five complete, upper and lower dentures were constructed. No other similar study has been reported.

*Excerpted from: Sarnat BG, Brodie AG, Kubacki HW. (1953) Fourteen-year report of facial growth in case of complete anodontia with ectodermal dysplasia. *AMA Am J Dis Child* **86**: 162–169.

REPORT OF A CASE

Period from 2 to 5 Years of Age

E. Z., a white boy aged 1 year and 9 months was referred to us, because no teeth had appeared in the oral cavity.

The mother had no difficulty during pregnancy and delivered an apparently normal, full-term, 3,775 g boy. The growth and development of the child during the neonatal and infancy periods were normal. He was given a diet consisting of breast milk (until 7 months of age), orange juice, and cod liver oil under the direction of the physician.

Because the child had no teeth, when he was about 10 months of age the mother consulted a physician, who assured her that the teeth would appear eventually. She was again assured on this point when the boy was 1 year and 6 months of age. At 1 year and 9 months the patient was referred to us, after a physician had taken intraoral roentgenographs and found no evidence of tooth development.

The presence of eczema and lack of hair were noticed. The patient did not perspire, and it was necessary to apply cold, wet packs to keep him cool on hot days.

The father and mother were of Polish descent and had no other children. Neither parent nor any relative of the parents was known to have a condition similar to that of the patient.

Physical examination revealed a well-developed, well-nourished, mentally alert boy with albinoid, lanugo-like hair sparsely distributed over the scalp. The skin was dry and scaly. There were neither eyebrows nor eyelashes and no axillary hair. There were no pigmentary changes in the iris; the lens and the fundus of the eye were normal. The skin of the lower eyelid toward the inner canthus was hyperpigmented and strikingly wrinkled. Lacrimation was observed. The bridge of the nose seemed to lack the normal prominence. On closure of the mouth the thickened lips pouted and gave the patient an aged appearance. The toe- and fingernails were present and normal. The remainder of the physical examination revealed no abnormalities. After a complete anthropometric examination, the patient was reported to be within the lower limit of normal.

The blood cell count and urine were normal. The Wassermann serologic reaction was negative. Examination of roentgenographs of the carpal bones taken when the patient was aged 4 years and 5 months showed four and five centers of ossification in the right and left wrists, respectively. Thus, carpal development was consistent with chronologic age. Microscopic examination of serial sections of skin obtained for biopsy from the right forearm failed to show the presence of either sweat or sebaceous glands or of hair follicles. A psychometric examination (revised Stanford–Binet, Form L) at a chronologic age of 3 years and 11 months revealed a mental age of 5 years and an intelligence quotient of 128.

Period from 6 to 16 Years of Age

During this period nothing unusually different occurred. General growth and development seemed to be well within the normal range. The albinoid, lanugo-like hair of the scalp was longer and less sparse. Fine, short, sparse eyelashes were now present. There was no evidence of either eyebrows or body hair. Four to five short, brown hairs were seen in each axilla and the pubic region. The skin was still dry and scaly, and a diagnosis of atopic dermatitis was made. Slight perspiration had been observed only in the axillae. There were no siblings.

Gross Study of Increase in the Size of the Jaws

When the patient was not yet 6 years of age, he was referred to the Department of Prosthodontia for the construction of full upper and lower dentures to improve masticatory function and facial appearance (Fig. 27.1).

Examination revealed a facial form and expression typical of an edentulous patient, with a loss of vertical dimension and protrusion of the lower jaw when the mouth was completely closed. Intraoral examination revealed the complete absence of teeth. The vestibule and the palate were well defined. There was no semblance of an upper or lower dental ridge other than a series of folds of soft, movable tissue.

Complete upper and lower dentures were constructed by the usual methods. The jaw relationship was determined, and the proper vertical dimension and free-way space were established. A total of 20 porcelain teeth

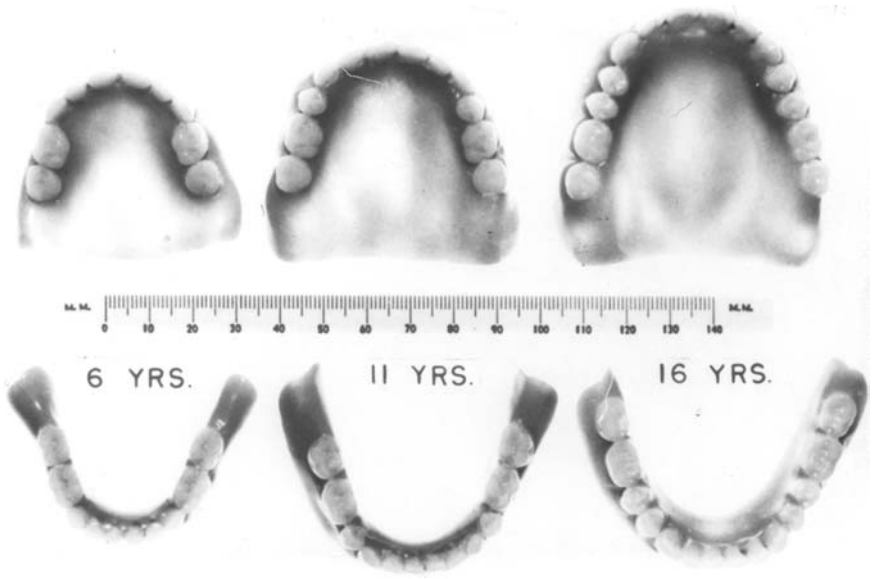

Fig. 27.1 Three of five sets of full upper and lower dentures made during the period from 6 to 16 years of age. Note the increase in the size of the dentures as well as the increase in the size and number of teeth.

were used in the upper and lower dentures. The full complement of posterior teeth was not supplied, because of the shortness of the arches (Fig. 27.1). The patient, despite his age, proved to be very cooperative. He learned to wear his dentures in a few days. In fact, after two days the patient had eaten popcorn for the first time in his life. The fact that he now had teeth was of tremendous value psychologically in his relation with other children.

Over the years, with increased growth, additional dentures were constructed, each time with larger and more teeth (Fig. 27.1). At one time, because the upper denture had been fractured, the patient refused to go to school until the denture had been repaired. The dentures had little, if any, restraining effect upon the growth of the jaws.

Serial Cephalometric-Roentgenographic Study

Cephalometric roentgenographs were taken at 6–12-month intervals from 22 months to 16 years of age (Fig. 27.2).

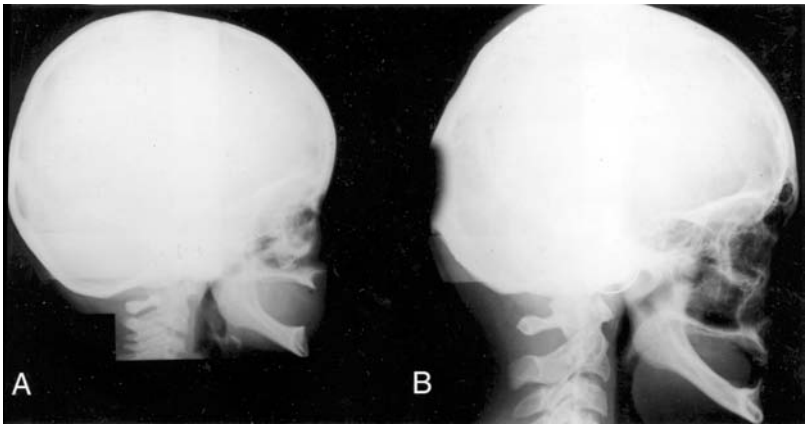

Fig. 27.2 Lateral cephalometric roentgenographs of the same patient with complete anodontia: (**A**) at 3 years of age; (**B**) at 16 years of age. Note the complete absence of teeth or tooth buds. Compare the lack of development of the face (**A**) and the development of the face (**B**). Also note the development of the frontal and maxillary sinuses and the ossification of the vertebrae in **B**.

One of the most striking features observed from the roentgenographs of the patient was the fragile appearance of the facial skeleton and the very high degree of pneumatization. All sinuses were extensive and were contained within extremely thin walls. The nasal cavity was developed far beyond the normal range except at its anterior apertures. No alveolar process was present. With these exceptions, the dimensions of the head, i.e. the cranium, cranial base, depth of face, and length of mandible, were all equal to or greater than small normal.

SUMMARY AND CONCLUSIONS

A patient with complete anodontia and ectodermal dysplasia has been studied clinically and roentgenographically from 2 to 16 years of age. Because of lack of sweat and sebaceous glands, he has been uncomfortable at times. The sparse, lanugo-like hair has increased in amount, but still lacks pigment. Five sets of full upper and lower dentures have been designed, constructed, and delivered during this time. Each successive denture was larger and contained more and larger teeth to accommodate the increase in the size of the jaws.

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Ameloblastoma*

INTRODUCTION

Ameloblastoma develops from the cells of the enamel organ during a particular phase of tooth development. It is found most frequently in the mandible, less so in the maxilla, and occasionally in the pituitary gland, tibia, ulna, and ovary. For the purposes of this report, only the ameloblastoma of the mandible will be considered. Although this tumor is considered to be uncommon, there have been over 400 reported.[1–5] The two sexes are affected at about equal frequency. The ameloblastoma has been recognized at birth and as late as the 76th year; the average age in Robinson's series was 37.6 years.[5] The ameloblastoma is generally described as a benign neoplasm, although in a study of 379 tumors, 4.5% showed metastases or historic evidence of malignancy.[6] A better-known characteristic of this tumor is its persistence and tendency to "recur" after operative intervention. This is probably due to inadequate surgical treatment. The purpose of this report is to consider (1) the surgical treatment of the ameloblastoma of the mandible and (2) the reconstruction necessary subsequently.

*Excerpted from: Byars LT, Sarnat BG. (1945) Surgery of the mandible: the ameloblastoma. *Surg Gynecol Obstet* **81**: 575–584.

DIAGNOSIS

Clinical Findings

The ameloblastoma which is most frequently seen in young adults, is characterized by a slow, progressive swelling of the jaw, usually near the angle. The tumor sometimes attains large proportions (Figs. 28.1A, 2), extends toward the clavicle, and weighs several pounds. The growth may be accompanied by pain. There is usually a history of a tooth or teeth having been extracted from the area several years previously and of several attempts surgically to eliminate the tumor. Fistulous tracts leading to the oral cavity and secondary infection of the tumor are not uncommon.

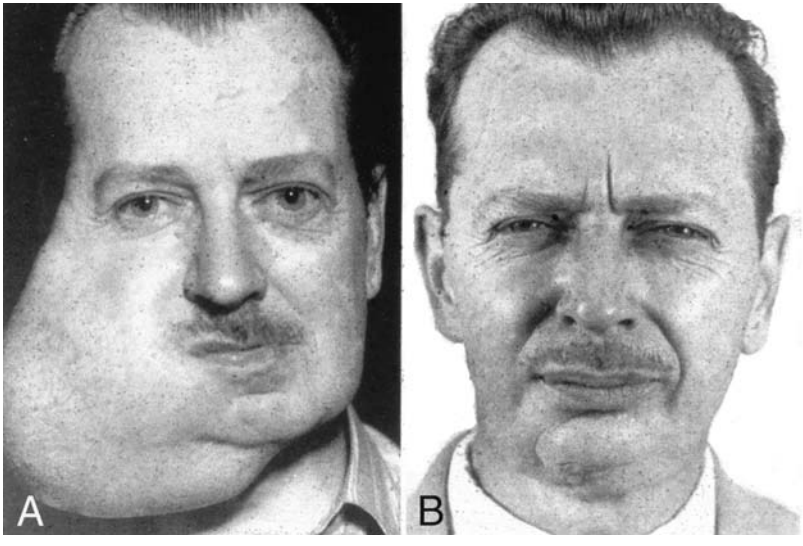

Fig. 28.1 (A, *left*) Photograph of a patient with a large ameloblastoma of the right side of the mandible. F. R., white male, aged 43 years. Swelling was first noticed inside the right side of the mouth 30 years previously. The mass had continued to grow notwithstanding numerous surgical procedures. The patient was told that the operation would be worse than the disease and was told to go home and forget about it. When the patient was seen he had been unable to work for the past few years. A hemisection of the mandible was done and he has worked ever since his recovery from the operation and has enjoyed good health. (B) Postoperative photograph after resection of the mandible.

The buccal plate of bone is usually expanded most, although the lingual bone may be expanded to push the tongue to the opposite side of the mouth. The bone is sometimes so thinned that it will crack like an eggshell. These are late findings, after the tumor has changed from the solid to the cystic phase. The patient may be seen only after pathologic fracture has occurred. Only occasionally do true signs of malignancy appear.

Roentgenographic Findings

The roentgenograph serves as a valuable adjunct to the diagnosis of cystic lesions of the jaw, but the final diagnosis depends on the gross and particularly the microscopic examinations. The roentgenograph is most valuable for the early diagnosis of ameloblastomas of the jaw when the tumor is still centrally located, has not expanded the bone, and is in the solid phase. It is at this time, when most of the mandible is as yet not destroyed, that the tumor can be removed completely, with no serious deformity resulting to the patient. When the ameloblastoma has become cystic and considerably larger, the clinical findings are obvious and the roentgenograph is of primary value in showing the extent of bone destruction. There is no constant characteristic roentgenographic description of the ameloblastoma. The multilocular appearance and the scalloped border are by no means pathognomonic. The ameloblastoma, giant cell tumor, carcinoma, and other lesions which are destructive cannot be positively differentiated from each other on the roentgenograph.[3]

Gross Findings

The findings on gross examination vary with the stage of development of the ameloblastoma. Analysis of 219 cases revealed that 57.5% were cystic, 24.2% were both cystic and solid, and 19.1% were solid.[6] This classification is arbitrary and combinations of the solid and cystic tumors are found in varying degrees. The solid tumor which usually represents an earlier stage of development is of fine granular consistency, and encapsulated. There may be one principal mass with numerous smaller daughter areas. The cystic type usually represents the solid tumor after cystic degeneration. The contained

fluid may be clear yellow to red and of either mucous or serous consistency. The bone is expanded and may be parchment-thin (Fig. 28.2C).

Microscopic Findings

Interpretation of the microscopic findings on the ameloblastoma is facilitated by an understanding of the histology of the enamel organ (Fig. 24.1).

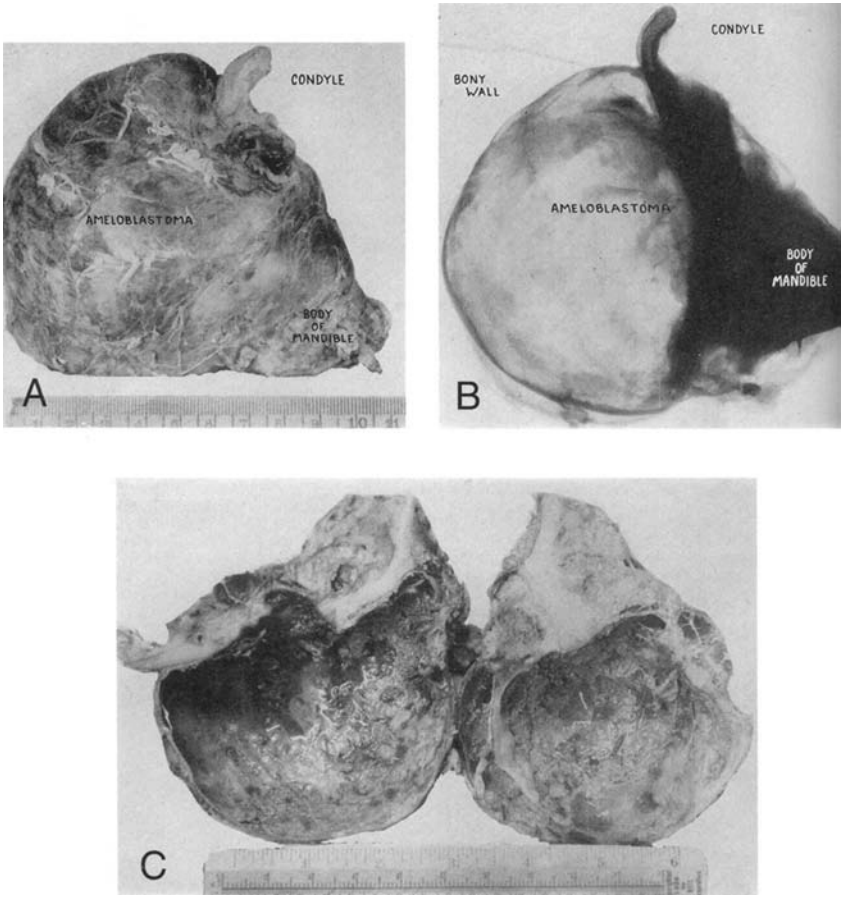

Fig. 28.2 Photograph (A) and roentgenograph (B) of the tumor and mandible which were resected. In B note the distortion of the condyle, ramus, and angle of the mandible and the absence of the coronoid process. (C) Photograph of a specimen after it was cut in two. Note the large single cyst, the small cysts, and the solid tumor.

Thoma[8] stated that there are many variations due to the stage of differentiation which the epithelium may attain when the tumor formation begins, the behavior of the stroma, and the malignant changes which may develop. Malignant changes, although uncommon, do occur.

Simmons[7] stated that where the cuboidal cells predominate, the growth is more malignant than in the cystic type with well-developed, ameloblast-like cells. Schweitzer and Barnfield[6] believed that there was no apparent correlation between the histologic pattern of the ameloblastoma and the ability to metastasize.

SURGICAL TREATMENT

Inasmuch as radiation does not affect the ameloblastoma materially, the treatment of this tumor of the jaw is primarily surgical. Both the surgical approach and the procedure which is carried out depend not only upon the diagnosis of the type of tumor but also upon its extent. In some instances the extent of the tumor will be such as to determine the type of surgical approach. In other cases, it is first necessary to know the type of tumor with which one is dealing and to determine, subsequently, the surgical approach and procedure. Clinical examination and roentgenography studies will sometimes be adequate for making the diagnosis. However, in a large group of mandibular tumors, diagnosis will still not be certain even after examination of both patient and roentgenograph.[2]

In this latter group, either preliminary biopsy for examination of a frozen section at the time of operation is of advantage. An accurate microscopic diagnosis will give the operator courage to do a radical operation if necessary or will give confidence in the less radical procedure. However, it has not been our practice routinely to do a resection of the jaw in dealing with the ameloblastoma. The more accessible lesions are first removed locally. The patient is warned that repeated postoperative examinations will be necessary over a long period of time in order to discover possible extension of the tumor. In many instances, (1) where a large portion of the mandible is involved, (2) where the tumor has definitely invaded beyond the confines of bone, or (3) where inaccessible areas of the mandible are involved so that local excision could not be adequate, resection of the mandible is the primary treatment of choice (Fig. 28.1). Sometimes the

choice of whether to do a local excision or radical resection must be made only after surgical exposure of the area of involvement. Especially is this true where the surgical approach is from the outside through the neck. In almost every instance where the surgical approach is from the inside of the mouth, local removal is done.

Intraoral Approach

Having made the decision to do a conservative local removal rather than a resection of the mandible, adequate exposure must be gained by freeing overlying soft tissues and attached mucoperiosteum over the complete extent of the tumor. Following this, overlying bone should be removed adequately, so as to give a complete exposure of the underlying tumor and to permit partial obliteration of the cavity which results from the removal of the tumor. This obliteration is accomplished by collapse of soft tissue into the cavity. It is preferable not to rupture the capsule of the tumor itself during the operation. In many instances of the less loculated type of tumor, the growth may be removed completely and without spillage. Under these circumstances there is less possibility of continued growth of the tumor.

Many of the multilocular tumors have irregular outlines and crevices in the bone at which point the tumor is usually broken into during the process of removal. One should never start out to do a curettement removal of this type of growth. It is much better to attempt total enucleation where possible. In multilocular or more invasive tumors one can become involved in a piecemeal removal of the tumor, however, and a certain amount of curettement will be necessary. Under these circumstances it is obvious that small fragments of growth will be left behind and necessitate removal at a later date.

To prevent this difficulty, cauterization of the cavity has been recommended. This cauterization may be either chemical or thermal. In general, the criticism of chemical cauterizing agents is that one cannot accurately determine the depth of penetration of the chemical so that cauterization tends to be either too great or too little in extent. The extent to which penetration goes and destruction is brought about with the thermal agent is better regulated than with the chemical. If the ameloblastoma has not been

removed completely, it has been our practice to use the electrosurgical unit or Bovie knife with the coagulating current and to go over the exposed bone surface. Heavier cauterization is done in areas of greater contamination with tumor tissue. The disadvantage of this procedure is that a certain amount of bone will be devitalized and sequestration will occur. In the meantime, the presence of the devitalized bone will delay healing. However, if the tumor and its immediate bony confines have been completely removed or destroyed, a cure is almost sure to result.

Extraoral Approach

The external approach for both resection of the mandible and local excision of the growth is the same. This incision should parallel the natural fold in the skin of the neck. It should be made underneath the mandible and should be adequate in extent to give complete exposure. The course of the lowest branch of the facial nerve in the neck should be remembered. This nerve can be preserved if the approach is carefully planned. The incision should be marked on the skin with the head in a normal position and should be 2 cm below the angle of the mandible. A flap containing skin, subcutaneous tissue, and platysma is then elevated. This includes the lower pole of the parotid gland and soft tissues anterior to it. Unless the lower pole of the parotid is elevated with this tissue, the facial nerve must inevitably be severed. The entire ramus as well as the angle and most of the body may be thus exposed. Having exposed the area of the tumor, removal may be done in one of three ways. The procedure of local removal by shelling out the tumor and applying the cauterizing agent may be followed in certain cases. In other instances it is possible to do a partial block resection of the mandible; the Albee saw is used to remove the tumor and a containing block of bone, but a bridge of bone is left to maintain the continuity of the mandible. This is rarely feasible. The third method is to resect the mandible (Figs. 28.1, 28.3).

The site of resection of the mandible has usually been determined beforehand by studying the roentgenograph. If possible, some portion of periosteum is left intact to bridge the gap. All bleeding is controlled. Where possible, mucosa is sutured so as to screen off the mouth from the neck portion of the wound, thus giving less contamination. The neck wound is closed accurately with a drain inserted.

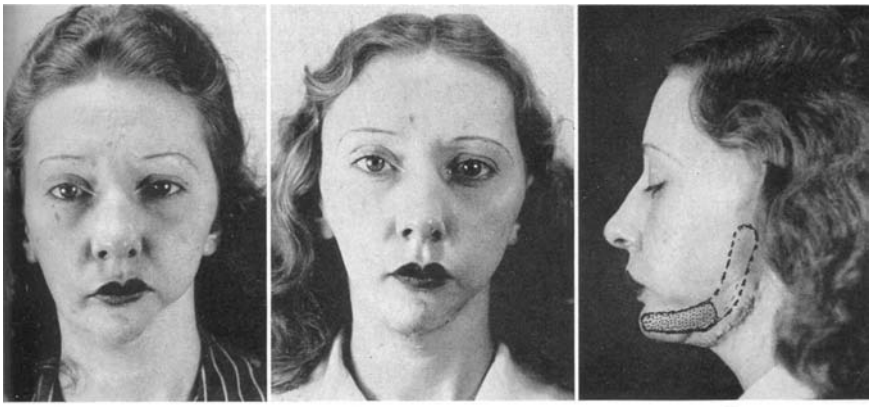

Fig. 28.3 (**A**) Preoperative and (**B**, **C**) postoperative photographs of a patient who had lost the entire left side of the mandible. The bony and cartilaginous portions of a rib were utilized. The bony portion was attached to the remaining mandible and the cartilaginous portion was adjusted and inserted into the temporomandibular fossa. Note the increased fullness of the left side of the face in **B**. (**C**) The dotted line indicates the position of the graft, the stippled area represents the bony portion of the graft, and the clear area represents the cartilaginous portion of the graft.

Maintenance of Jaw Fragments

Wherever a resection is done some provision must be made to maintain the remaining fragments of the mandible in as near proper position as possible prior to bone graft repair. If there has been disarticulation in removal of the ramus, then only the anterior fragment must be considered, and in this case the simplest and best method of maintaining the position is to wire the remaining teeth in occlusion until complete soft tissue healing has taken place. This same procedure may be the simplest also where there are teeth on both the anterior and posterior fragments. However, if the resection has been near the angle of the mandible so that the angle and ramus remain as the posterior segment, some means must be taken to maintain not only the space between fragments but also the posterior fragment in its proper position. Various methods have been used to control the posterior fragment. It is essential that this space retention is maintained until there is complete soft tissue healing.

Otherwise, as soft tissue healing occurs, there will be progressive dislocation of the fragments by the pull of the new, forming scar tissue and the various muscles. This dislocation will interfere with later repair by bone grafting. This is especially common where mucosa has been removed and a granulating wound has been left inside the mouth to heal by secondary intention.

Reconstruction of the Defect

Many patients have apparently been content to continue without having the defect in the mandible repaired. In some instances it has been possible for them to wear dentures. Unquestionably, the patient is more comfortable and the situation is more normal if a repair of the resected area of the mandible can be obtained with bony union. A number of methods may be employed but in general a free bone graft is the most desirable procedure.

To carry out the procedure of a free bone graft satisfactorily, certain essentials should be present. The fragments of the mandible which remain must be free enough so that they can be not only placed but also maintained in their proper position during the time that the bone graft is healing in place. It is extremely important that the covering soft tissue is adequate in quality and amount to give good covering and nourishment to a bone graft. If the overlying tissue has been damaged to the point where it is scarred and tight, the graft is likely to be extruded. If it is necessary to dissect dense scar tissue from between the ends of the bone before they can be restored to their proper position, then this must be done prior to the insertion of the bone graft, to prevent mouth contamination. In certain instances it may even be necessary to apply additional soft tissue by means of flaps to replace the scar or to supplement inadequate covering material.

The bone graft either may be massive, using the half or full thickness of the rib or a section of the ilium, or it may be thin, as in the case of the osteoperiosteal graft taken from the tibia. This type of graft may be applied in several thicknesses. Regardless of the type of graft used, it is desirable to overlay the ends of the mandible with an inch or so of the bone graft where possible, making the bone graft two inches longer than the defect. In some

instances the portion of the graft which overlaps the ends of the mandible may be thin while the portion between the ends is thicker. Sometimes a T-shaped graft may be employed, the thick arm of the T projecting in between the ends of the mandible. In all instances the bone grafts should be in as close contact with the mandible as possible and anchored to soft tissues or even to the bone itself with silk or fine tantalum wire sutures.

Where there has been a disarticulation of one side of the mandible, a rib graft containing cartilage and bone can be utilized. The cartilage end can be fitted into the temporomandibular fossa and the bony end attached to the remaining mandible (Fig. 28.3).

SUMMARY AND CONCLUSIONS

The ameloblastoma arises from the enamel organ during a particular phase of tooth development, namely morphodifferentiation. Because the cells from which this tumor arises are not as yet differentiated into ameloblasts, the term "preameloblastoma" is more accurate.

This tumor is found most frequently near the angle of the mandible in young adults. Although the clinical history and roentgenographic findings are an aid, the final diagnosis depends upon microscopic examination.

The tumor is slow-growing and unless completely removed will continue to grow (rather than recur). It seldom becomes truly malignant.

Curettement, cauterization with drugs, and radiation are inadequate therapeutic measures. The lesion should be (1) completely enucleated if unilocular, (2) cauterized by heat if not too large and multilocular, or (3) if extensive, resected, including a small amount of normal bone. These are the best methods of treatment because they give the greatest assurance of no tumor being left.

The surgical approach and procedure for various ameloblastomas and the necessary subsequent reconstruction surgery have been considered.

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Congenital Syphilis*

This report shows the value of routine intraoral roentgenographs of unerupted permanent teeth as an aid in the early diagnosis of congenital syphilis (Fig. 29.1). The growing teeth, like the bones and other organs, may be affected in congenital syphilis. The screwdriver-shaped and notched permanent upper central incisors are the most common and characteristic clinical dental abnormality. In congenital syphilis, the form (size and shape) of the tooth is altered during the stage of morphodifferentiation (Fig. 24.1). The primary requisite of the upper permanent central incisor and of the first permanent molar is a convergence of the lateral surfaces, with a resulting narrowed mesiodistal diameter of the crown.

A group of 73 patients with congenital syphilis were studied. Twenty-two (30%) had dental changes characteristic of this disease: permanent upper central (Hutchinson) incisors and first (Moon) molars. Congenital syphilis, a systemic disease which is exacerbated during the neonatal period and infancy, may affect the particular stage of tooth development active at the time (Fig. 24.1). No correlation was made between the severity of the disease in the neonatal period and earliest infancy and the dental development. These developmental disturbances of the teeth are permanent and have been found only in congenital syphilis. They can be

*Excerpted from: Sarnat BG, Shaw NG. (1942) Dental development in congenital syphilis. *Am J Dis Child* **64**: 771–778.

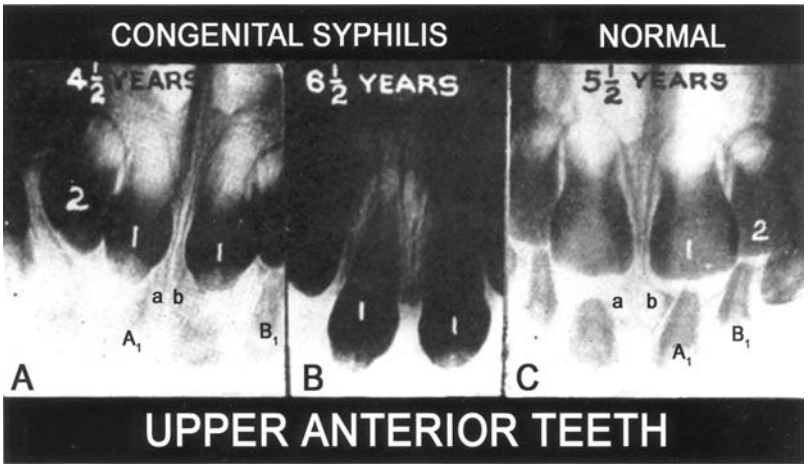

Fig. 29.1 (A) Deciduous upper central (A_1) and lateral (B_1) incisors in congenital syphilis. Unerupted permanent central (1) incisor. Note the convergence of the proximal surfaces at about the midcoronal level. The incisal third is irregular in density. The upper lateral incisors (2) are not affected. ab — alveolar bone. (**B**) Central incisors have erupted. The coronal portion is similar to that in **A**. The roots are now nearly completely formed and calcified. (**C**) Note the normal contour of the crowns and the divergence of the proximal surfaces. [From: Sarnat BG, Schour I, Heupel R. (1941) Roentgenographic diagnosis of congenital syphilis. *JAMA* **116**: 2745–2747.]

demonstrated roentgenographically prior to eruption (Fig. 29.1). In the 1930's and 1940's, Herman Bundeson, M.D., Director of the Chicago Public Health System, had in his program brought this condition under good control.

Enamel Hypoplasia*

Enamel hypoplasia occurs in the stage of dental development of appositional growth (Fig. 24.1). An extensive investigation was undertaken of the chronologic incidence, the morphologic pattern, and the possible etiologic factor or factors of enamel hypoplasia in relation to systemic disease (Fig. 30.1). Two-thirds of the enamel hypoplasia occurred during the infancy period (from birth to the end of about the first year), about one-third occurred during the early childhood period (about 13–34 months), and less than 2% occurred during the late childhood period (about 35–80 months). No specific cause was found. Exanthematous disease was not so frequent a cause of enamel hypoplasia as has been commonly believed. Possible causative factors were rickets, hypoparathyroidism, and fluorosis, but development of hypoplasia cannot be predicted with any reliability even in the severe forms of these diseases. In more than 50% of the patients studied, no causative factors could be determined. Except in fluorosis, enamel hypoplasia was not restricted to certain geographic localities, but was as ubiquitous as disease.

*Excerpted from: Sarnat BG, Schour I. (1941) Enamel hypoplasia (chronologic enamel aplasia) in relation to systemic disease: a chronologic, morphologic and etiologic classification, Part I. *JADA* **28**(12): 1989–2000. Sarnat BG, Schour I. (1942) Enamel hypoplasia (chronologic enamel aplasia) in relation to systemic disease: a chronologic, morphologic and etiologic classification, Part II. *JADA* **29**(1): 67–75. Winner of Capp's Prize, Institute of Medicine, Chicago; and the Noyes Award, College of Dentistry, University of Illinois.

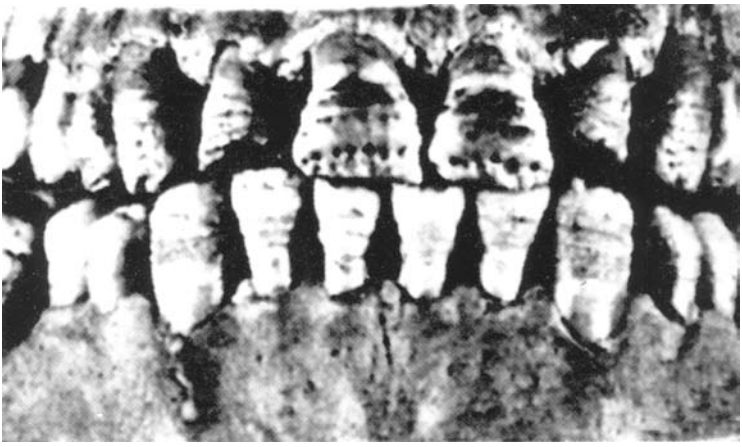

Fig. 30.1 Multiple enamel hypoplasias, characteristic of recurrent periods of disturbed metabolism.

PART V

THE CRANIUM

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The Skull Base, Sutures, and Long Bones*

INTRODUCTION

The purpose of this investigation was to study and compare the effects of prolonged administration of yellow phosphorus on growing bones and to determine, if possible, the mechanisms of these effects.

Wegner,[1] in 1872, was the first to experimentally produce transverse bands of increased density in the metaphysial regions of growing long bones by feeding yellow phosphorus over prolonged periods. We have chosen to designate these bone changes as *phosphorus bands.* Phemister,[2] in 1918, was the first to describe the roentgenographic appearance of phosphorus bands. No reports on the effects of yellow phosphorus on growing teeth have been found.

METHODS AND MATERIALS

Yellow phosphorus was given to 14 rats for periods varying from 22 to 57 days by replacing the cod liver oil of the diet with standard phosphorized cod liver oil. This contains 0.01% yellow phosphorus. In the diets of

*Excerpted from: Adams CO, Sarnat BG. (1940) Effects of yellow phosphorous and arsenic trioxide on growing bones and growing teeth. *Arch Pathol* **30**: 1192–1202.

6 of these rats, the yellow phosphorus was increased fourfold during the last weeks of the experiment.

RESULTS

The phosphorus bands in the proximal end of the tibia corresponded to the periods during which the animal received yellow phosphorus (Fig. 31A.1). In some of the animals which received yellow phosphorus over a period of four or more weeks, there was definite retardation in the normal process of tubulation.

In the roentgenographs of the skulls, there is a phosphorus band on both sides of the basispheno-occipital and basisphenopresphenoid junctions (Fig. 31A.1). Growth of these basal skull bones is by endochondral ossification, whereas most of the remaining skull bones grow by membranous ossification. The latter bones appear to be unaffected by the administration of yellow phosphorus.

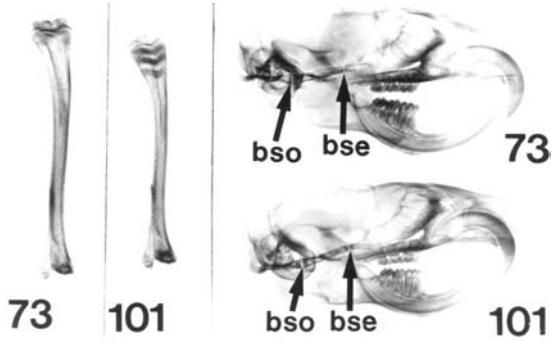

Fig. 31A.1 Roentgenographs of tibias and midsagitally sectioned skulls of rat No. 73, normal, and rat No. 101, which had 0.01% yellow phosphorus added to the cod liver oil of its diet in the first, third, and fifth weeks of the experiment. Both animals were killed at the end of the sixth week of the experiment. Three dense metaphysial bands corresponding to the periods of ingestion of yellow phosphorus are present in the proximal end of the tibia of rat No. 101. An increased density is seen on both sides of the basisphenooccipital (BSO) and basisphenopresphenoid (BSE) junctions. No changes are noted in the incisor or molar of rat No. 101. Note the lesser growth of both the tibia and the skull base in the experimental animal that received the phosphorized cod liver oil.

COMMENT

Growing Bone

Yellow phosphorus in the dosages stated has a general effect on the animal, as evidenced by failure to gain weight normally and retardation of longitudinal bone growth. The reduction in the rate of growth of the long bones may be the direct effect of the drug on the epiphysial cartilages.

Microscopic study shows that the increase in the number of trabeculae is apparently due to a reduced resorption of the intercellular calcified cartilage matrix which is left when the cartilage cells are released and disappear on the diaphysial side of the epiphysial cartilage plate. Normally, a large percentage of this matrix is resorbed, leaving only a few spicules on which bone is deposited. Yellow phosphorus evidently reduces this resorption and leaves many more spicules of matrix on which new bone is laid down. There results a great increase in the number of trabeculae in the metaphysis. Resorption of these newly formed trabeculae occurs less readily than normal, as evidenced by the retardation of tubulation and by the abnormal persistence of these trabeculae in the diaphysis. Additional new bone is deposited only in the portion destined to become the cortex of the shaft. The trabeculae in the metaphyses of the animals fed yellow phosphorus persist longer than normal.

SUMMARY

In the case of the animal given yellow phosphorus, a roentgenograph of the metaphysis of any growing long bone shows a zone of increased density — the phosphorus band. This same band can be seen grossly in the split specimen and histologically. There is a reduction in the process of tubulation of the shaft. *These effects are due to diminished resorption of cartilage matrix and bone.* This diminished resorption of bone is probably generalized but is readily evident only in the metaphyses, where extremely active bone resorption is a prominent feature of the process of normal endochondral bone growth.

Because of this increased density of metaphysial bone, children during the early 1900's were given phosphorized cod liver oil, particularly for rickets.

However, as demonstrated in this experiment, because bone growth was decelerated, use of this medication was discontinued.

Metaphysial bands of increased density caused by acute illnesses or lead, arsenic, bismuth, and other substances are probably produced by the same change as phosphorus bands, i.e. by diminution of the resorption of bone and cartilage matrix.

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2. Phemister DB. (1918) *JAMA* **70**: 1737.

Cranial Sutures: Clinical Considerations

CRANIOSYNOSTOSIS

Calvarial plates originate from neural-crest-derived cranial connective tissue and ossify from the center to the periphery. At the periphery fibrous cranial sutures develop between the calvarial plates. At the cranial base synchondroses occur. At birth, cranial sutures allow for necessary molding during passage through the birth canal. Postnatally, cranial sutures are growth centers for the expanding calvarium.[1] Growth of the skullcap is based on underlying brain growth and the cranial suture response to this growth.[2] Coordinated growth is achieved through tissue interactions among the brain, dura mater, suture mesenchyme and calvarial osteogenic fronts.[3] Important cell-to-cell communication is achieved by cytokine signaling and osteogenic factors.

Growth of the calvarial bone plates is perpendicular to the cranial sutures. Craniosynostosis, or premature fusion of the cranial sutures during this growth phase, results in an abnormal head shape and may lead to functional problems like increased intracranial pressure and/or vision problems. The most common type of craniosynostosis is the isolated form: 1 in 2000 live births.[2]

Single or multiple premature suture fusion results in characteristic head shapes[4] (Fig. 31B.1). Sagittal synostosis leads to scaphocephaly ("boat-shaped" head). Unilateral coronal synostosis leads to (anterior) plagiocephaly (oblique-shaped head). Bilateral coronal synostosis results in brachycephaly (wide, high anterior head). Premature metopic suture fusion leads to trigonocephaly ("triangle-shaped" forehead). (The metopic suture

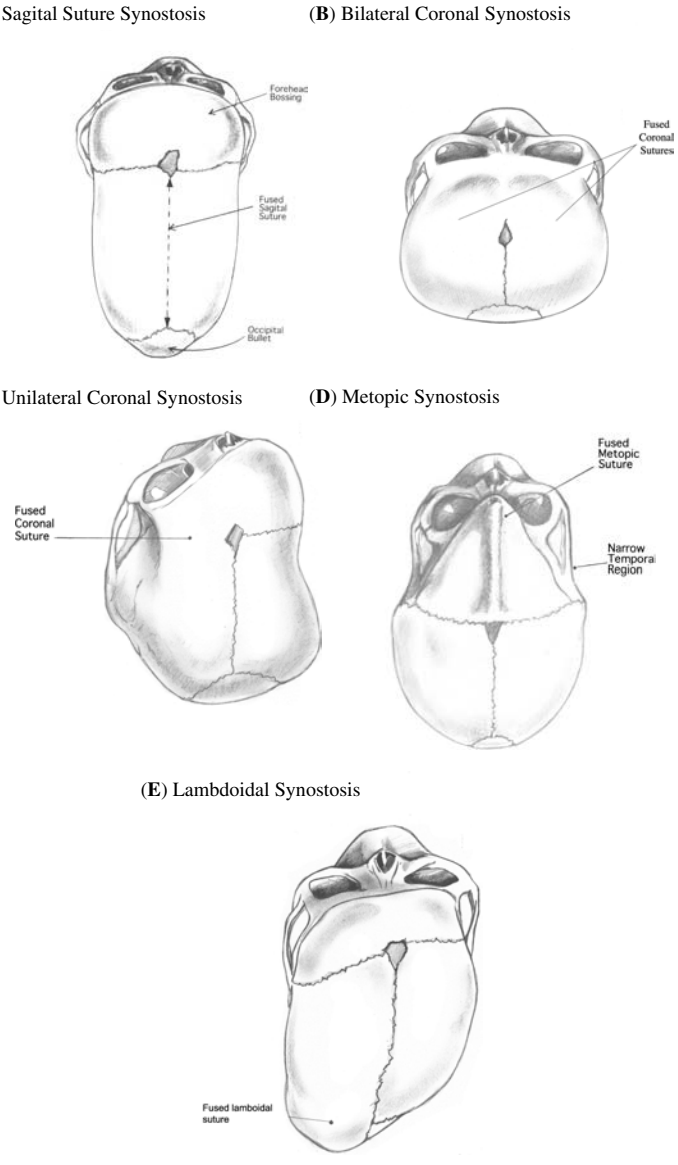

Fig. 31B.1 Characteristic head shapes from craniosynotosis. (**A**) Sagittal synostosis with scaphocephalic elongation and biparietal restriction. (**B**) Bilateral coronal synostosis with brachycephalic forehead flattening. (**C**) Left coronal synostosis with plagiocephaly, left forehead flattening, temporal bulging, and contralateral right forehead bossing. (**D**) Metopic synostosis with midforehead ridging and temporal narrowing. (**E**) Lambdoidal synostosis with posterior vault asymmetry and mastoid bossing.

normally fuses between birth and one year of age, so premature fusion occurs prenatally.) Lambdoidal synostosis leads to posterior plagiocephaly. Finally, multiple or even pansynostosis may result in a *kleeblattschädel* ("cloverleaf") head shape or a "normal-shaped" but smaller head.

Craniosynostotic syndromes have various phenotypic manifestations and include Apert syndrome, Crouzon syndrome, Saethre–Chotzen syndrome, Jackson–Weiss syndrome, Pfeiffer syndrome, carpenter syndrome, craniofrontonasal dysplasia, Antley–Bixler syndrome, and others. Genetic mapping has documented chromosomal gain of function mutations in fibroblast growth factor receptors (FGFR-1, FGFR-2, FGFR-3). Although FGFR mutations are the most commonly identified ones, MSX and TWIST syndrome mutations have also been found. These genetic findings provide important clues in investigating the biology of cranial suture fusion.[3]

Normal Suture Fusion: Rodent Model

When performing research at the Institute of Reconstructive Plastic Surgery, New York University, with Michael T. Longaker, M.D. and Joseph G. McCarthy, M.D., our laboratory began a series of investigations based on a model described by Moss in the 1950s.[1] He described posterior frontal suture fusion in a Sprague–Dawley rat. In this model the posterior frontal (PF) suture normally fuses between 12 and 20 days of life (Fig. 31B.2). This

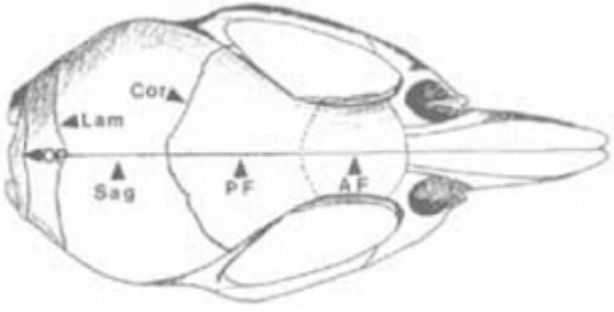

Fig. 31B.2 Normal suture fusion: rodent model experiment. Line drawing of a mouse skull and cranial sutures. OP = occipitointerparietal; Lam = lambdoidal suture; Sag = sagittal suture; Cor = coronal suture; PF = posterior frontal suture and AF = anterior frontal suture are labeled with arrows designating the location of each suture. The *jugum limitans* separates the AF and PF sutures and is represented by the dotted line. The *bregma* is the intersection of the coronal, sagittal, and PF sutures.

suture is analogous to the human metopic suture. All other rat cranial sutures (sagittal, coronal, lambdoidal, and anterior frontal) remain patent until senescence.

Moss also theorized that cranial base tensional forces acted through the dura mater to cause cranial suture fusion. Historically, investigators suggested that there was a problem intrinsic to the suture.[5] Virchow felt that the cranial suture acted independently of the surrounding neurocranial environment. Park and Powers theorized that craniosynostosis was a result of an abnormality in the suture mesenchymal tissue.[6]

Dura mater influence

Our initial investigation into Moss's normal suture fusion model involved exploring which regional tissue (suture mesenchyme, periosteum, or dura mater) was most important for cranial suture fusion. A series of investigations led to the finding that dura mater communication with the overlying suture was critical for suture fusion. In addition, this dura-mater–suture communication was most likely in the form of soluble factors.

Silastic barrier experiment

This experiment involved the study of placement of a silastic sheet barrier separating the dura mater from the overlying PF (fusing) suture.[7] Six-day-old Sprague–Dawley rats (a time point prior to the initiation of PF suture fusion) were divided into four groups: Group 1 — no operation (control); Group 2 — craniotomy only; Group 3 — craniotomy, dural dissection, and replacement of the bone flap; and Group 4 — silastic membrane interposition between the dura mater and the cranial suture (Fig. 31B.3). Both the PF (fusing) and sagittal (patent, control) sutures were studied in these groups.

Results of the silastic interposition study showed that the unoperated-on and craniotomy PF sutures fused (Groups 1 and 2), as expected, during the normal time frame (Fig. 31B.4). There was a slight delay in the elevated dura PF sutures (Group 3), which initiated delayed fusion at 22 days and completed it on day 30. Most interestingly, Group 4 animals with the dura mater silicone sheet separation remained patent throughout

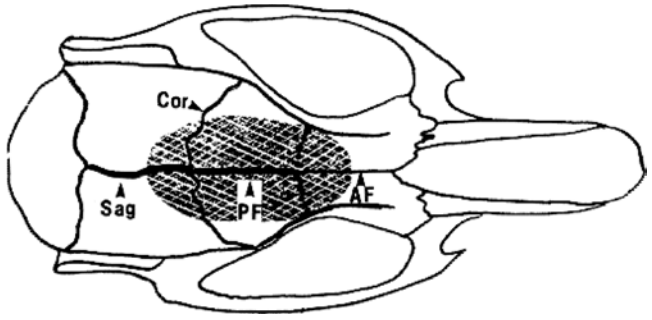

Fig. 31B.3 Silastic barrier experiment. Line drawing of a Sprague–Dawley rat skull and cranial sutures. Sagittal suture (Sag), coronal suture (Cor), posterior frontal suture (PF), and anterior frontal suture (AF) are labeled with arrows designating the location of each cranial suture. Note: The location of silicone sheeting placed surgically beneath the sutures and calvariae and above the underlying dura is identified by the oval shaded central area.

the normal PF suture time period of 12–20 days and did not initiate suture fusion until day 30 (Fig. 31B.5). Also, the sagittal suture remained patent in all four groups, including the silastic interposition group.

From these data we postulated that for normal cranial suture fusion dura mater communication was fundamental. In addition, we thought that the regional dura mater beneath the PF suture must secrete soluble factors to the overlying PF suture necessary for initiating cranial suture fusion. These osteoinductive factors are necessary for stimulating osteoblasts and augmenting the suture osteogenic front. Once this initiation occurred, the necessary extracellular matrix proteins could be laid down and ossification could take place. We found that normal suture fusion was in a consistent direction anterior to posterior and endocranial to ectocranial. Our next investigation was a mechanical rotation study designed to examine the regional specialization of dura mater.

Suture rotation experiment

Was dura mater signaling beneath the patent sutures acting to maintain suture patency or was it providing inadequate signaling for fusion? In this study we rotated the PF and sagittal sutures with respect to the underlying dura mater.[8]

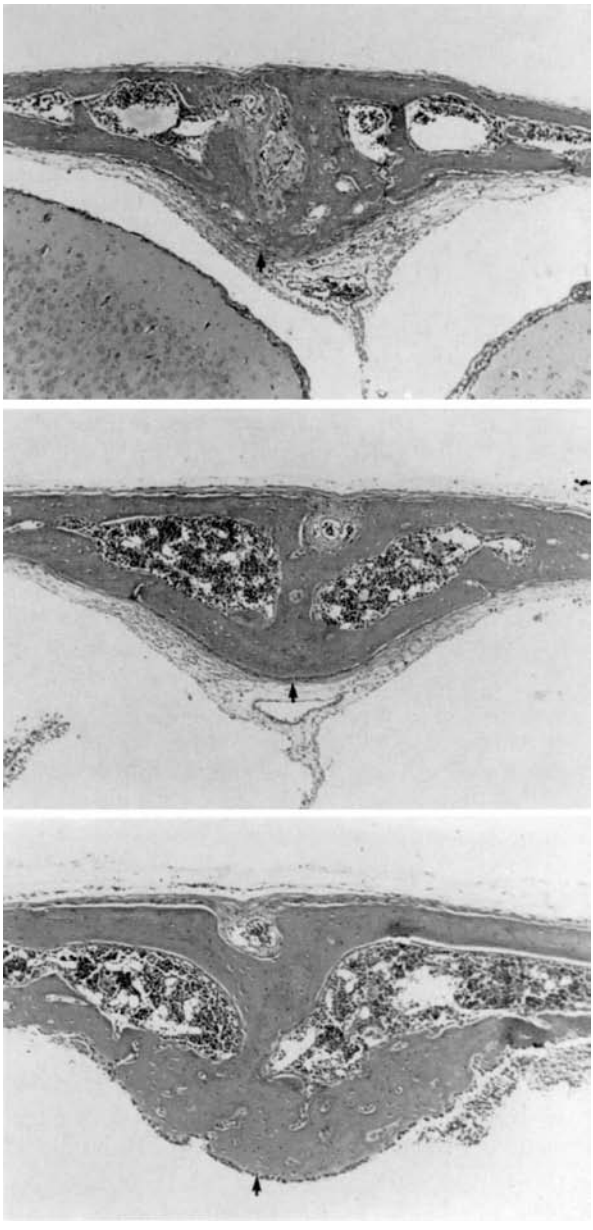

Fig. 31B.4 Silastic barrier experiment. Photomicrograph of Group A, unoperated-on control group (×250). *Top*: Day 15; fusion begins (up arrow) on the endocranial side of the suture. *Middle*: Day 22; the PF suture is completely fused (up arrow). *Bottom*: Day 30; the suture is fused (up arrow).

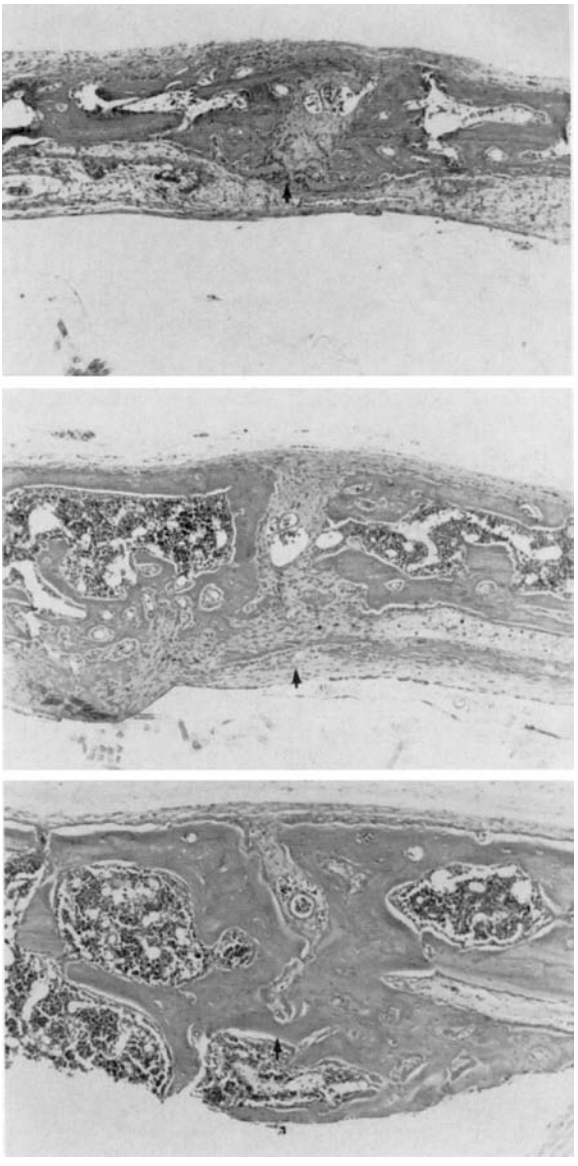

Fig. 31B.5 Silastic barrier experiment. Photomicrograph of Group B, experimental group (×250). *Top*: Day 15; the PF suture is patent (up arrow); silicone polymer remnants are seen in the lower left corner. *Middle*: Day 22; the suture remains patent (up arrow). *Bottom*: Day 30; the suture is beginning to fuse, as seen by the osteal bridge (up arrow) beneath the fibrous suture.

Eight-day-old Sprague–Dawley rats (at a time point prior to the initiation of PF suture fusion) were divided into two groups: Group 1 (control) — a rectangular osteotomy inclusive of the PF and sagittal sutures from the lambdoidal suture to the *jugum limitans* was made, and the flap was elevated and then replaced in an anatomic position in its original orientation; Group 2 (experimental) — the same craniotomy was performed, and the excised strip was rotated 180° about the midsagittal axis and then replaced on the dura (Fig. 31B.6). In the experimental group the PF (fusing) suture was rotated to overlay the sagittal dura and the sagittal (patent) suture was rotated to overlay the PF dura. Animals were euthanized at 20, 30, 40, and 50 days (12, 22, 32, and 42 days postoperatively), and tissue sections were examined with hematoxylin and eosin staining.

The control animals with the unrotated strip craniectomy showed sagittal suture patency and PF suture fusion in the normal, anterior-to-posterior and endocranial-to-ectocranial directions (Fig. 31B.7). By contrast, in the experimental group the PF suture (overlaying the sagittal dura mater) remained patent and the sagittal suture (overlaying the PF dura mater) fused (Fig. 31B.8). In addition, the rotated sagittal suture fused in the normal anatomic directions — anterior-to-posterior

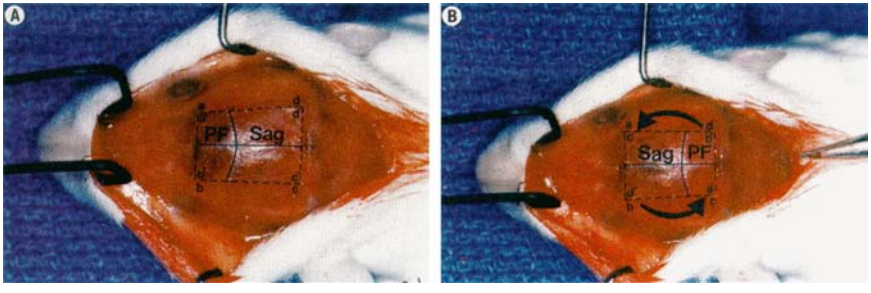

Fig. 31B.6 Suture rotation experiment. Photographs of the operative procedure. (**A**) Operative photograph of the control group (Group A). Elevation of the calvarial strip is inclusive of the posterior frontal (PF) and sagittal (Sag) sutures replaced in an anatomic position. a and a′, b and b′, c and c′, d and d′ are adjacent. (**B**) Operative photograph of experimental group (Group B). Elevation of the calvarial strip is inclusive of the posterior frontal (PF) and sagittal (Sag) sutures rotated 180° and positioned so that the posterior frontal suture overlies the sagittal dura mater and the sagittal suture overlies the posterior frontal dura mater. a is adjacent to c′, b is adjacent to d′, c is adjacent to a′, and d is adjacent to b′.

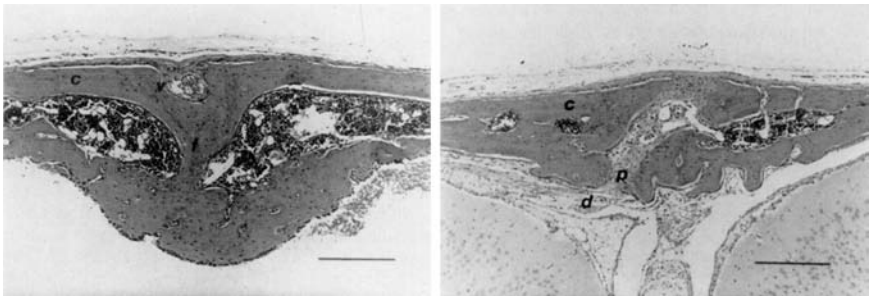

Fig. 31B.7 Suture rotation experiment. Schematic illustration of histologic cross section of a patent and a fused cranial suture (×250) (S — suture; D — dura; C — calvaria). *Left*: Patent cranial suture; the fibrous suture separates the opposing calvarial bone plates. *Right*: Fused cranial suture; the calvarial bone has obliterated the cranial suture.

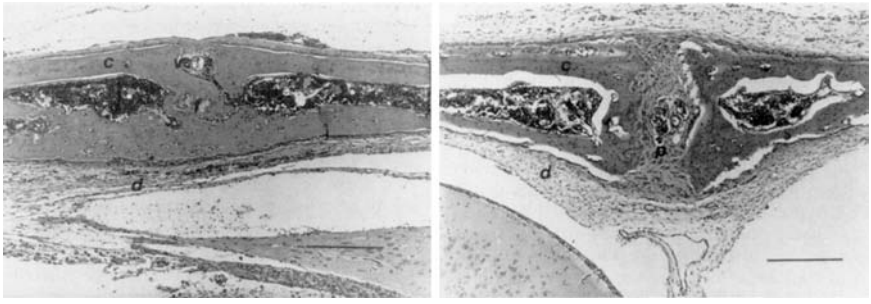

Fig. 31B.8 Suture rotation experiment. Histologic cross section of Group A: unrotated control sutures after 30 days in culture (×250) (S — suture; D — dura; C — calvaria). *Left*: Patent sagittal suture (↑) over sagittal dura. *Right*: Fused posterior frontal suture (↑) over posterior frontal dura.

and endocranial-to-ectocranial. This pattern of ossification persisted despite having the rotated sagittal suture positioned in a reverse fashion.

From the above data we concluded that the cranial suture fate was determined by specific regional dura mater signaling. The rat PF dura mater during the 12- and 20-day postnatal time periods was capable of initiating and completing cranial suture fusion. Signaling from this PF dura mater was unique, both temporally and spatially, in the way it promoted cranial suture fusion. Next, a series of experiments were performed to investigate mouse cranial sutures.[9]

Murine cranial suture fusion

We felt that it would be important to document normal cranial suture fusion in the mouse, since this animal is frequently used in biomechanical and genetic studies. In addition, the mouse cranial sutures would be better for *in vitro*, organ culture studies because of their smaller size.

All the cranial sutures of three distinct strains of mice (CD-1, CF-1, and C57bl-6) were studied histologically for fusion at sequential time points. Two studies were set up using Group A mice ($n = 72$; all sutures studied) and Group B mice ($n = 78$; only the posterior frontal suture was studied, but more precisely along its anatomic length). In the Group A cranial suture study, mice were sacrificed starting at the newborn age and then every 5 days until age 50 days. In addition, two mature mice (250 days old) from each strain were sacrificed. In all three mouse strains, histologic examinations showed that the anterior frontal, sagittal, coronal, lambdoid, and occipitointerparietal sutures remained patent at up to 50 days of age and were patent in the 250-day mature mice. However, examination of the midpoint of the posterior frontal suture showed patency at 30 days, partial fusion at 35 days, and complete fusion by 40 days (Fig. 31B.9).

These data prompted the posterior frontal suture fusion study. In the Group B posterior frontal suture fusion study, mice were sacrificed at age 23 days and then every 2 days until 47 days of age. The anterior, midpoint, and posterior aspects of the posterior frontal suture were examined: the anterior aspect fused between 25 and 29 days; the midpoint fused between 31 and 37 days; and the posterior aspect fused between 39 and 45 days. These data indicate that fusion of the posterior frontal cranial suture in the mouse proceeds in a defined temporal sequence from an anterior to a posterior direction in three distinct strains of mice, while in the same mice all other cranial sutures remain patent. Thus, we found that mouse CF suture fusion is slightly later than in the rat but the directions (anterior-to-posterior and endocranial-to-ectocranial) are similar.

Murine in vitro study

In a subsequent study, we investigated the same murine cranial sutures with an organ culture model.[10] We felt that this model would be ideal for

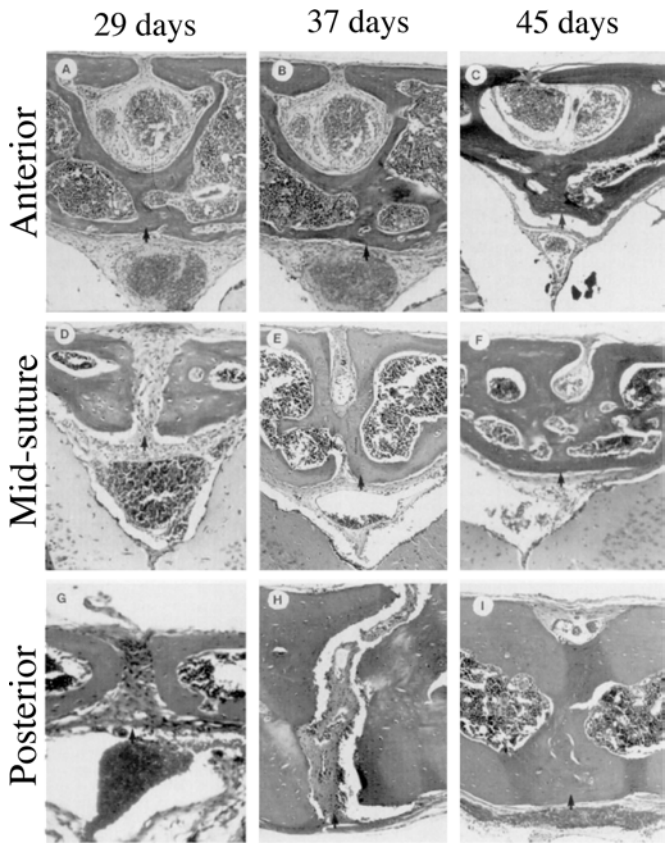

Fig. 31B.9 Murine cranial suture fusion. Photomicrographs of the anterior, midpoint, and posterior aspects of the mouse posterior frontal suture at 29, 37, and 45 days (×250). (**A**) The anterior aspect of the posterior frontal suture at 29 days demonstrated fusion (bold upward arrow) beneath the superior sagittal vein on the ectocranial surface. (**B**) The anterior aspect of the posterior frontal suture at 37 days showed continued fusion (bold upward arrow). (**C**) The anterior aspect of the posterior frontal suture at 45 days showed continued fusion (bold upward arrow). (**D**) The midpoint of the posterior frontal suture at 29 days demonstrated patency (bold upward arrow). (**E**) The midpoint of the posterior frontal suture at 37 days demonstrated fusion (bold upward arrow). (**F**) The midpoint of the posterior frontal suture at 45 days showed continued fusion (bold upward arrow). (**G**) The posterior aspect of the posterior frontal suture at 29 days demonstrated patency (bold upward arrow). (**H**) The posterior aspect of the posterior frontal suture at 37 days was still patent (bold upward arrow). (**I**) The posterior aspect of the posterior frontal suture at 45 days demonstrated fusion (bold upward arrow). The entire posterior frontal suture demonstrated fusion by 45 days.

studying the suture–dura-mater interaction without the influence of other extrinsic forces. In such an organ culture system, the sutures are free both from the influence of dural forces transmitted from the cranial base and from hormonal influences only available in a perfused system.

For this murine *in vitro* study, the sagittal sutures (controls that remain patent *in vivo*) and PF sutures (that fuse *in vivo*) *with* the underlying dura were excised from 24-day-old euthanized mice, cut into $5 \times 4 \times 2$ mm specimens, and cultured in a chemically defined, serum-free medium. One hundred sutures were harvested on the day of sacrifice, then every 2 days thereafter until 30 days in culture, stained with H & E, and analyzed. A subsequent, related experiment — a cranial suture *without* dura *in vitro* study — was performed in a similar fashion to the first study, but only the calvariae with the posterior frontal or sagittal sutures (without the underlying dura) were cultured.[9]

Results from the murine *in vitro* study with dura showed that all sagittal sutures placed in organ culture with the underlying dura remained patent (Fig. 31B.10). We found that specimens grew 25% in size over a 30-day culture period. More importantly, the PF sutures *with* the underlying dura, which were plated down as patent at 24 days of age, demonstrated fusion after various growth periods in organ culture (Fig. 31B.11). *In vitro* PF mouse suture fusion occurred in an anterior-to-posterior direction but in a delayed fashion, 4–7 days later than *in vivo* PF mouse suture fusion. In contrast, the subsequent related

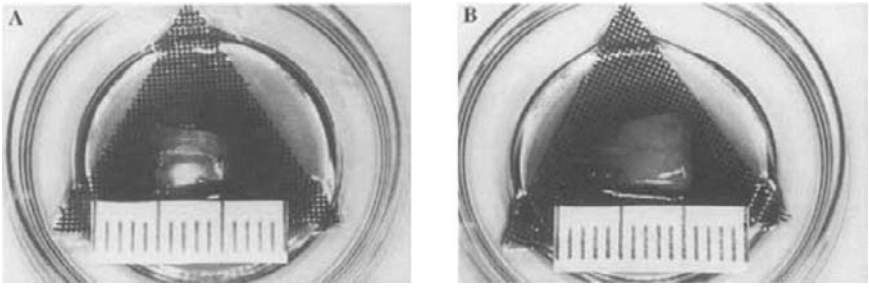

Fig. 31B.10 Murine *in vitro* study. Photograph of a suture specimen in an organ culture system. (**A**) Twenty-four-day-old calvarial specimen in an organ culture system measuring $5 \times 4 \times 2$ mm. (**B**) Fifty-four-day-old postnatal calvarial specimen (grown for 30 days in culture) measuring approximately $6.3 \times 5 \times 2.5$ mm, representing a 25% increase in size.

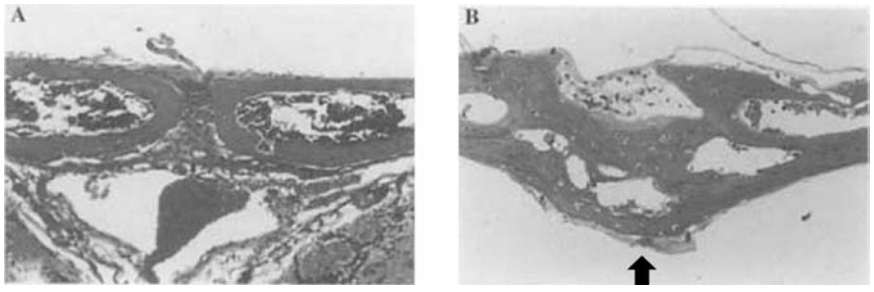

Fig. 31B.11 Murine *in vitro* study. Photomicrograph of the midportion of the PF suture (original magnification ×250). (**A**) PF suture; 24 days old at the time of excision for culturing. The arrow shows suture patency. (**B**) PF suture grown in organ culture with dura mater for 16 days (40 days postnatal). The arrow shows suture fusion. An average increase in calvarial thickness of 40% was noted.

murine *in vitro* study *without* dura showed patency of all sutures, including the PF suture.

At the time, these data from *in vitro* experiments indicated to us that: (1) mouse calvariae, sutures, and the underlying dura survive and grow in organ culture systems for 30 days; (2) the local dura, free from external influences transmitted from the cranial base and hormones from distant sites, influences the cells of its overlying suture to cause fusion (but in a delayed fashion compared to *in vivo*); and (3) without dura influence, all *in vitro* cranial sutures remained patent. At the time, we suggested that the dura-mater–suture communication was independent of tensional forces or other endocrine signaling since the PF suture, dura mater, and brain tissue were isolated, in a culture system. However, it is possible that tensional or other external factors influenced the PF dura tissue prior to harvesting the organ culture tissue, and that the signaling occurred once *in vitro*. After this external influence, by 24 days the PF dura mater was able to provide signaling while in the organ culture system to the overlying tissue of suture mesenchyme and osteogenic fronts for ossification.

Murine in vitro suture rotation

This final cranial suture–dura-mater manipulation study was aimed at emphasizing the influence of the regional dura mater over the overlying

cranial suture.[11] We hypothesized that the regional dura mater could induce suture fusion while in an organ culture system in cranial sutures programmed to remain patent.

For this murine *in vitro* suture rotation study, we used 24-day-old CD-1 mice (at a time when the PF suture was patent) divided into three groups of 50 (n = 165; three groups of 50 cultured controls and three groups of 5 uncultured controls). Group A (unrotated control group) was characterized by a strip of PF and sagittal suture with underlying dural tissue grown in organ culture systems for up to 30 days; Group B (*rotated* experimental group) was characterized by 180° suture rotation while *in vitro*; Group C (*translocated* experimental group) was characterized by translocation or shifting of sutures while *in vitro* (Fig. 31B.12).

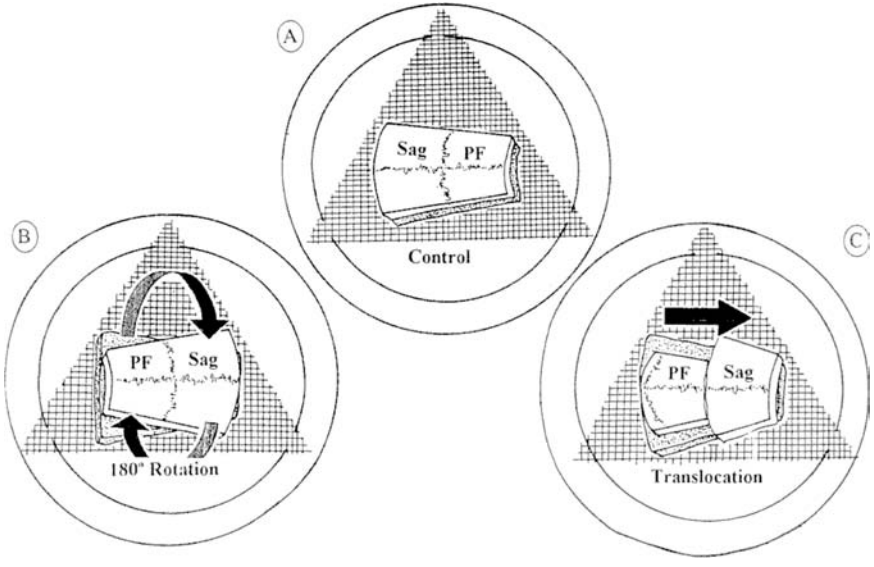

Fig. 31B.12 Murine *in vitro* suture rotation. Schematic illustration of the organ culture systems for each experimental group. A strip craniectomy specimen with underlying dura mater and brain is placed on wire mesh screens in a serum-free medium and grown in organ culture systems. (**A**) Group A: unrotated control. The unmanipulated calvarial strip is over the dura mater. (**B**) Group B: experimental rotation. The calvarial strip is rotated 180° over the dura mater so that the posterior frontal suture lies over the sagittal dura and the sagittal suture lies over the posterior frontal dura. (**C**) Group C: experimental translocation. The calvaria was bisected at the posterior frontal–sagittal suture junction; the posterior frontal suture was slid posteriorly over the sagittal dura, and the sagittal suture was slid anteriorly over the posterior frontal dura.

Results from this murine *in vitro* rotation experiment showed that Group A (control) specimens had persistent patency of the sagittal suture and fusion of the PF suture in an anterior-to-posterior direction. Group B (rotation) resulted in patency of the PF suture over the sagittal dura and fusion of the sagittal suture over the PF dura in a posterior-to-anterior direction. And Group C (translocation) resulted in patency of the PF suture over the sagittal dura and fusion of the sagittal suture over the PF dura in an anterior-to-posterior direction.

Data from this study re-emphasized the regional specialization of the PF dura with regard to temporal and spatial uniqueness in cranial suture fusion. In our next investigations we looked into molecular mechanisms behind this process. We began by studying growth-factor-mediated signal pathways thought to involve inductive tissue interactions of the dura cells with the suture cells.

Cytokine signaling

From the above experiments it appeared that regional dura mater with paracrine signaling was critical to the cranial suture fate. However, the factors involved in dura-mater–suture communication and the precise mechanisms were not understood. We used immunolocalization and *in situ* hybridization techniques to identify these important osetogenic factors.[12–15]

Insulin-like growth factors

As an initial cytokine study investigating the dura-mater–suture paracrine signaling that results in osteogenic differentiation and suture fusion, we investigated the possible role of insulin-like growth factors (IGFs) I and II. We studied the temporal and spatial patterns of the expression of IGF-I and IGF-II mRNA and IGF-I peptide and osteocalcin (bone morphogenetic protein 4) protein in fusing PF rat sutures, and then compared them with patent coronal (control) sutures.[12] Ten Sprague–Dawley rats were studied at the following time points: 16, 18, and 20 days of gestation and 2, 5, 10, 15, 20, 30, 50, and 80 days after birth ($n = 110$). PF and coronal (patent, control) sutures were analyzed for IGF-I and IGF-II mRNA expression by *in situ* hybridization through the use of 35S-labeled IGF-I

and IGF-II antisense riboprobes. Levels of IGF-I and IGF-II mRNA were quantified by counting the number of autoradiograph signals per cell. IGF-I and osteocalcin immunoreactivity were identified by avidin–biotin peroxidase immunohistochemistry.

Our results showed that IGF-I and IGF-II mRNA were expressed in dural cells beneath fusing sutures, and the relative mRNA abundance increased between 2 and 10 days before initiation of fusion (Fig. 31B.13). Subsequently, IGF-I and IGF-II mRNA were detected in the suture connective tissue cells at 15 and 20 days during the time of active fusion (Fig. 31B.14). In contrast, within large osteoblasts of the osteogenic front, the expression of IGF-I and IGF-II mRNA was minimal. However, IGF-I peptide was intensely immunoreactive within these osteoblasts at 15 days (during the period of suture fusion) (Fig. 31B.15). Osteocalcin was also demonstrated within osteoblasts of the osteogenic front (Fig. 31B.16).

These data from our IGF study suggested that PF dura mater cells were producing IGFs and that this appeared to colocalize IGF and osteocalcin (a marker for the mature osteoblast phenotype) proteins within the above suture tissue. Thus, we suggested that dura-mater–suture interaction may be signaled in a paracrine fashion by dura-mater-derived growth factors, such as IGF-I and IGF-II. These peptides, in turn, stimulate nearby osteoblasts to produce bone-promoting growth factors, such as osteocalcin.

Transforming growth factor beta, fibroblast growth factors, and other candidate genes

TGF-βs are regulatory molecules that are known to stimulate osteoblast proliferation and induce extracellular matrix proteins.[13] FGFs are a family of monomeric peptides that act with heparin-sulfate-containing proteoglycans to modulate cell migration, angiogenesis, bone development and repair, and FGFR mutations have been mapped to craniosynostosis syndromes.[15]

For these candidate gene cytokine experiments, the sagittal (patent) suture was used as the control group and the PF (fusing) suture was used as the experimental group. Both temporal and spatial data were collected.

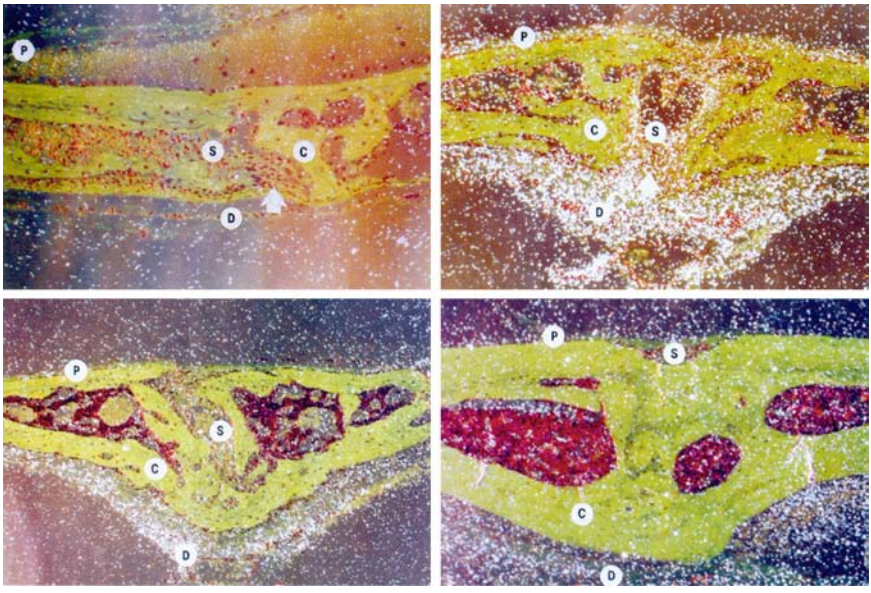

Fig. 31B.13 Insulin-like growth factor experiment. Dark field photomicrographs of the coronal and posterior frontal sutures after IGF-I *in situ* hybridization with ^{35}S-radiolabeled IGF-I antisense RNA and exposure to photoemulsion for 40 days (×250). D — dura mater; C — calvarium; S — suture; P — periosteum. *Top, left*: Patent coronal suture at 15 days of life. IGF-I is minimally expressed in the dura cells, suture cells, and periosteal cells. The arrow marks the patent suture. *Top, right*: The posterior frontal suture is still patent at 10 days of life (prefusion). IGF-I mRNA is markedly expressed within dural cells beneath the suture and also present within connective tissue cells in the endocranial half of the suture. The arrow marks the patent suture. *Bottom, left*: The posterior frontal suture begins to fuse on the endocranial surface at 15 days of life (active fusion). IGF-I mRNA is present within dural cells beneath the fusing suture, but less so than at 10 days of life. IGF-I mRNA is now expressed within connective tissue cells in the ectocranial half of the suture. *Bottom, right*: The posterior frontal suture is completely fused at 50 days of life (postfusion). IGF-I mRNA is only minimally expressed within dural cells beneath the fused suture and within connective tissue cells of the ectocranial suture remnant.

We found an increase in TGF-β1 transcription prior to and during PF suture fusion.[16] Patent sutures were less immunoreactive for TGF-β isoforms than fusing sutures but TGF-βs localized to the margin of the patent sutures. In addition, TGF-βRI and TGF-βRII were immunolocalized to the osteoblasts of the osteogenic fronts surrounding the suture and in the

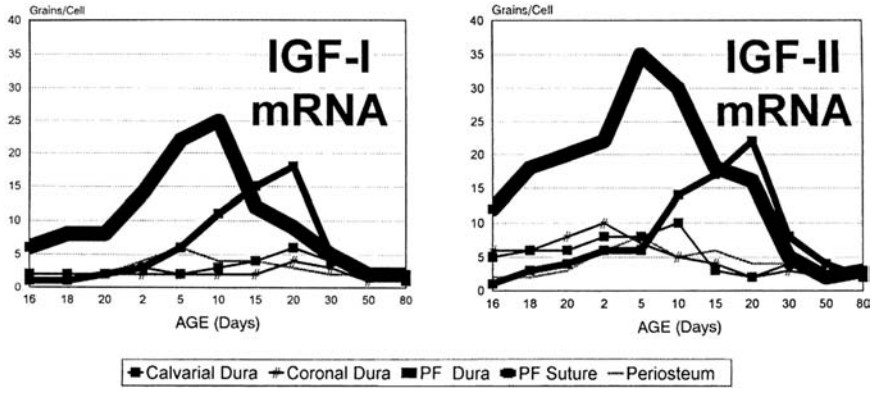

Fig. 31B.14 Insulin-like growth factor experiment. Line graph drawing of IGF-I and IGF-II mRNA expression within dural, suture, and periosteal cells. Values are grains/cell; age is in days, starting with days of gestation and moving on to days after birth. The posterior frontal dura cells (thick bold line) showed the most prominent up-slope or increase in both IGF-I and IGF-II mRNA at 5 and 10 days (just before suture fusion). The posterior frontal suture cells (thinner bold line with bold boxes) showed a later up-slope or increase in both IGF-I and IGF-II mRNA at 15 and 20 days (time during suture fusion). The posterior frontal suture values are the mean values of the cells within the ectocranial and endocranial areas of the suture. The calvarial dura cells, the coronal dura cells, and the periosteal cells did not show a marked increase in IGF-I or IGF-II mRNA during any of the time periods.

dura mater subjacent to the active fusing suture.[17] Also, a relative abundance of FGF-2 mRNA (a factor known to augment healing of critical size bone defects) was seen in PF (fusing) suture dura tissue compared to sagittal (patent) suture dura tissue.[15]

Further studies by the laboratory of Michael T. Longaker, M.D. on the normal rodent cranial suture fusion model focused on the bone morphogenetic protein (BMP) pathway. They showed that Noggin (a secreted antagonist of BMP) and Runx2 (a transcription factor that is a marker of osteoblast differentiation) are localized to osteogenic fronts of fusing PF sutures. They were able to change the frontonasal phenotype of a rat by maintaining PF suture patency with overexpression of Noggin (Fig. 31B.17).[18] We compared this normal suture model to a pathologic model described below with respect to this pathway.

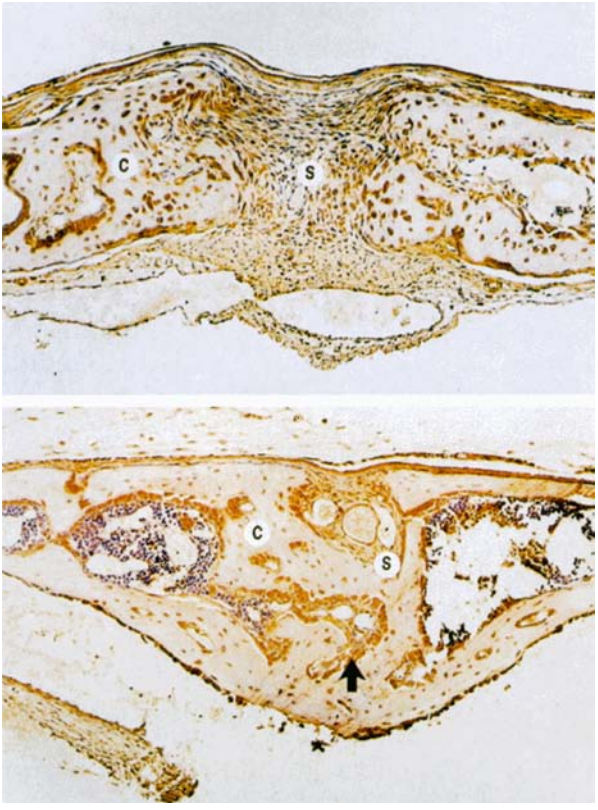

Fig. 31B.15 Insulin-like growth factor experiment. Photomicrographs of IGF-I immunoreactivity (×400). C — calvarium; S — suture. *Top*: The posterior frontal suture, patent at 10 days of life (prefusion), also shows only minimal IGF-I immunoreactivity. *Bottom*: The posterior frontal suture begins to fuse on the endocranial surface at 15 days of life (during fusion). IGF-I immunoreactivity is present within large osteoblasts in the area of active suture fusion. The arrow denotes osteoblasts with IGF-I immunoreactivity.

Pathologic Suture Fusion: Rabbit Model

Currently the most representative animal model of this human condition is the rabbit craniosynostosis strain at the University of Pittsburgh.[19–21] In this model pathologic suture fusion begins *in utero*, causing cranial vault deformities like plagiocephaly in unilateral coronal suture synostosis and

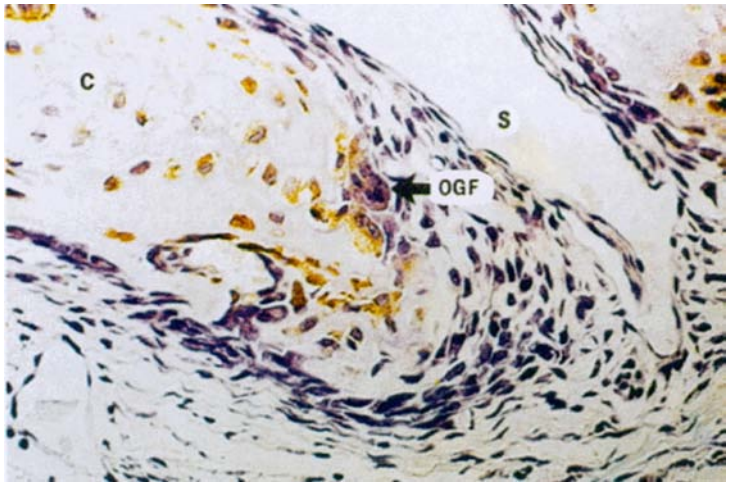

Fig. 31B.16 Insulin-like growth factor experiment. Photomicrographs of osteocalcin immunoreactivity. Osteocalcin immunoreactivity is demonstrated within the large osteoblasts (arrow, OGF) of the osteogenic front of the fusing posterior frontal suture at 15 days of life (×400). C — calvarium; S — suture.

brachycephaly in bilateral synostosis (Fig. 31B.18). Mark Mooney, Ph.D. has characterized this unique strain of craniosynostic rabbits with regard to incidence and occurrence and embryologic, anatomic, functional anomalies with a series of investigations over the last 13 years. A series of surgical manipulations of the pathologic sutures has shed light on surgical outcomes and growth factor treatment. With Dr. Mooney we performed a series of experiments investigating pathologic suture fusion in the growing rabbit. The studies described below include: (1) a study of facial growth and intracranial volume after surgical correction of synostosis, (2) a study of osteogenic factors with neonatal sutures, and (3) biochemical manipulation with growth factors to prevent suture refusion.[22–25]

Correction of unilateral coronal synostosis in rabbits leads to resolution of mandibular asymmetry

Mandibular dysmorphology in unilateral coronal synostosis has been recognized clinically (Fig. 31B.19). In patients with unilateral coronal

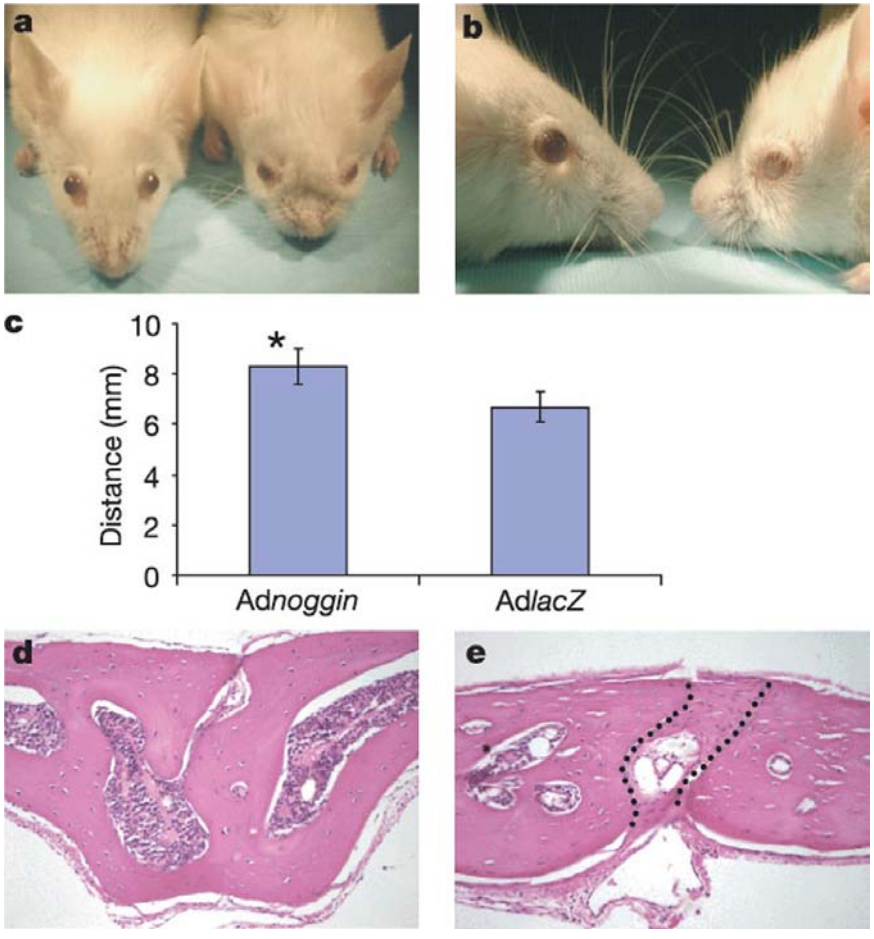

Fig. 31B.17 Frontal view of 53-day-old CD-1 mice demonstrating a normal phenotype on the left and reduced midface projection and wide-set eyes on the right secondary to abnormal persistent patency of the PR sutures from Noggin underexpression.

synostosis, the chin point deviates away from the affected side. In this study the Pittsburgh familial nonsyndromic rabbits were used to investigate whether this mandibular asymmetry resolves after correction of unilateral coronal synostosis.[22]

Rabbits with unilateral coronal synostosis that underwent "correction" with resection of the affected suture (study group) were

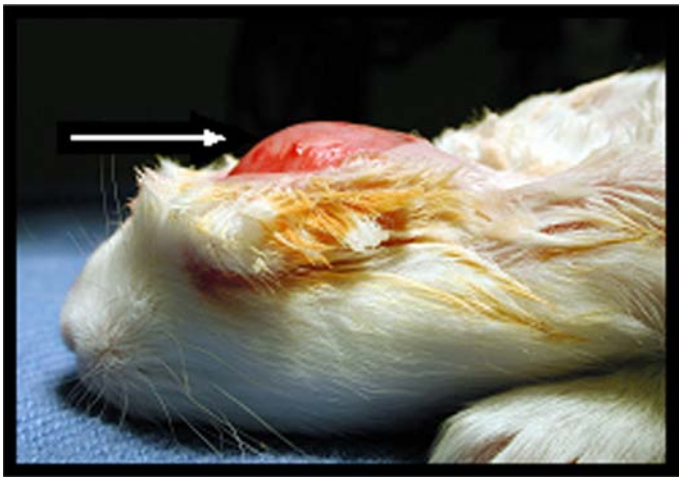

Fig. 31B.18 Coronal synostotic rabbit model demonstrating a high, dome-shaped forehead (brachycephaly).

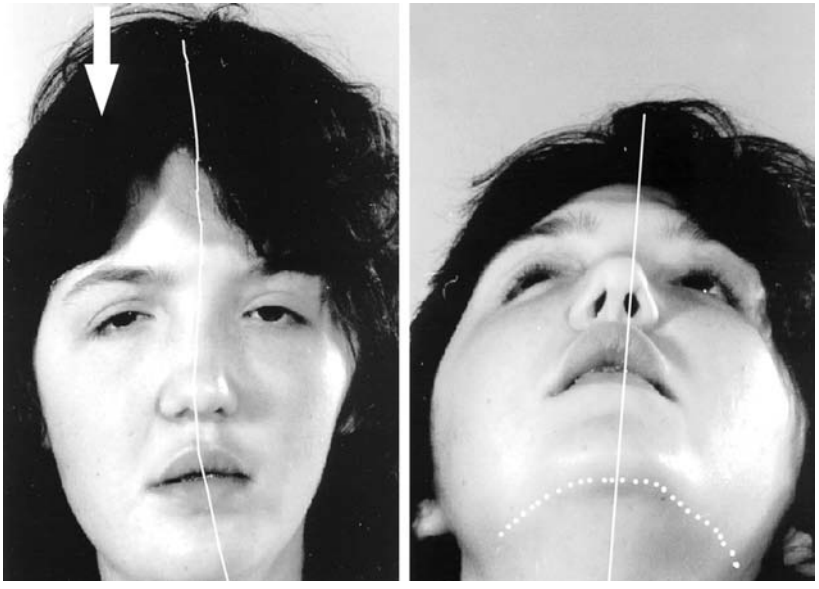

Fig. 31B.19 Skeletally mature patient with mild uncorrected right unilateral coronal synostosis, showing a shift of her chin point away from the affected side. *Left*: Anterior view. *Right*: Caudad (worm's-eye) view.

compared with "uncorrected" rabbits with unilateral coronal synostosis and normal, wild-type rabbits (control — unoperated-on)($n = 36$; three equal groups of 12).

Serial lateral cephalograms were obtained at 10, 25, 42, and 84 days for growth measurements including mandibular length and ramal height. Mature mandibular gross specimens were also used for comparative measurements. In addition, these specimens were used for cranial base measurements and condylar shape and volume measurements.

Our data, from the serial lateral cephalograms, showed that there were no asymmetries in wild-type rabbits and progressive asymmetries in the ramal height and mandibular length in uncorrected unilateral coronal synostosis rabbits (controls). However, in corrected unilateral coronal synostosis rabbits, existing asymmetries at 10 and 25 days improved by 42 days and were not seen by maturity, at 84 days (Figs. 31B.20 and 31B.21). In dry, mature, mandibular specimens, wild-type rabbits showed equal side-to-side measurements and uncorrected unilateral coronal synostosis rabbits showed the following on the affected side: longer ramal height

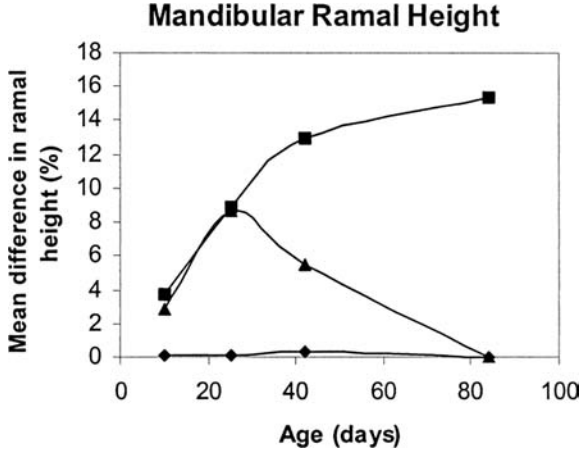

Fig. 31B.20 Correction of unilateral coronal synostosis in rabbits. Mean difference in mandibular height. The wild-type rabbits (♦) showed no difference, the uncorrected unilateral coronal synostosis rabbits (■) showed progression of difference or asymmetry, and the corrected unilateral coronal synostosis rabbits (π) showed resolution of difference or asymmetry after the procedure.

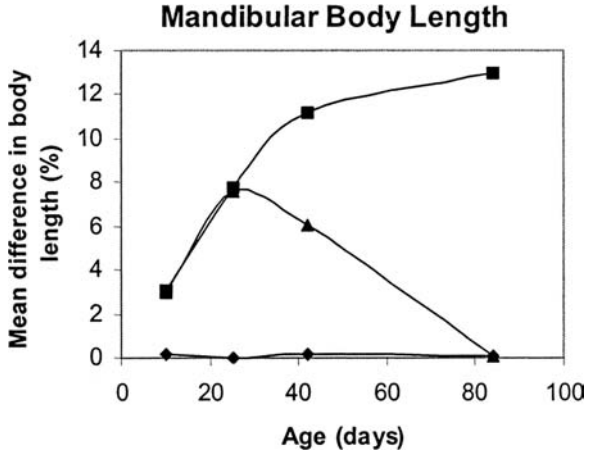

Fig. 31B.21 Correction of unilateral coronal synostosis in rabbits. Mean difference in mandibular body length. The wild-type rabbits (◆) showed no difference, the uncorrected unilateral coronal synostosis rabbits (■) showed progression of difference or asymmetry, and the corrected unilateral coronal synostosis rabbits (π) showed resolution of difference or asymmetry after the procedure.

(15%), shorter ramal width (13%), longer body height (10%), and shorter body width (13%) (Figs. 31B.22–31B.24). By contrast, 10 of the 11 corrected unilateral coronal synostosis specimens showed no side-to-side differences.

There were no asymmetries in condylar shape or condylar volume in any of the three groups. Cranial base measurements showed asymmetries of the uncorrected unilateral coronal synostosis specimens that were consistent with an anteriorly positioned glenoid fossa on the affected side (Fig. 31B.25). However, only 1 of the 11 corrected unilateral coronal synostosis specimens showed similar cranial base asymmetries.

From this experiment we concluded that mandibular asymmetries in nonsyndromic, familial rabbits with unilateral coronal synostosis are progressive with growth but improve after correction of synostosis. However, clinical experience suggests that mandibular asymmetries do not resolve after correction of all unilateral coronal synostosis in humans. The reasons for this discrepancy include species differences, timing of surgery, type of procedure, follow-up, and the fact that syndromic cases were not studied.[16]

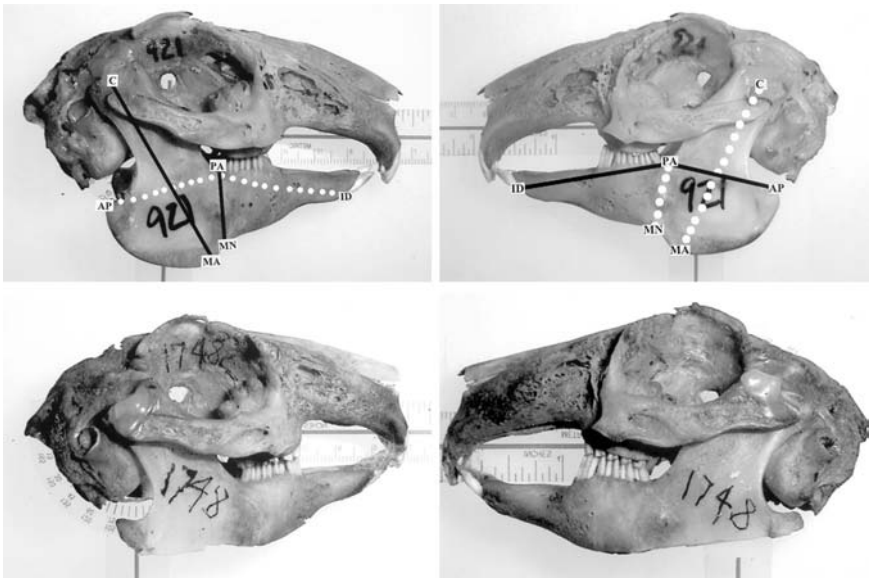

Fig. 31B.22 Correction of unilateral coronal synostosis in rabbits. Lateral view of mature rabbit skulls. C — midcondylar; AP — angular process; MA — mandibular angle; MN — mandibular (angular) notch; ID — infradental; PA — posterior alveolus. *Top*: Uncorrected unilateral coronal synostosis — right side affected. *Top, left*: Right-side view demonstrating larger ramal and body height when compared with the contralateral side (black solid line) and smaller ramal and body height when compared with the contralateral side (white dotted line). *Top, right*: Left-side view demonstrating smaller ramal and body height when compared with the contralateral side (white dotted line) and larger ramal and body length when compared with the contralateral side (black solid line). *Bottom*: Corrected unilateral coronal synostosis: right-side suturectomy. *Bottom, left*: Right-side view demonstrating no difference compared to the contralateral side. *Bottom, right*: Left-side view demonstrating no difference compared to the contralateral side.

First, there may be differences between human and rabbit mandibular growth. The rabbit is known to experience masticatory function at an earlier time and also has the unique ability to generate bone. Second, due to the early age at diagnosis and during surgical procedures, a significant amount of corrective growth was allowed. Third, the differences in procedure might affect the outcome, and release of the synostosis down to the cranial base near the sphenoid region (as done

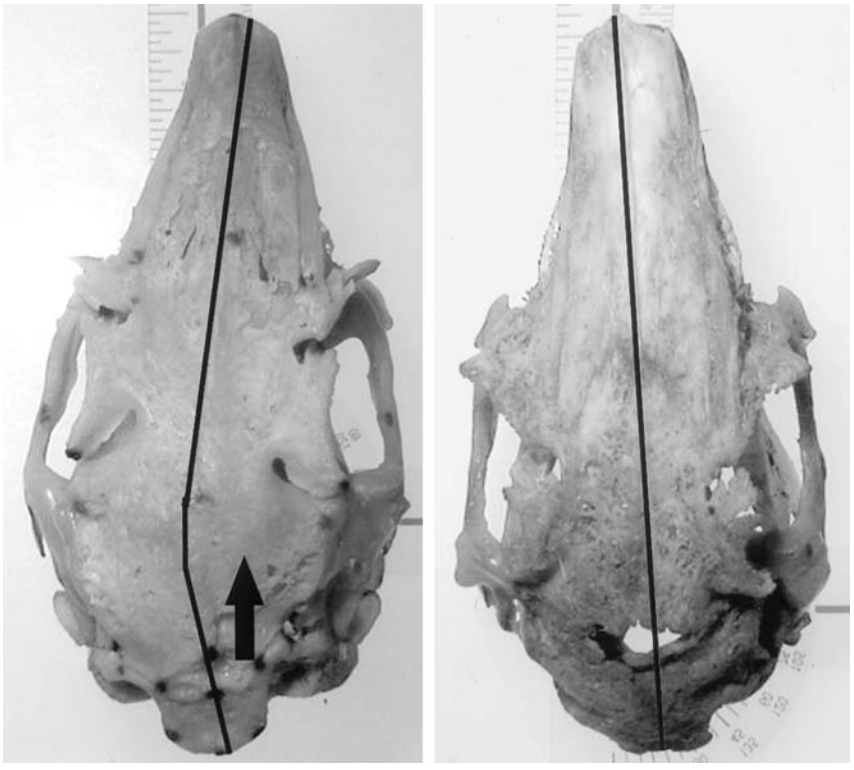

Fig. 31B.23 Apical view of mature rabbit skulls. *Left*: Uncorrected unilateral coronal synostosis demonstrating nasal deviation to the *right* or ipsilateral to the affected side. *Right*: Corrected unilateral coronal synostosis demonstrating a midline nasal root.

with the rabbits) may be necessary. Fourth, in our study the near-correction of asymmetry is not seen until maturity, so that human patients must be followed into their teenage years. Fifth, the model used in this study is a nonsyndromic unilateral coronal synostosis model. It is possible that clinical cases with genetic abnormalities, including those localized to the fibroblast growth factor receptor, may not behave the same with respect to correction of mandibular asymmetries. Finally, in our series, not all animals showed correction of asymmetries. Likewise, there may be a subset of human cases that will not show correction of asymmetries.

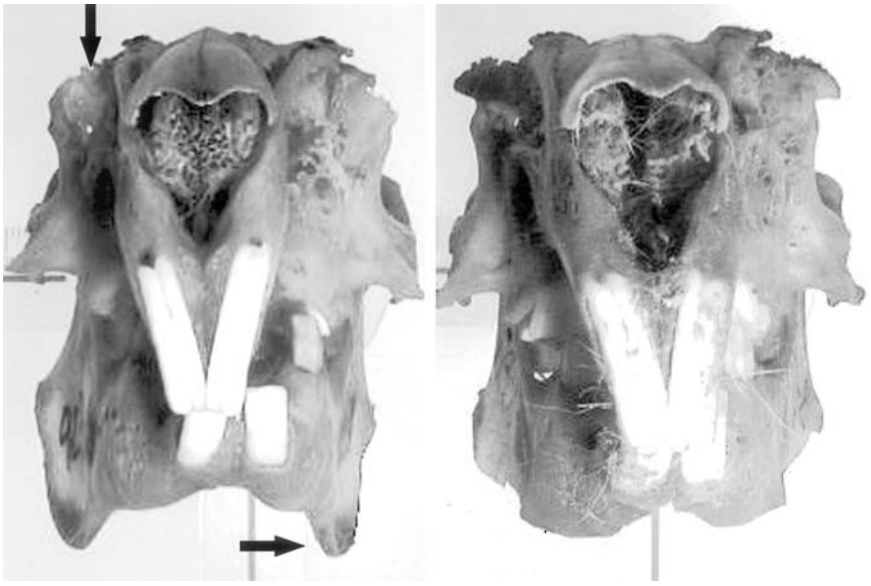

Fig. 31B.24 Frontal view of mature rabbit skulls. *Left*: Uncorrected unilateral coronal synostosis (the *top* arrow indicates the region of the fused suture) demonstrating chin point deviation to the *left* or contralateral to the affected side (the *bottom* arrow indicates left-side deviation of the chin point). *Right*: Corrected unilateral coronal synostosis demonstrating a midline chin point.

Intracranial pressure changes in craniosynostotic rabbits

Individuals with craniosynostosis are known to have cranial vault deformities and thought to be at risk for brain anomalies related to changes in intracranial pressure. We investigated the intracranial pressure changes in a rabbit model with naturally occurring, uncorrected coronal suture synostosis.[23]

Longitudinal and cross-sectional intracranial pressure data were collected from 241 New Zealand white rabbits, divided into four groups: normal controls ($n = 81$); rabbits with delayed onset coronal suture synostosis ($n = 78$); rabbits with early onset unilateral coronal suture synostosis ($n = 32$); and rabbits with early onset bilateral coronal suture synostosis ($n = 50$) (Fig. 31B.26). Epidural intracranial pressure measurements were obtained at 10, 25, 42, and 84 days of age using a NeuroMonitor microsensor transducer (Fig. 31B.27).

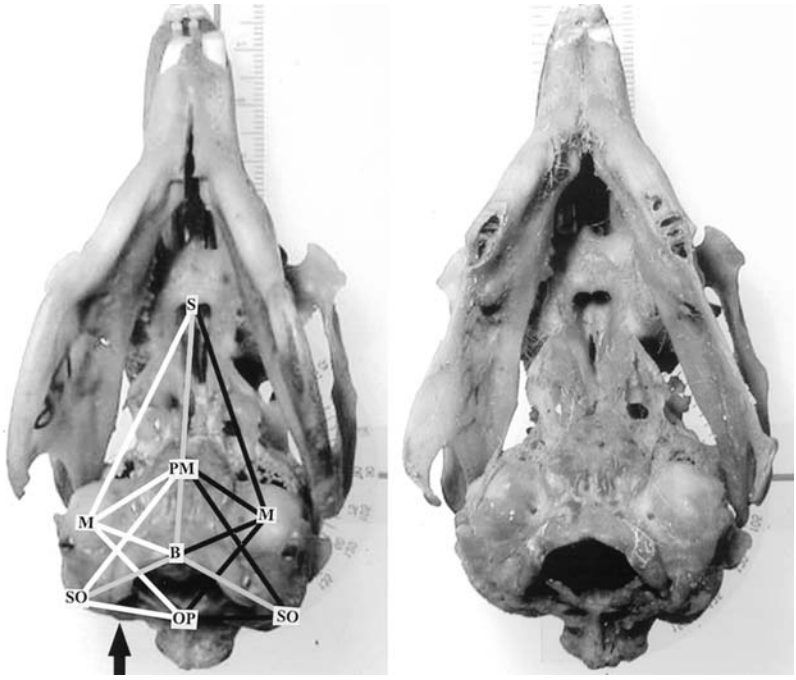

Fig. 31B.25 Caudal view of mature rabbit skulls showing the cranial base. M — mastoid; S — septum; B — basion; OP — opisthion; PM — pterygomaxillary; SO — spheno-occiput. *Left*: Uncorrected unilateral coronal synostosis demonstrating slightly shorter lengths on the synostosed side (white lines) compared with the unaffected side (black lines). *Right*: Corrected unilateral coronal synostosis demonstrating no significant differences in the cranial base measurements.

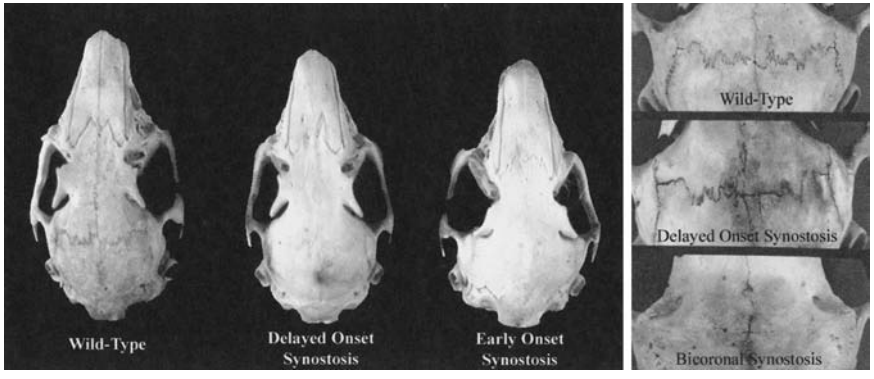

Fig. 31B.26 Superior view of cleaned and dried skulls of 42-day-old rabbits showing wild-type, delayed onset, and early onset phenotypes.

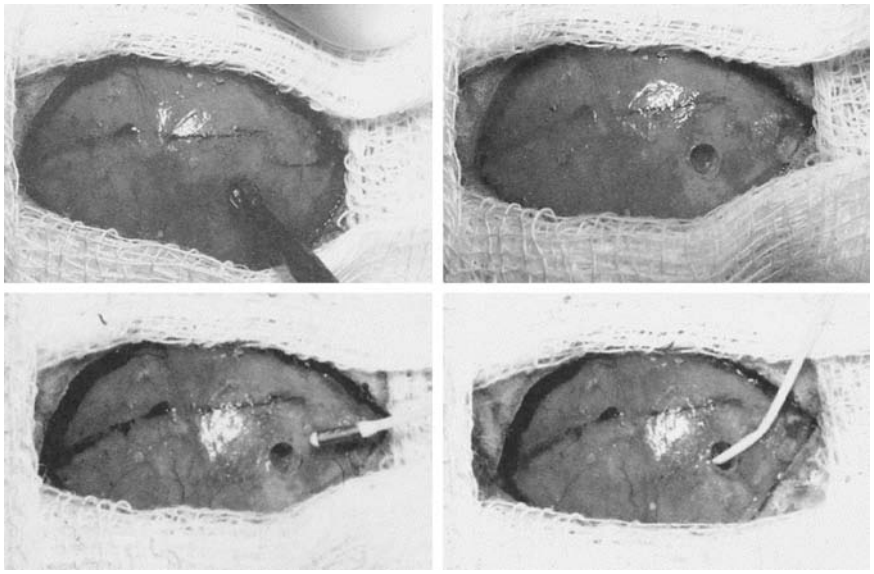

Fig. 31B.27 Superior view of the bur hole location in the parietal bone of the rabbit calvaria and microsensor intracranial pressure transducer placement.

Our results indicated that normal rabbits and rabbits with delayed onset coronal suture synostosis and early onset unilateral coronal suture synostosis showed a similar oscillating pattern of age-related changes in normal and head-down intracranial pressure from 10 to 84 days of age. In contrast, rabbits with early onset bilateral coronal suture synostosis showed markedly elevated normal and head-down intracranial pressure levels from 10 to 25 days and showed a different pattern through 84 days (Fig. 31B.28). Results from one-way analysis of variance revealed significant ($p < 0.01$) group differences only at 25 days of age. Rabbits with early onset bilateral coronal suture synostosis had significantly greater ($p < 0.05$) normal and head-down intracranial pressure (by 42%) than the other three groups.

These results showed differing intracranial pressure compensations in rabbits with uncorrected multiple-suture synostosis compared with normal rabbits or rabbits with uncorrected single-suture synostosis, possibly through progressive cerebral atrophy and decreased intracranial volume, abnormal intracranial vascular patterns and blood volume, and/or differing cranial vault compensatory changes. The pathologic

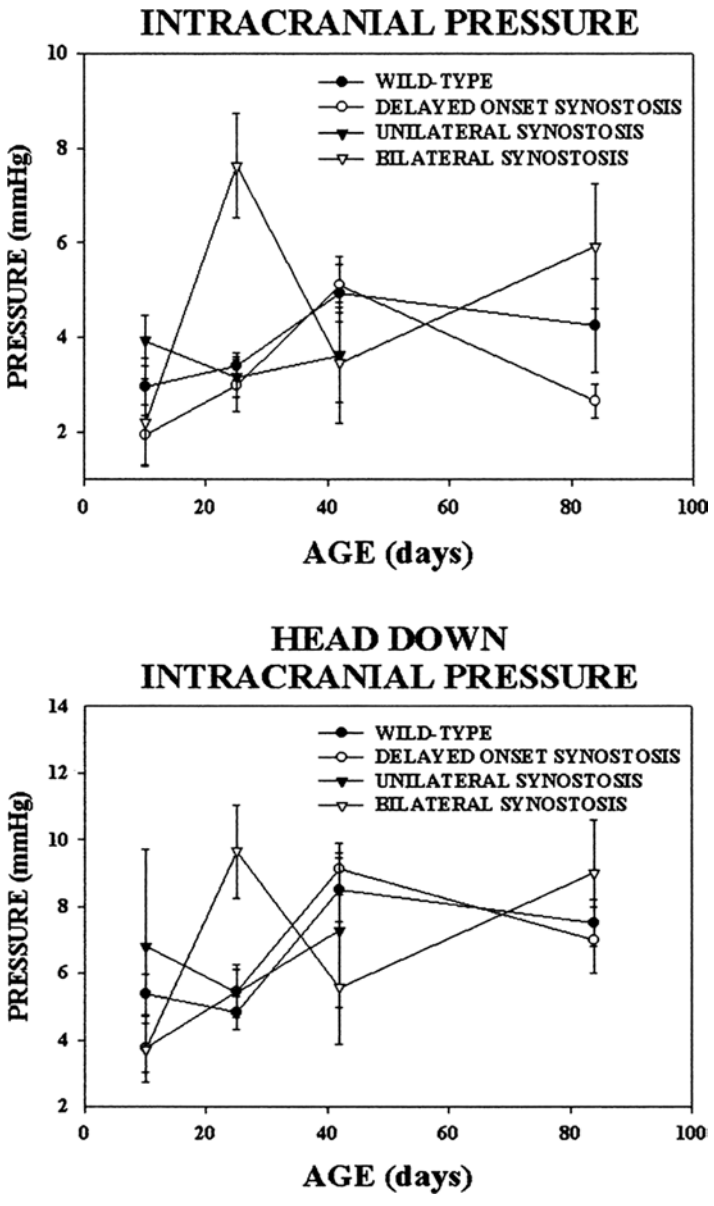

Fig. 31B.28 Mean (±SE) normal and head-down intracranial pressure changes among the four groups under study. Note the marked increase in intracranial pressure from 10 to 25 days in rabbits with early onset bilateral coronal suture synostosis compared with the other groups.

rabbit suture fusion model has been used to provide clues for clinical care, as in these two studies on postcorrection facial growth changes and on intracranial pressure changes. In the following two studies the biology of craniosynostosis in the pathologic rabbit craniosynostotic fusion model was investigated.

Noggin and Runx2 in craniosynostotic rabbits

Normal suture fusion in the rodent models (described above) was shown to be driven by the molecular signals elucidated by the underlying dura mater. In order to investigate the pathogenesis of suture fusion in craniosynostosis, we chose to examine the expression patterns of two important molecular signals (Noggin and Runx2) in the same congenital craniosynostotic rabbits.[24]

Coronal (fusing) and sagittal (patent) rabbit cranial sutures from our congenitally synostosed rabbits and wild-type (control) rabbits were harvested at a neonatal time point. These sections were then grown in organ culture and harvested for histology at 0, 7, or 14 days of culture (Fig. 31B.29). The fusion percentage was then assessed and an overall

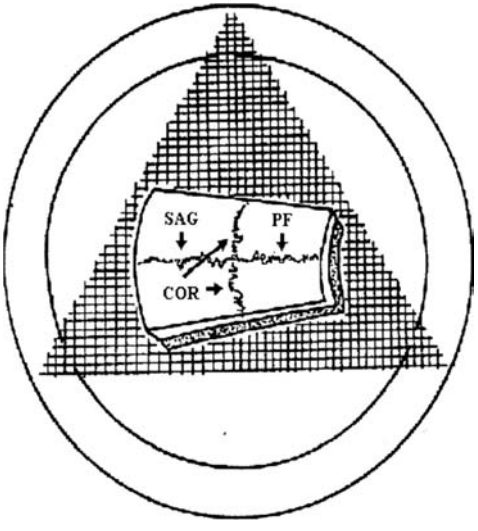

Fig. 31B.29 Representation of the organ culture system used in our study. In the study, we divided the calvariae into separate isolated groups, examining the sagittal suture and the coronal suture for signs of fusion.

fusion score was calculated. Expression of Noggin and Runx2 was then localized by immunohistochemistry and quantified by Western blot analysis.

Histologic results of the wild-type cranial sutures (control) showed suture patency (a score of 0%) for all coronal and sagittal sutures at 0, 7, and 14 days of organ culture. Sagittal sutures of craniosynostotic animals also showed suture patency (a score of 0%) at all culture times (0, 7, and 14 days). Of the 18 coronal sutures from the craniosynostotic animals, 8 remained patent and 10 fused. For the coronal sutures that fused, fusion scores of 14%, 41%, and 84% were documented at 0, 7, and 14 days of organ culture, respectively (Fig. 31B.30).

With immunolocalization, Noggin was found to be expressed in both the dura and the suture cells underlying patent sutures, but not in fusing sutures *in vitro* (Fig. 31B.31). Runx2 was found to be expressed in the dura beneath the suture and suture cells of fusing sutures, not patent sutures. Western blot densitometry confirmed these findings (Fig. 31B.32).

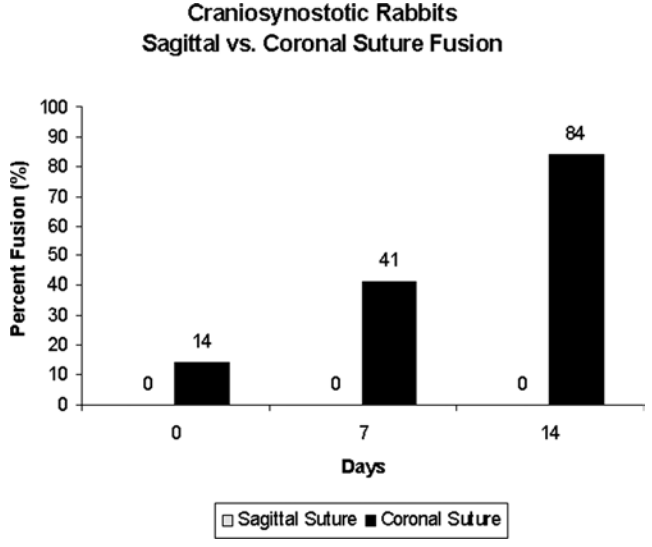

Fig. 31B.30 Percent fusion observed in the sagittal sutures and fusing coronal sutures in the craniosynostotic rabbit model at three time intervals: 0, 7, and 14 days. The sagittal suture remained patent at all culture times. For the coronal sutures that fused, suture fusion progressed in the *in vitro* system.

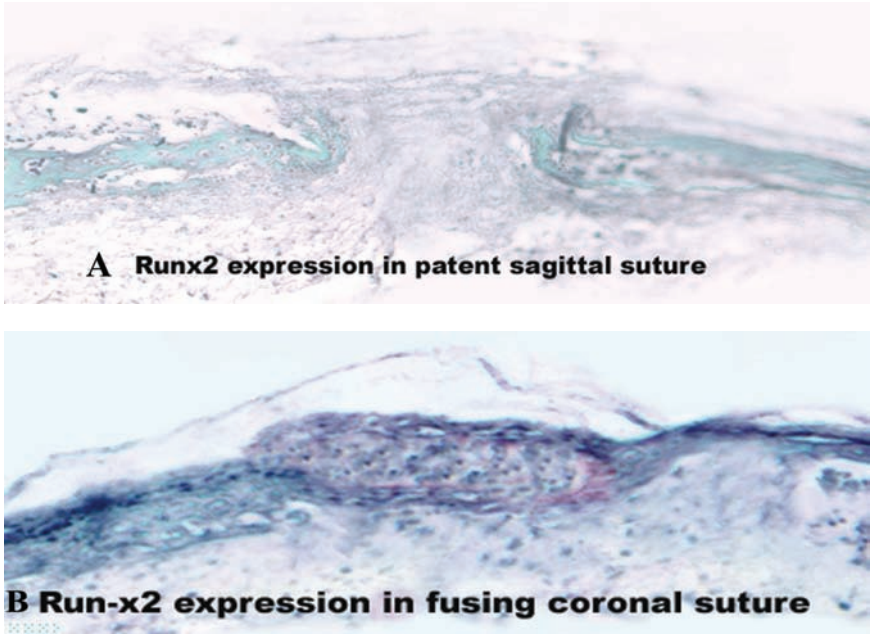

Fig. 31B.31 Expression pattern of Runx2 in (**A**) patent sagittal suture and (**B**) fusing coronal suture. Runx2 was expressed in the dura beneath the suture and suture cells of fusing sutures but not patent sutures.

Our neonatal organ culture data suggested that pathologic rabbit coronal sutures progress toward complete suture fusion *in vitro*, and expression patterns of Noggin and Runx2 paralleled that of our well-studied normal suture fusion model.

Noggin is a BMP-2/4 antagonist. Both BMP-2 and BMP-4 are present in osteogenic fronts of fetal mice (Fig. 31B.33). In the normal suture fusion murine model, Noggin was expressed by the patent sagittal suture but not by the fused PF suture. Also, the expression of Noggin was decreased by FGF2 and syndromic Fgfr and that overexpression of Noggin, induced by transfection, resulted in suture patency of the normally fused PF suture. Our data suggest an important role for Noggin in pathologic suture fusion as well. Underexpression of Noggin was found in the dura and coronal mesenchyme prior to suture fusion. In the same system control, patent coronal and sagittal sutures expressed Noggin.

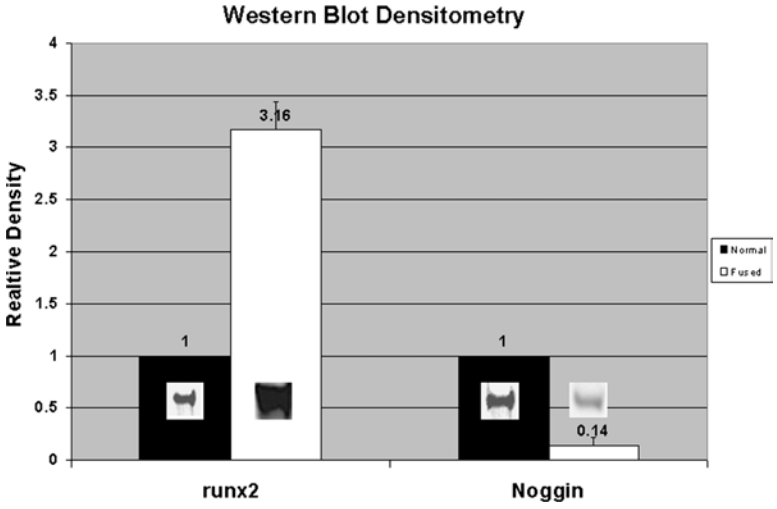

Fig. 31B.32 Relative densities of Noggin and Runx2 in patent and fusing sutures as determined by Western blot densitometry. Fusing sutures showed significantly lower Noggin expression and significantly higher Runx2 expression when compared with patent sutures.

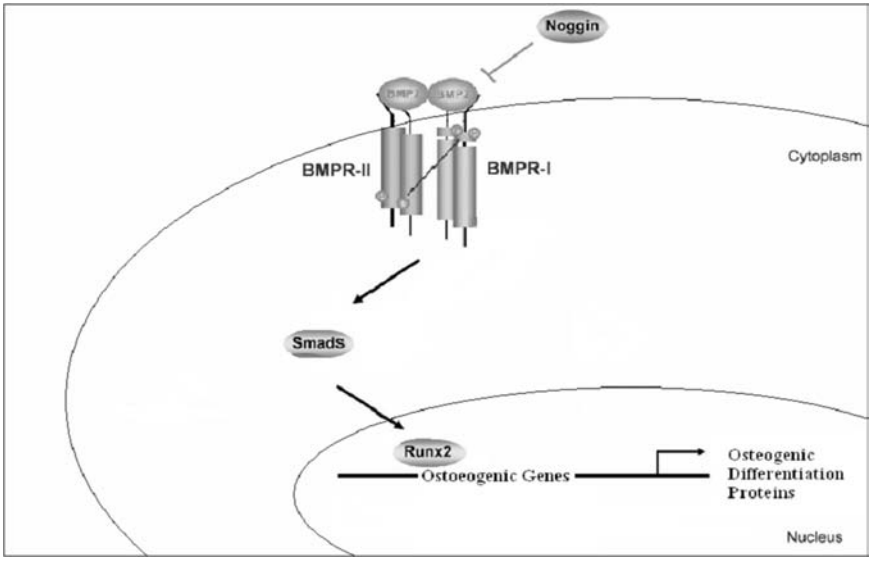

Fig. 31B.33 Role of Noggin and Runx2 in BMP signaling.

Rescue of coronal suture fusion using transforming growth factor beta 3 (TGF-β3)

Developmental studies in our normal suture fusion rodent model showed that low levels of transforming growth factor beta 3 (TGF-β3) were associated with normal fusion of the PF suture. Also, TGF-β3 prevented PF suture fusion in a dose-dependent fashion. A study was designed with the rabbit craniosynostotic model to test the hypothesis that TGF-β3 can also prevent or "rescue" fusing sutures.

One hundred coronal sutures from 50 rabbits with delayed onset, coronal suture synostosis were examined in the present study. The rabbits were divided into 5 groups of 10 rabbits each: (1) sham controls, (2) bovine serum albumin (BSA, 500 ng) low-dose protein controls, (3) low-dose TGF-β3 (500 ng), (4) high-dose BSA (1000 ng) controls, and (5) high-dose TGF-β3 (1000 ng). At 10 days of age, radiopaque amalgam markers were implanted in all of the rabbits on either side of the coronal suture to monitor sutural growth. At 25 days of age, the BSA or TGF-β3 was combined with a slow-absorbing collagen vehicle and injected subperiosteally above the coronal suture.

Radiographic results revealed that high-dose TGF-β3 rabbits had significantly greater ($p < 0.05$) coronal suture marker separation than the other groups. Histomorphometric analysis revealed that high-dose TGF-β3 rabbits also had patent coronal sutures and significantly greater ($p < 0.01$) sutural widths and areas than the other groups (Figs. 31B.34 and 31B.35).[19]

The results suggest that there is a dose-dependent effect of TGF-β3 on suture morphology and area in these rabbits, and that the manipulation of such growth factors may have clinical applications in the treatment of craniosynostosis.

Stress-induced Suture Fusion

There is clinical evidence that fetal head constraint may contribute to many cases of nonsyndromic craniosynostosis. Models inducing intrauterine constraint with cervical cerclage, delayed birth, and fetal crowding have been used to study cranial suture fusion. Richard Kirschner

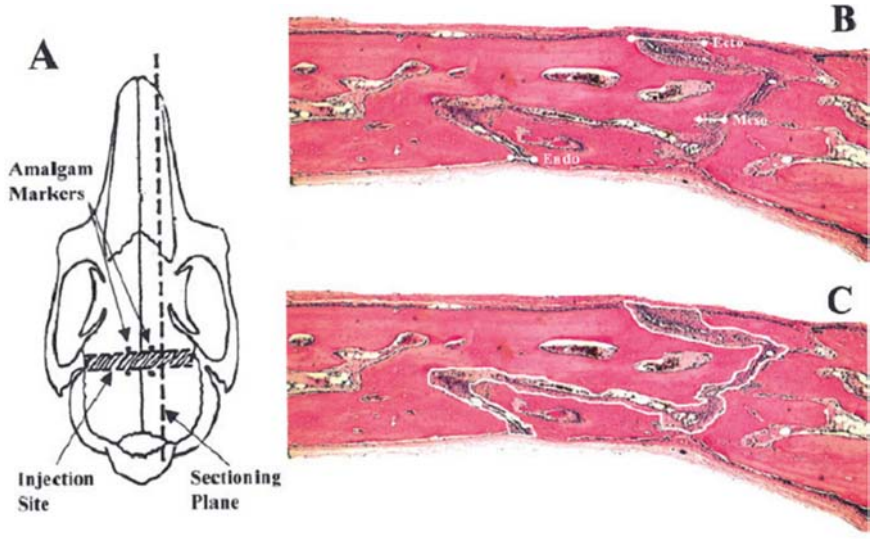

Fig. 31B.34 (A) Drawing of a rabbit skull showing the amalgam marker placement, collagen injection site and harvesting area (hatched area), and sagittal sectioning plane (dashed line) in the middle of a right coronal suture. Although it was not drawn, the *left* coronal suture was sectioned in the same plane. Histophotomicrographs (original magnification 25×) of a rabbit coronal suture in the sagittal plane showing the ecto-, meso-, and endocortical landmarks used for measuring coronal suture width (**B**) and the boundaries of the coronal suture that were traced (white lines) to quantify the coronal suture area (C).

and his associates used this model to try and replicate some of the data obtained with the normal suture fusion rodent models.[26] They found that fetal head constraint was associated with increased TGF-β1 immunoreactivity in the suture and dura areas of fusing sutures. In our laboratory we also investigated cranial suture response to stress using an *in vitro* system.[28]

Stress-induced in vitro cranial suture fusion

We modified an organ culture system that was initially set up to provide distraction and oscillation stress forces on preosteoblasts and stem cells suspended in a three-dimensional collagen matrix (Fig. 31B.36). Using this modified system we investigated sutural changes related to fusion.

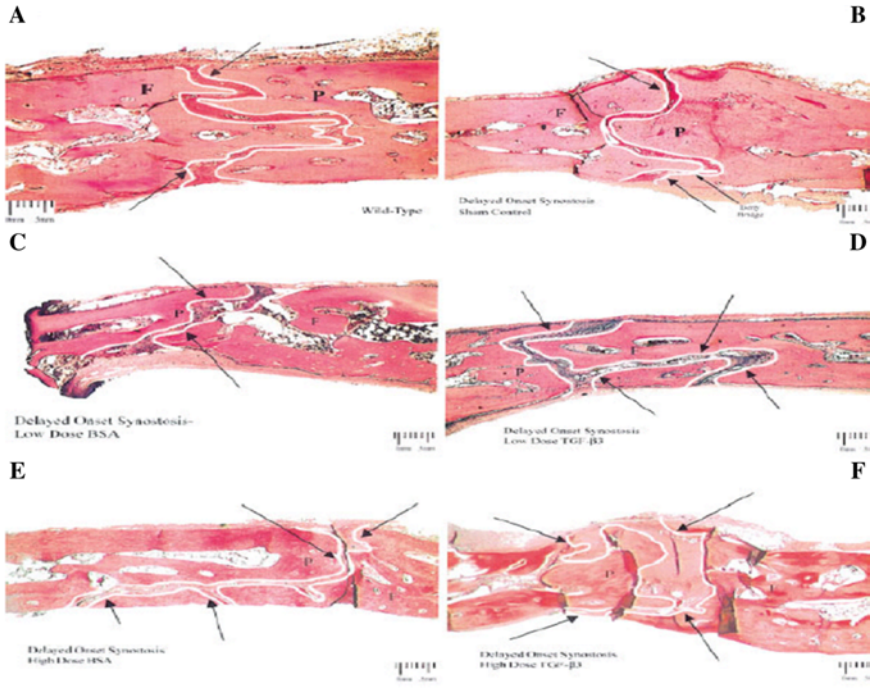

Fig. 31B.35(A–F) Histophotomicrographs (original magnification 25×) of coronal sutures from 84-day-old rabbits, showing the osteogenic fronts of the parietal (P) and frontal (F) bones and the coronal suture (arrows) for the various groups. The suture mesenchyme is outlined in white for comparison. Note the very narrow coronal suture with bony bridging (arrow) in the sham control group (**B**) and the widened and patent coronal suture in the high-dose TGF-β3 suture (**F**) compared to the other groups.

In addition, based on our above data from the normal suture rodent models and pathologic suture rabbit model, we looked at expression changes of Noggin, Runx2, and alkaline phosphatase (AP) in response to mechanical stress.

For this stress-induced suture fusion experiment, PF (fusing) and sagittal (patent) rat cranial sutures were held static, oscillated, or distracted for 10 days in our organ culture microdistraction device, beginning at 5 days of age (10 days prior to the onset of suture fusion) ($n = 15$) (Fig. 31B.37). Fusion scoring was done with 0 for patent, 1 for

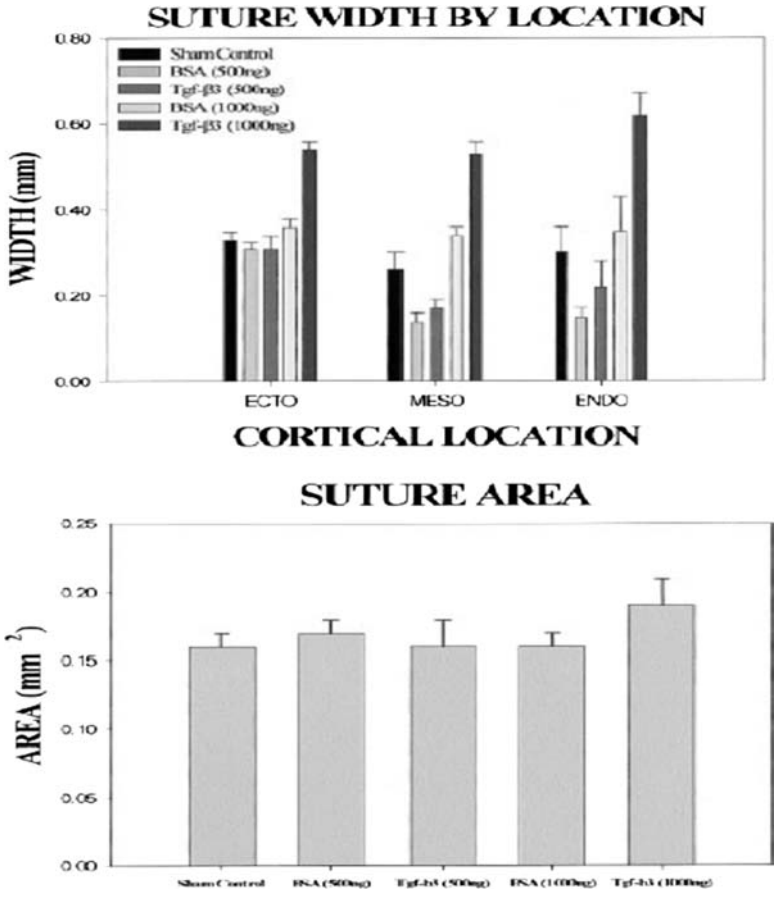

Fig. 31B.36 Graphs showing mean (±SE) coronal suture width (*top*) and coronal suture area (*bottom*) by group. Note the significantly increased coronal suture width and coronal suture area in the rabbits receiving high-dose TGF-β3 (1000 ng) compared to the other four groups.

fusing or partial fusion, and 2 for complete fusion. Percent fusion equaled the score received for bony closure. Expression of noggin, Runx2, and AP was also localized by immunohistochemistry for all groups.[20]

Our results showed that both the PF and the sagittal suture demonstrated a statistically significant ($p < 0.05$) increase in fusion percentage

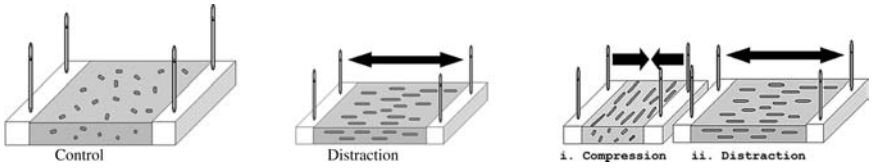

Fig. 31B.37 Illustration of three experimental groups with MC3T3 cells within the collagen matrix and Kirschner wires placed in peripheral polyethylene bars. (**a**) Control group: no stress was applied. (**b**) Distraction group: the bars were moved away from each other 0.5 mm/day (the arrow indicates the vector of linear force). (**c**) In the oscillation group, stress was applied in an alternating manner: (i) during periods of compression, the bars were moved toward each other (1.0 mm/day); (ii) during periods of distraction, the bars were moved away from each other (1.0 mm/day).

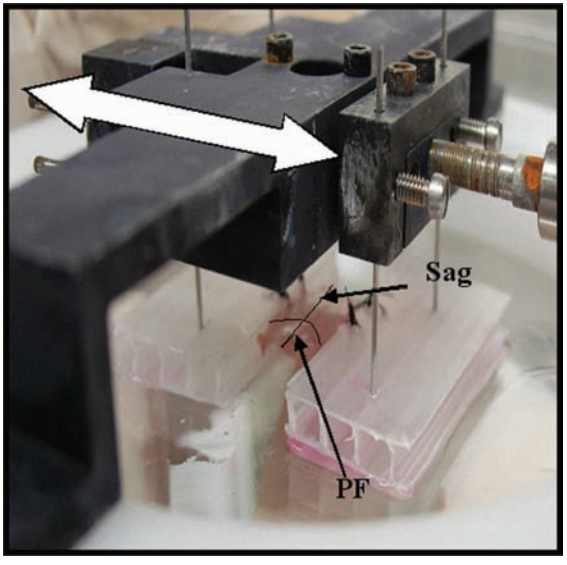

Fig. 31B.38 Cranial sutures within a microdistractor: the PF and sagittal sutures are positioned to allow perpendicular stress with activation of the microdistractor.

with *oscillation* relative to the static control, from 39% to 73% for the PF (fusing) suture and from 0% to 56% for the sagittal (patent) suture, respectively (Fig. 31B.38). Immunohistochemistry of our static control demonstrated that Noggin expression was low in the fusing PF suture, but high in the normally patent sagittal suture (Fig. 31B.39). Inversely,

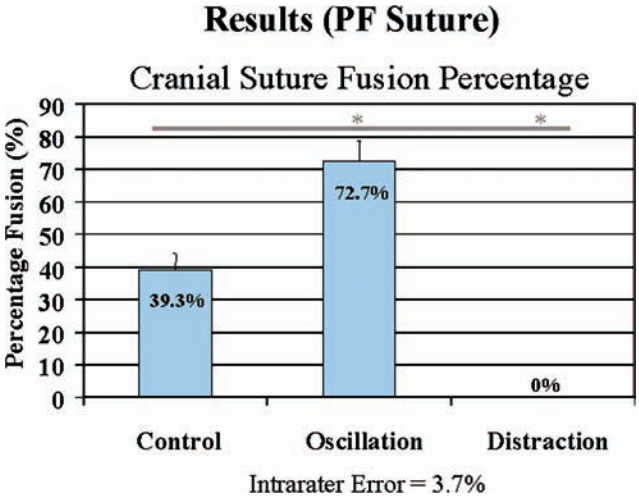

Fig. 31B.39a Posterior frontal suture: percentage of suture fusion in control, oscillation, and distraction groups ($n = 5$ per group). Oscillation showed a significant increase in the fusion percentage compared to static control. Distraction showed a zero fusion percentage. The symbol * denotes "statistically significant" compared to control.

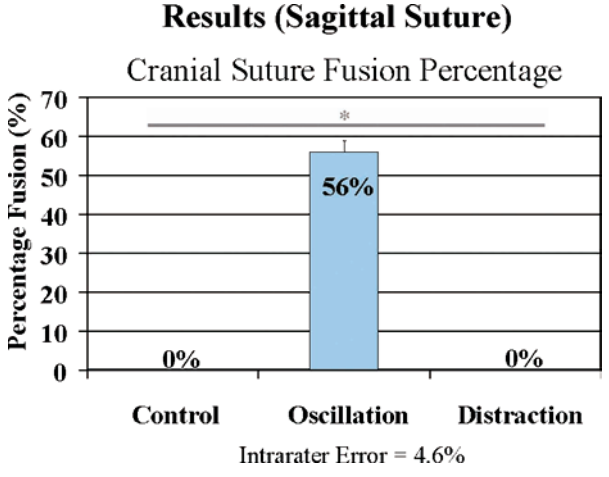

Fig. 31B.39b Sagittal suture: percentage of suture fusion in control, oscillation, and distraction groups ($n = 5$ per group). Over half of the patent sagittal sutures fused when subjected to oscillation. The symbol * denotes "statistically significant" compared to control.

Runx2 and AP were high in the PF suture but low in the sagittal suture. However, when a mechanical stress was applied via either oscillation or distraction, Noggin expression decreased significantly, whereas Runx2 and AP expression increased in both the PF and sagittal sutures (Figs. 31B.40 and 31B.41).

From our above data we concluded that the application of stress to cranial sutures results in fusion of both the PF and the normally patent sagittal suture. Noggin expression is decreased and Runx2 and

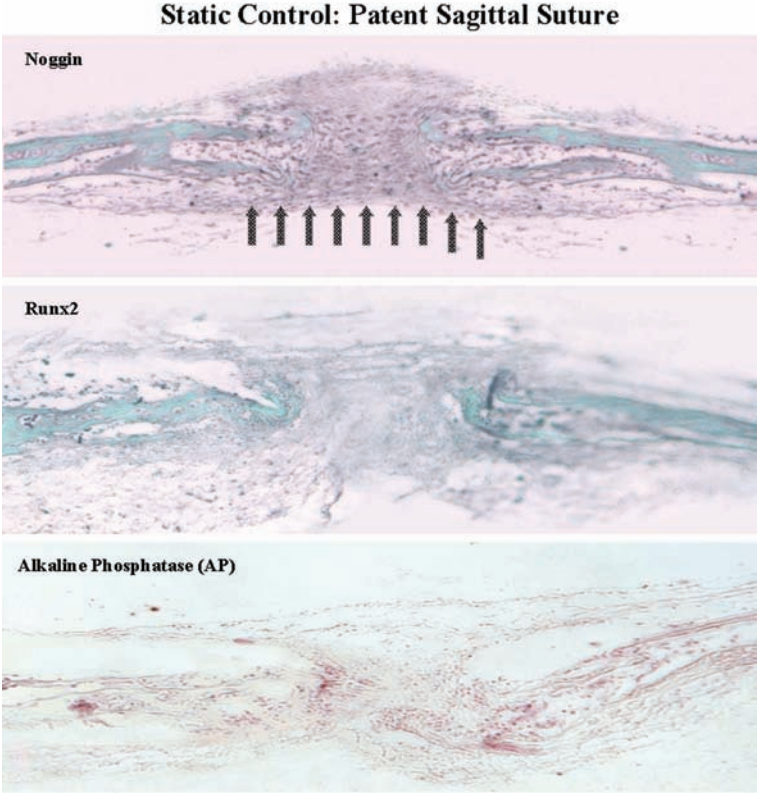

Fig. 31B.40 Digital immunohistochemistry image of a static (Group 1) sagittal suture. Noggin is expressed within sutural cells (↑) (upper panel) but Runx2 and alkaline phosphatase are not expressed (lower two panels).

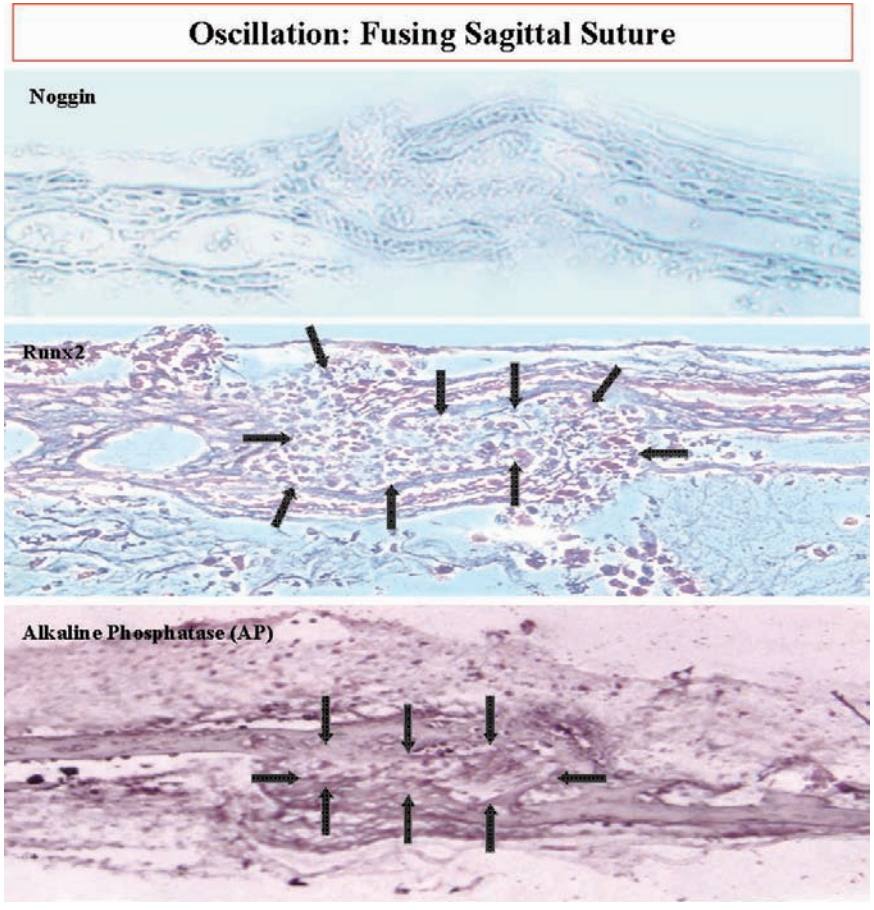

Fig. 31B.41a Digital immunohistochemistry image of an oscillation-stressed (Group 2) sagittal suture. Noggin is expressed within cells (upper panel). Runx2 and alkaline phosphatase expression is seen in sutural cells (↑) (lower two panels).

AP expression are increased. Thus, mechanical stress influences sutural fusion.[20]

The three models of cranial suture fusion presented have similarities with respect to regional tissue interaction and involvement of osteogenic factors. However, there may be subtle differences that will add to the biologic understanding of cranial suture fusion. Currently, these differences are under investigation.

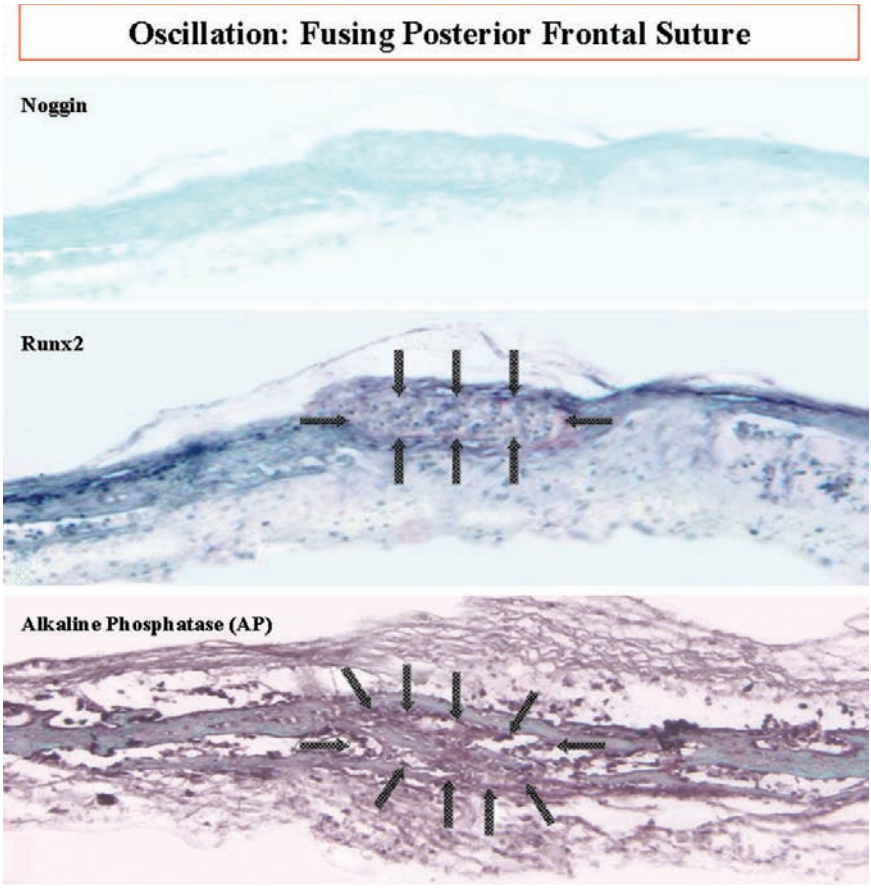

Fig. 31B.41b Digital immunohistochemistry image of an oscillation-stressed (Group 2) posterior frontal suture. Noggin is not expressed within cells (upper panel). Runx2 and alkaline phosphatase expression is seen in sutural cells (↑) (lower two panels).

CLINICAL CONSIDERATIONS

Children with craniosynostosis are evaluated by a multidisciplinary craniofacial team, including the following areas: plastic surgery, neurosurgery, genetics, orthodontics, audiology, speech pathology, head and neck surgery, pediatric dentistry, ophthalmology, and other subspecialties. Initial screening for functional problems and genetic syndromic associations is performed.

Roentgenographic confirmation of suture fusion may be necessary. A plane skull series is typically sufficient for visualizing the cranial sutures or opacification of the pathologic sutures. In addition, findings like the Harlequin deformity for unilateral coronal synostosis can be identified. (The Harlequinn deformity is the abnormal superiolateral oblique shape of the orbit from the coronal–sphenoid suture fusion.) CT scans may be necessary if hydrocephalus or another irregularity is a concern.[21] Three-dimensional CT scans may be helpful for long-term outcome research but are not typically necessary.

For patients with syndromic causes of craniosynostosis or families having multiple siblings with isolated craniosynostosis, genetic testing of FGFR is available. If one parent is affected, the risk of a child inheriting the mutation is 50%.[3]

The optimal timing of surgery varies by institution. Surgeons who prefer earlier procedures (3 months of age or younger) want to take advantage of the normal brain growth after the cranial suture release and cranial vault reshaping. Surgeons who prefer later procedures (1 year or older) suggest that the procedure is safer (with a larger child) and the relapse is less (skull bones are thicker for fixation). At UCLA we prefer around 6 months of age (4–7 months) for correction of craniosynostosis. Even when functional problems arise, like increased intracranial pressure, procedures are not delayed. Although with a single suture fusion there is a less-than-7% chance of increased ICP, with multiple synostosis the chance may be as high as 62%.[3]

The therapeutic goals of craniosynostotic correction are to release the growth restriction of the fused cranial suture, to allow for adequate volume for the expanding brain, and to provide an esthetically pleasing head shape. Technical procedures have advanced from the initial linear suture craniectomy with a high relapse rate and poor head shape results. Complete craniectomy led to incomplete ossification and poor results. Improved results were seen with full mobilization of the orbits and affected skull regions with fronto-orbital advancement for coronal and metopic synostosis and cranial vault remodeling for sagittal synostosis. Recently more minimally invasive approaches have been tried for reduced morbidity. Endoscopic procedures are less invasive but require 6–12 months of

postoperative helmet therapy. Regulated springs have also been used for simple cranial expansions. At UCLA we prefer cranial vault procedures like a reverse PI procedure that is less invasive than a total cranial vault remodeling but does not require postoperative helmet therapy. In addition, blood-conserving therapy with preoperative erythropoeitin and intraoperative cell saver are often used.

Most cases of craniosynostosis are diagnosed after birth; however, ultrasonic prenatal detection is becoming more common, especially with the 3D mode. Although *in utero* invasive surgical treatment should not be performed owing to the high risk of preterm labor, future minimally invasive biological manipulations may be possible. Further investigations into the biology of cranial suture fusion and translational studies may make this a future option.

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PART VI

SOME LESSONS LEARNED

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CHAPTER 32

Differential Growth and Healing of Bones and Teeth*

INTRODUCTION

A series of experiments was conceived, designed, and performed in regard to bones and teeth in turtles, rats, gophers, lagomorphs, pigs, dogs, and monkeys. The purpose of this selective and limited review, analysis, and summary of personal experiments was to correlate certain aspects of differential growth and healing with age, sites, rates, factors, and mechanisms. No similar report was found in the literature.

The studies included (1) sutural growth of the turtle shell, monkey face, and rabbit snout; (2) cartilaginous growth of the long bones and the base of the skull in the rat, the costochondral junction in the rabbit, the mandibular condyle in the monkey and pig, and the nasal septum in the rabbit; (3) appositional and resorptive growth of the rabbit nasal bone region and the pig mandible; (4) normal and abnormal growth of the rabbit orbit and changes in the dog maxillary sinus; (5) growth of the gopher incisor during hibernation and under normal laboratory conditions, and effects of yellow phosphorus on rat teeth (and bones); and (6) reaction of both bones and teeth in the rat to a single inclusive fracture.

From these studies the following observations will be considered specifically: (1) differential sutural bone growth within the same site;

*Excerpted from: Sarnat BG. (1984) Differential growth and healing of bones and teeth. *Clin Orthop Relat Res* **183**: 219–237.

(2) differential sutural bone growth at the same site in relation to age and other factors; (3) differential sutural bone growth of various related sites; (4) differential endochondral bone growth at various sites; (5) differential growth of the cartilaginous nasal septum; (6) differential appositional and resorptive bone growth at various sites; and (7) differential healing of bone, cementum, dentin, and enamel to simultaneous fracture of these tissues at the same related site.

EXPERIMENTAL CONSIDERATIONS

Bone Growth

Sutural growth

Several facial sutures

The contribution to the growth of the face of the frontomaxillary, frontozygomatic, zygomaticomaxillary, zygomaticotemporal, and premaxillomaxillary sutures was studied in eight young Macaca rhesus monkeys (see Chap. 15).

Shell

Except for the turtle shell, sutural (synarthroses) bone growth is found only in the skull. The total amount and periodic increments of bone growth at the hyohypoplastron (length) and interhyoplastron (width) sutures were investigated in 28 turtles from 233 to 1154 days of age by means of serial roentgenographic studies of the increase in separation of radiopaque implants on either side of the selected sutures (see Chap. 33).

Cartilaginous growth

Long bone; base of the skull

In this part of the investigation, the effects of yellow phosphorus on growing bones and growing teeth were studied and compared, and the mechanisms of these effects were determined (see Chap. 31). In the experimental animals, the lengths of the long bones and skulls were found to be less than

in the control animals (Fig. 31.1). A phosphorus band in the metaphyses of the growing long bones and the basal bones of the skull was visible as a zone of increased density on roentgenographs. This same area was observed in the sectioned specimens both grossly and histologically. The effect was believed to be due to a diminution in the resorption of cartilage matrix and bone during endochondral bone formation.

Mandibular condyle

See Chaps. 2–4.

Nasal septum

Autoroentgenographic studies with tritiated thymidine were undertaken to determine normal levels of proliferative activity in the young rabbit cartilaginous nasal septum (see Chaps. 11 and 14).

Appositional and resorptive (remodeling) growth

Nasal bone

Differential growth activity at several borders of the nasal bone region was studied (see Chap. 13).

Mandible

A combined method of serial roentgenography and metallic implants was used to study the growth pattern of the mandible in 9 Hampshire pigs from 8 to 20 weeks of age (see Chap. 2).

Growth of Cavities

Orbit

Normal orbital volume

One hundred and ninety-nine postnatal volumetric determinations were made of orbits from 159 young and adult rabbits (64 New Zealand,

95 Dutch) by means of either linear measurements or removable permanent elastic rubber base imprints (see Chaps. 20 and 21).

Maxillary sinus

In this part of the investigation, the volumes of the left and right maxillary sinuses were compared in the dog after extraction of the teeth adjacent to the left maxillary sinus (see Chap. 16).

Growth of Teeth

Hibernation

Developing teeth reflect metabolic changes promptly and accurately. During hibernation there is an extreme depression of general metabolism. This part of the investigation sought to determine the effect of hibernation on the rate of dentin apposition in the 13-lined ground squirrel (see Chap. 25).

Sutural Growth

By the use of implants on either side of a suture, information was obtained about the total amount, rate, and direction of bone growth, and highlight periods of maximum/minimum growth activity at a particular time. Many instances of differential sutural growth were demonstrated (see Chap. 33).

Cartilaginous Growth

Differential cartilaginous growth was found within a particular region and between different regions. In the rabbit nasal septum, the sites of greatest activity were in the anterior and posterior areas (Fig. 11.3). In the third, fifth, and seventh rabbit ribs, the third rib had the lowest rate of growth while the seventh had the highest at the costochondral junctions. Endochondral growth of the rat tibia was found to be considerably greater than endochondral growth at the base of the skull (Fig. 31.1). In addition, the toxic effects of yellow phosphorous on endochondral bone growth were demonstrated, in that in the experimental animals the length of both

the tibia and the skull was less than in the control animals (Fig. 31.1). The radiopaque phosphorus bands in the tibia could be compared with lines of arrested growth. Endochondral growth of the mandibular condyle made a major and differential contribution to growth of the mandible in terms of both site and time (Fig. 2.5).

Appositional and Resorptive (Remodeling) Growth

This type of growth was well demonstrated in the pig mandible, in which the greatest amount of growth occurred at the posterior border of the ramus (with actual loss of bone at the anterior border of the ramus) and the least amount at the inferior border of the body of the mandible (Fig. 2.5). There was a deceleration in the amount of growth at all borders with age. Differential growth was found in the rabbit nasal bone region, with the greatest at the distal and proximal borders.

Cavities

Deceleration of the increase in the size of the orbital cavity is related to a decrease in the orbital contents, whereas acceleration of the increase in the size of the orbital cavity is partially explained on the basis of increased volume of the contents (see Chaps. 20 and 21). What are the factors related to the change in the volume of air-filled cavities, e.g. the sphenoidal, ethmoidal, frontal, and maxillary sinuses? The maxillary sinus was reported to be larger when the adjacent teeth were absent (see Chap. 16).

During mastication forces are brought to bear on the dentition and its supporting structure. The maxillary sinus occupies the region between the palatine process of the maxilla, the facial surface, and the base of the alveolar process. Thus, it lies at the point of intersection of the forces transmitted from the teeth to the cranium. Since a large part of the walls of the antrum, and especially the floor, are devoid of muscular attachment, the masticatory forces contribute most of the functional forces. After the extraction of maxillary teeth, the sinus is bounded by walls in which the functional forces have been reduced. While remodeling, the bulk of the walls is reduced, leading to enlargement of the sinus.

Teeth

Lowering of the environmental temperature during hibernation produced severe depression of general body metabolism as well as of dentin apposition, as measured by vital staining with alizarin red S (Fig. 25.1). This offers an easy, accurate method for determining the differential rate of growth of mineralizing structures under normal and pathologic conditions in various experimental animals.

Histologically, in the incisors and molars of the rats that received phosphorized cod liver oil, the daily incremental pattern of the dentin (Fig. 26.1) could be closely correlated with the time of injection of the drug and the changes in the long bones (Fig. 31.1).

Healing of Mineralized Tissues

Experimental complete transverse fractures of the mandible in the rat offered a unique opportunity to study and compare the effects of simultaneous fractures on the growing bone and the growing tooth (see Chap. 6, Fig. 6.1). While the enamel, dentin, cementum, and bone are all hard, mineralized structures, they differ significantly in their response to injury and their capacity for repair. The dental tissues that were capable only of apposition were generally nonreactive, while bone and cementum, which were capable of both apposition and resorption, were highly reactive and able to recover from the trauma. The fractured tooth changed from an actively functioning organ to one of deformity and dysfunction, while the repair of bone was frequently effective in restoration of normal function.

Sutural Growth*

A series of experiments was performed on young monkeys, rabbits, and turtles to study gross sutural growth of bones. Radiopaque implants in conjunction with serial, direct gross, and indirect roentgenographic measurements were employed. Differences in growth were observed in the monkey among five facial sutures and also in the same suture at different times. Growth was greatest at the zygomaticotemporal suture and least at the premaxillomaxillary suture (see Chap. 15, Fig. 15.2). In the rabbit, the nasal bone side of the frontonasal suture grew about twice as fast as the frontal bone side (see Chap. 13). In the turtle shell, the midsagittal suture grew faster than the transverse suture (Fig. 33.1). In all of the animals, the rate of sutural growth decreased with an increase in age. No gross regional growth disturbance was noted after resection of the frontonasal (see Chap. 12B, Fig. 12B.2), midpalatine, and transpalatine sutures (see Chap. 17, Fig. 17.1). The frontonasal suture reformed presumably because of the underlying nasomucoperiosteum, as in a cranial suture, also because of the underlying dura. After extirpation of the midpalatine suture with the formation of a complete cleft and despite there being no underlying membrane, a new suture reformed in an eccentric position in a number of instances. Bone growth at sutures is secondary or compensatory to some other factors.

Local resection of a suture in a child with craniosynostosis inevitably results in its reformation presumably because of the presence of the

*Excerpted from: Sarnat BG. (2003) Gross growth and regrowth of sutures: reflections on some personal research. *J Craniofac Surg* **14**: 438–444.

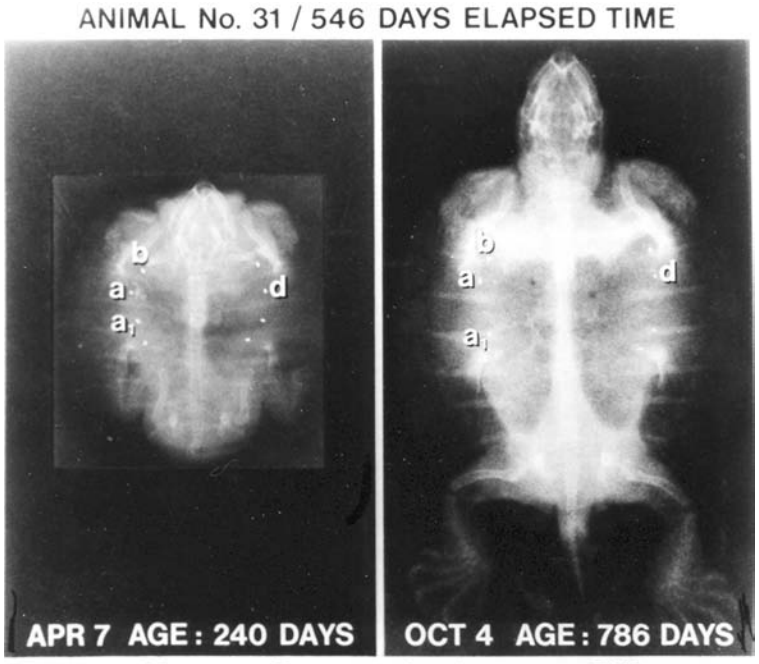

Fig. 33.1 Dorsoventral roentgenographs of turtle No. 31 at 240 and 786 days of age. Two radiopaque implants were inserted into each of the left (a and b) and right hypoplastron and hyohypoplastron bones at 233 days of age. Note, during the 546-day period, the greater increase in separation of implants in width (ad) — 7.7 mm at the midsagittal suture — than in length (aa_1) — 4.3 mm at the hyohypoplastron suture. Of course, more than one suture contributed to increase in length. Also note that there was no increase in separation between the implants ab, which were in the same bone during the 546-day period. This demonstrated that there was no interstitial growth of bone. [Reproduced with permission from Sarnat BG: Differential growth and healing of bones and teeth. *Clin Orthop* **183**: 225, 1984.]

underlying dura mater. Similarly, local resection of the frontonasal suture in young rabbits results in reformation presumably because of the presence of the underlying nasal mucoperiosteum. The challenge was to find a free bounding suture with no underlying membrane.[1] In selecting the

midpalatine suture (see Chap. 17, Fig. 17.1), the following questions were raised. After total resection of the midpalatine suture and its related soft tissues, creating a surgical cleft of the palate with complete communication between the oral and nasal cavities, what would be the status of (1) the resected suture region; (2) the related soft tissue; (3) the growth of the bony palate, midface, and face; and (4) the suture as either a primary or secondary site of growth? This seemed to be the ideal model for testing the issue of sutural regrowth.

REGROWTH OF SUTURES

Extirpation of the median and transverse palatine sutures in young monkeys (see Chap. 17).

HISTOLOGICAL FINDINGS

Examination of the tissue revealed that on the side not operated on, the mucous membrane and the submucosa were normal in a wide lateral area.[1] The edge of the cleft, however, was formed by dense connective tissue that showed some subepithelial lymphocytic infiltration. The lamina propria of the mucosa and the submucosa was replaced by dense collagenous scar tissue. The regenerated tissue shelf consisted of a core of dense collagenous scar tissue covered on the oral surface by stratified squamous epithelium and on the nasal surface by pseudostratified columnar epithelium. This finding duplicates the relations in a case of congenital cleft palate.

The total surgical cleft showed an extreme tendency for healing by proliferation of the tissues at the edges of the cleft. This proliferation of tissues may lead to almost functional closure between the oral and nasal cavities by an overlapping of the two shelves that grow from the sites of resection. In areas where the two soft tissue shelves touched, no fusion (i.e. no anatomical closure of the defect) occurred in these animals. There were signs of the formation of new bone and progressive growth of the newly formed trabeculae. This formation of bone, however, should not be classified as growth of the maxilla or the palatine bone, but rather as growth of bone tissue within young, proliferating connective tissue.

The difference — biologically speaking — between a congenital and a surgical cleft is the static behavior of the former, whereas the unprotected edges of the wound in the latter cause a proliferative reaction of the injured tissues. It may be permissible to consider that even in the congenital cleft, the static relations could be changed to dynamic tissue behavior by surgical interference at the edges of the cleft. An interesting observation was made by Adams[2] when he found bony union of the hard palate of the repaired soft tissue cleft. Adams[2] stated, "… this was an unexpected finding, since all previous teachings and beliefs were that following repair of complete cleft palate by the use of mucoperiosteal flaps one could expect only a soft tissue repair of the defect."

THE SNOUT AFTER EXTIRPATION OF THE FRONTONASAL SUTURE REGION IN YOUNG RABBITS

See Chap. 12B and Fig. 12.2B.

SUTURAL GROWTH

Growth a: several facial sutures in young monkeys (see Chap. 15 and Fig. 15.2).

GROWTH AT THE FRONTONASAL SUTURE IN YOUNG RABBITS

See Chap. 12A and Fig. 12A.1.

GROWTH AT SEVERAL SUTURES IN YOUNG TURTLE SHELLS

The total amount and periodic increments of bone growth of the hyohypoplastron (length) and interhyoplastron (width) sutures were investigated in 28 turtles from 233 to 1,154 days of age by serial roentgenographic studies of the increase in separation of radiopaque tantalum implants on either side of the selected sutures.[3] The turtles were maintained in aquaria under constant laboratory conditions (16 h of artificial light and 8 h of darkness, temperature of 27°C, humidity factor of 30%, and fed twice a week). The mean sutural bone growth was greatest in the

period of 233–317 days of age and decelerated thereafter in each successive period. In the period of 606–786 days of age, the mean growth at the hyohypoplastron suture was about one-fourth to one-third that of the earliest period. At the interhyoplastron suture, the mean bone growth was about 40% that of the earliest period. Comparison of width (midsagittal) versus length (hyohypoplastron) sutures showed significantly greater growth of the turtle shell in length than in width (Fig. 33.1). More sutures, however, contributed to greater growth of the turtle shell in length than in width. (Turtle shell is unique, in that the turtle is the only animal with sutural bone growth outside the skull. Growth of the turtle shell can be compared with growth of the cranium. The turtle is an easy-to-raise, readily available, and inexpensive experimental animal. For example, a variety of experiments could be undertaken, such as restraint, extirpation, rotation, and transplantation of sutures.)

PATTERN OF SUTURAL GROWTH OF BONES

The pattern of sutural bone growth may be quite varied. Several different theoretical possibilities may occur, either separately or in combination (Fig. 33.2). Thus, sutural bone growth can be classified according to whether the total amounts of growth at various sites along a suture are equal or unequal.

If the total amounts of growth are equal, three variations in this group may be considered: (1) the amount of bone growth is equal on either side of the suture and along each border (Fig. 33.2A), (2) the amount of bone growth is greater on one side of the suture than on the other but equal along a given border at several points (Fig. 33.2B), or (3) the amount of bone growth is unequal not only on each side of the suture at any point but also along a given border at several points (Fig. 33.2C).

In contrast, in a second group, the total amounts of bone growth are unequal at various sites along a suture. Three possibilities may be considered: (1) at any one site on the suture, the amount of bone growth is equal on each side but varies at different sites (Fig. 33.2D); (2) the amount of bone growth is unequal on each side of the suture at any one point but equal along one of the borders at several points (Fig. 33.2E); or

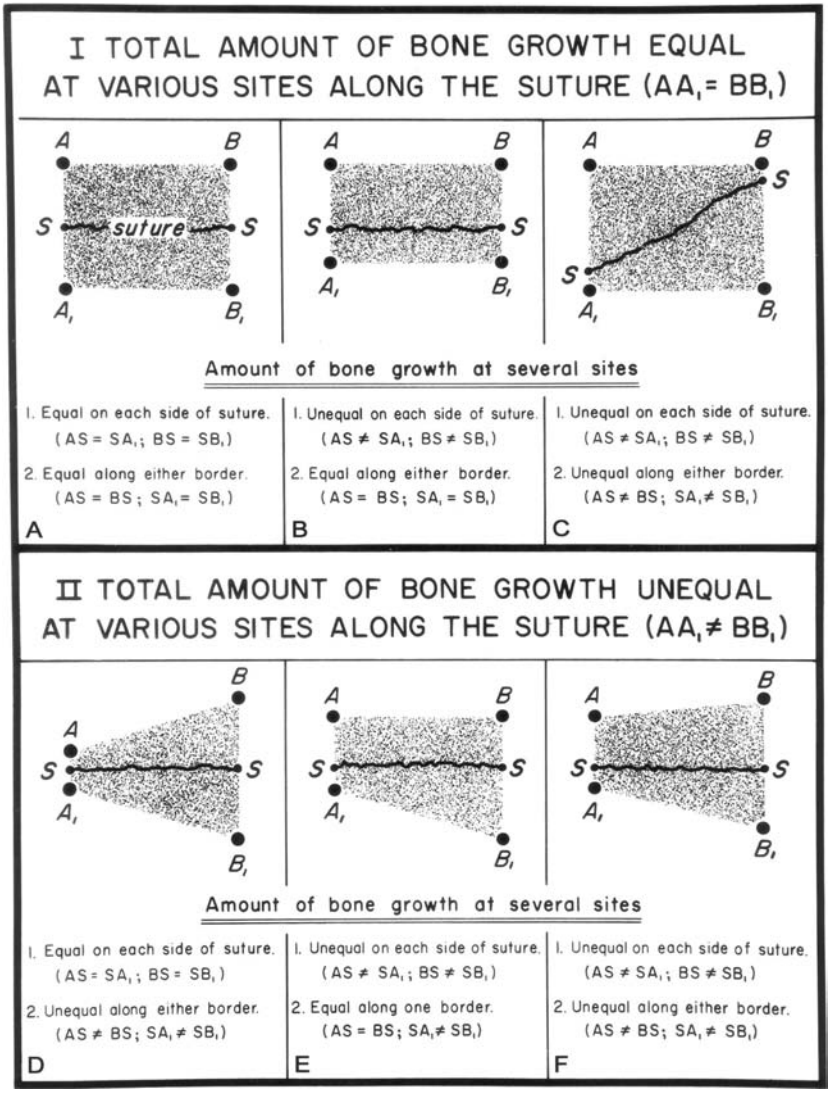

Fig. 33.2 Diagrammatic representation of some possible patterns of gross sutural bone growth that could be determined from the changes in position of implants along a suture. AS, SA1, BS, and SB1, for example, represent an amount of bone growth along a suture at particular points for a unit period of time. A, Al, B, and Bl represent implants. S — suture. [Reproduced with permission from Selman AJ, Sarnat BG: Sutural bone growth of the rabbit snout: a gross and serial roentgenographic study by means of metallic implants. *Am J Anat* **97**: 395–408, 1955.]

(3) the amount at any one site on the suture is unequal on each side as well as at different sites along the borders (Fig. 33.2F).

If a skull bone grows at its sutures, the form of the bone is influenced by and represents in part the past pattern of activity of its sutures. One might thus expect that the pattern of activity would be the same on each side of a suture bordering bones similar in form and different on each side of a suture bordering bones differing in form. Identical bones in the skull would then be bordered by identical suture complexes, and dissimilar ones would be bordered by dissimilar suture complexes.

Contiguous bones that are identical or mirror images must be joined by a suture with identical bone growth activity on both sides, such as the sagittal or internasal suture (Figs. 33.2A, D). The essentially straight interfrontal suture of the growing rabbit, for example, joins symmetrical frontal bones, which taper in the region of the nasal process (see Fig. 33.2A). A progressive decrease anteriorly in the rate of sutural bone growth accentuates this tapering (see Fig. 33.2D). Constancy of an equal amount of bone growth on either side of the suture maintains the symmetrical bone and straight suture form. The particular anteroposterior shape of the snout (e.g. narrower anteriorly and wider posteriorly) raises a question as to the growth gradient all along the internasal and interfrontal sutures.

Conversely, inequality of activity on either side of the suture may be expected between dissimilar bones that are contiguous, as are the frontals and nasals (see Figs. 33.2B, C). The bow-shaped frontonasal suture is characterized not only by an unequal amount of bone growth on each side of the suture at any site but also by variation along a border. However, the total amounts of bone growth at various sites along the suture are equal. To be unidirectional, growth must be equal in all planes along a suture (Fig. 33.2C).

COMMENT

Because of the number of varied sutures and other structures, the face has proven to be a rich source of study. By the use of implants on either side of the suture, information was obtained about the amount, rate, and direction of bone growth, highlighting periods of maximum and minimum

growth activity at a particular time. Many instances of differential sutural growth were demonstrated. Of particular interest was the finding in the rabbit that the nasal side of the frontonasal suture contributed about twice as much as the frontal side to growth of that suture. That different sutures at a particular time in the same animal have different rates of growth was shown in the monkey. Of five facial sutures studied, the zygomaticotemporal suture had the greatest rate of growth and the premaxillomaxillary suture had the smallest. This was also found for the turtle shell, where the midsagittal suture made a greater contribution to growth in width than the hyohypoplastron suture to growth in length. In the animals (turtle, rabbit, and monkey), the rate of sutural growth decreased with age.

So, what is the nature of gross sutural growth and regrowth?

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Effects and Noneffects of Personal Environmental Experimentation on Postnatal Craniofacial Growth*

EDITOR'S NOTE

In this issue of *The Journal of Craniofacial Surgery*, Dr. Bernard Sarnat, renowned for his work on craniofacial growth for the past 50 years, has a distillate of his work presented. The presentation is based on a keynote lecture at the American Association of Pediatric Plastic Surgeons in Los Angeles, California, during the American Society of Plastic Surgeons Annual Meeting. Dr. Sarnat received the honors of the association and was made an honorary member of the association. His original work, which was scholarly, motivated individual scientists worldwide to further their studies in the field of craniofacial growth and proceed further with a new understanding based on his original contribution to the field of craniofacial growth. The editorial board of *The Journal of Craniofacial Surgery* is delighted to have those experiences shared with all the readers around the world. On a final note, to Dr. Sarnat from the editorial board of the journal: "Bravo Bernie!" It is by your scientific work that the craniofacial surgeons will always treasure.

— *Mutaz B. Habal, Editor*

*Excerpted from: Sarnat BG. (2001) Effect and noneffects of personal environmental experimentation on postnatal craniofacial growth. *J Craniofac Surg* **12**: 205, 217.

INTRODUCTION

The purposes of this personal, selective, organized, limited review, analysis, and summary are to present some of the significant basic science methods used for evaluating the effects and noneffects of several environmental factors (a variety of surgical trauma, chemical, and cold) on craniofacial growth. Some principles of the biology of bone(s) are central to this presentation.

What follows serves as a brief, general introduction for consideration of some of the various factors and their subtleties and nuances, which may or may not affect craniofacial growth. In planning experiments to determine either change or nonchange in size and shape with time, as accurately as possible, various approaches were considered and used, both direct and indirect. Although the design of the experiments was such as to obtain either a "yes" or "no" answer, at times a "maybe" answer was the result. Invariably, after completion of the experiments, more questions were raised than answers. The findings were unequivocal, but the explanations sometimes left some doubt.

This report will be limited to a few selected examples of extensive gross morphological change: (1) resection of the mandibular condyle with severe changes not only of the mandible but also as a consequence of the ventral skull and midface; (2) resection of the nasal septum with extreme changes in the midface; (3) either decrease or increase in the volume of orbital contents, with a resulting orbit either less large or larger than normal; (4) administration of a chemical, yellow phosphorus, with retarded long bone and skull base growth and altered dental calcium metabolism; and (5) the effects of hibernation on dental growth and eruption. Thus, these models are representative of the lower face, the midface, the orbit, the lateral face, the ventral skull, and the basicranium, as well as the general skeleton. Other experiments, with either alteration or nonalteration of bone growth, are mentioned in Tables 34.1 and 34.2.

LOCAL SURGICAL INTERVENTION

Changes After Mandibular Condylectomy

What might be the effects of prenatal and postnatal disorders, trauma, or disease of the condyle? To find some answers to these questions, unilateral

Table 34.1 Craniofacial Surgical and Other Experiments that Produced Gross Bony Changes. Sarnat BG. Effect and noneffects of personal environmental experimentation on postnatal craniofacial growth. *J Craniofac Surg* 12: 205, 217*

Site	Animal	Procedure	Findings
Temporomandibular joint	Young monkey, adult monkey	Unilateral resection of mandibular condyle and lateral pterygoid myotomy	Severe upper and lower facial and ventral cranial asymmetry
Cartilaginous nasal system	Young rabbit	Extensive resection of cartilaginous nasal septum	Severe upper and lower facial deformity
Maxillary sinus	Adult dog	Extraction of adjacent teeth	Increase in volume of maxillary sinus
Orbit	Young rabbit	a. Evisceration of eye b. Enucleation of eye c. Exenteration of orbit d. Increase in volume of eye	Deceleration of orbital growth directly related to volume of tissue removed; increase in volume of orbit
Basicranium, tibia	Young rat	Systemic administration of yellow phosphorus	Decrease at growth at basicranium and tibia

*Modified with permission from Sarnat BG (1997). *Plast Reconstr Surg* **100**: 132–153 (Copyright © 1997 by American Society of Plastic Surgeons, Inc.)

mandibular condylectomies were performed on both young and adult monkeys (see Chaps. 3 and 4). With the use of cartilage implants to build up facial deficiencies (see Chap. 28), metabolic and histochemical studies were initiated (see Chap. 37).

Effects of Extirpation of the Nasal Septum

Major amounts of the septovomeral regions and/or the cartilaginous nasal septum were resected in both young and adult rabbits (see Chap. 14).

Table 34.2 Craniofacial Surgical and Other Experiments that Produced No Gross Bony Changes. Sarnat BG. Effect and noneffects of personal environmental experimentation on postnatal craniofacial growth. *J Craniofac Surg* 12: 205, 217*

Site	Animal	Procedure	Findings
Temporalis muscle/ coronoid process	Adult monkey	Unilateral intracranial resection of motor root V nerve	Atrophy of temporalis muscle; no change of coronoid process
Cartilaginous nasal system	Adult rabbit	Extensive resection of cartilaginous nasal septum	Local defect as a result of surgical procedure; no gross deformity
Frontonasal suture	Young rabbit	Unilateral and bilateral wide resection of suture not including mucoperiosteum	Regrowth of suture; no gross deformity
Mipalatine and transpalatine sutures	Young monkey	Complete resection of sutures including periosteum producing a complete cleft palate	Regrowth of sutures and scar tissue; no gross deformity
Orbit	Adult rabbit	Enucleation of eye	No change in volume of orbit
Eye, orbit	Adult rabbit	Unable to increase volume of eye as in young	No change in volume of either eye or orbit
Upper and lower jaws	Young human	Experiment of nature, complete absence of both primary and secondary dentitions	Growth of jaws and face within normal limits except for alveolar bone

*Modified with permission from Sarnat BG (1997). *Plast Reconstr Surg* **100**: 132–153 (Copyright © 1997 by American Society of Plastic Surgeons, Inc.)

Experimental Changes After Decrease and Increase in Orbital Contents Volume

Facial growth is related to orbital growth. The shape and size of the orbit result from the balance of a number of genetic and epigenetic factors that may function on a systemic, regional, and local basis (see Chaps. 19–22).

SYSTEMIC FACTORS

Yellow Phosphorus and Its Effect on Long Bones, the Base of the Skull, and Teeth

In this investigation on young rats, the effects of yellow phosphorus on growing bones and growing teeth were studied and compared and the mechanisms of these effects were determined (see Chaps. 26, 31, and 38B).

Effect of Decreased Temperature on Growth

Developing teeth reflect and record metabolic changes promptly, accurately, and permanently. During hibernation there is an extreme depression of general metabolism. In this investigation, we sought to determine the effect of hibernation on the rate of dentin apposition and dental eruption in the 13-lined ground squirrel (see Chap. 25).

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Interstitial Growth of Bones*

INTRODUCTION

As early as 1743, Duhamel (cited from Payton 1932)[1] demonstrated grossly that long bones grow at their ends and that there is no interstitial growth. This report is unique, in that it deals not with long bones but with what are essentially flat bones of young Hampshire pigs (mandible),[2] New Zealand white rabbits (frontal and nasal),[3] and turtles (hyoplastron and hypoplastron).[4]

MATERIALS AND METHODS

The general method of study was to insert two or more radiopaque dental amalgam or tantalum implants in each of several bones of young pigs,[2] rabbits,[3] and turtles[4] and to follow the subsequent growth with serial roentgenographs. Special head-holders were designed for the pig (see Chap. 2, Fig. 2.3) and the rabbit (see Chap. 12A, Fig. 12A.1).

Turtle Hyoplastron and Hypoplastron[1]

See Chap. 33.

*Excerpted from: Sarnat BG. (2004) Interstitial growth of bone revisited. *J Craniofac Surg* **15**(2): 283–287. Awarded Best Paper of 2004.

RESULTS

Pig Mandible

Measurements between implant images were the same on all the serial roentgenographs for each animal (see Chap. 2, Fig. 2.4); these implants were used as points of reference for superpositioning the tracings of the roentgenographs.

Rabbit Frontal and Nasal Bones

Of the 200 implants inserted, 7 were missing and 13 were loose. Four of these were associated with inflammatory reaction. Most of the difficulties were encountered in the nasal bones. The remaining 180 implants were well tolerated and invariably covered by a thin layer of bone. Measurements taken between implants in the same bone (frontal and nasal) were the same at the beginning as at the end of the experiment (see Chap. 12A, Fig. 12A.2).[1]

Measurements between the implant images within the same bones showed no changes in relationship during the entire experimental period (see Chap. 33, Fig. 33.1).

DISCUSSION

In 1743, Duhamel (cited from Payton 1932)[1] cut holes in the shafts of growing bones and inserted silver stylets. At a later period, he found that the distance between the stylets remained the same. From this he concluded that growth in length occurred at the extremities of a bone and that there was no interstitial growth. He made no mention of the epiphyses. In 1770, Hunter (cited from Dobson 1948)[5] implanted two lead pellets along the length of a growing tubular bone and measured the distance between them. When the animal (bone) was fully grown, he found that the distance between the pellets had remained the same (Fig. 35.1). Flourens (cited from Keith 1919)[6] in 1842 and Ollier (cited from Keith 1919)[7] in the 1860's confirmed Duhamel's findings that there was no interstitial growth of long bones. Adams and Sarnat[8] demonstrated, by the use of yellow phosphorus,

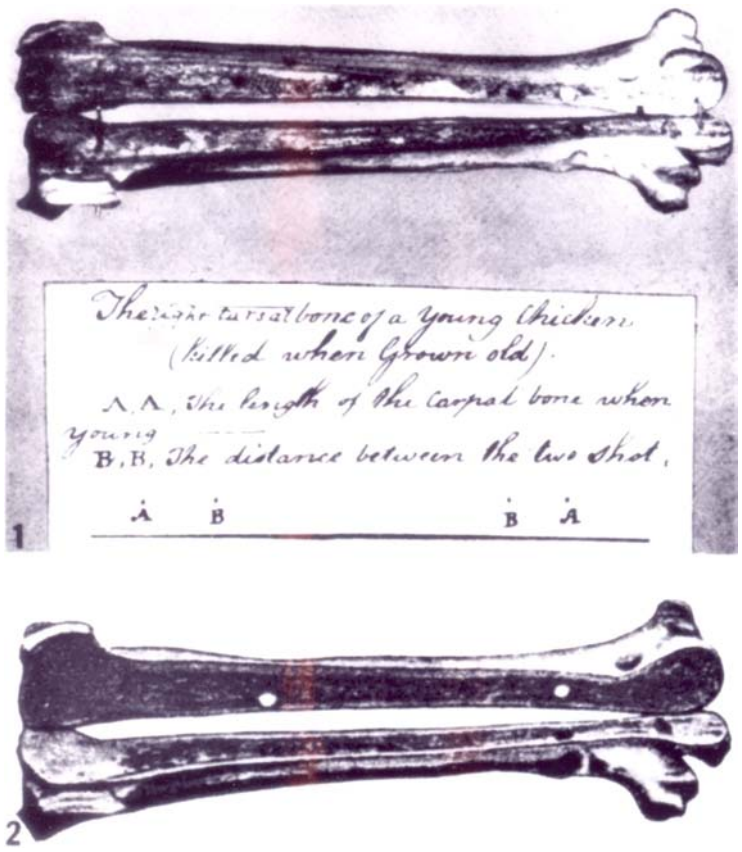

Fig. 35.1 Photograph of one of John Hunter's specimens, with the original note illustrating experiments in the investigation of growth of bones by the insertion of lead shots into drill holes. [From: Dobson J. (1948) Pioneers of osteogeny: Hunter, 1782–1793. *J Bone Joint Surg* **30B**: 361–364.]

endochondral bone growth, not only at the end of the tibia but also at the skull base. However, in 1868, Wolff (cited from Keith 1919)[9] concluded that the conception of interstitial growth of bone was not true. Weinmann and Sicher stated, "One of the most important advancements in bone biology is the conclusive demonstration that there is no interstitial bone growth. Growth of bone tissue always occurs by the addition of new bone tissue to free bone surfaces, in other words by appositional growth.

It is both interesting and discouraging that the concept of interstitial growth of bone, long since disproved and discarded, is still exhumed from time to time by some writers."

Because the design of these experiments included at least two implants within the same flat bone, measurements between these implants were taken. No change in the relationship was found. The evidence obtained agrees with that of others who do not subscribe to the theory of interstitial growth of bone. The mandible, nasal, frontal, hyoplastron, and hypoplastron bones grow by apposition and resorption. At their sutures, they grow only by apposition. In addition, the mandible grows at its condyle by epiphysis-like growth.

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CHAPTER 36

Some Methods of Assessing Growth of Bones*

Dr. Bernard G. Sarnat has, over many years, contributed a substantial amount of information to the field of craniofacial biology. His influence has been most significant. Dr. Sarnat has submitted this article as a review of his extensive contributions. I believe it is extremely valuable for younger members of our Association to understand the basis of how and from where information we use today comes. I believe that Dr. Sarnat's article facilitates such an understanding. I hope that you enjoy reading his publication.

— *Stewart R. Rood, Ph.D. Editor*

INTRODUCTION

The purposes of this personal, selective review and summary are to present some of the significant clinical and basic science methods used for assessing and evaluating growth of bone(s) and in particular the determination of craniofaciodental growth. In part, this report includes anthropometry, impressions and casts, vital markers, histology, radiopaque implant markers with and without serial cephalometric roentgenographs, and autoroentgenography. Knowledge obtained from the use of these various

*Excerpted from: Sarnat BG. (1997) Some methods of assessing postnatal craniofaciodental growth: a retrospective of personal research. *Cleft Palate Craniofac J* **34**: 159–172.

methods on rats, ground squirrels, rabbits, pigs, dogs, monkeys, and humans has contributed to a deeper and more fundamental understanding of both the processes and the roles that craniofaciodental biology plays in the advancement not only of basic biology but also of craniofacial surgery.

Each method has its limitations. One might yield information about the sites of growth (vital and implant markers), another about the rate (vital and implant markers), and still another about direction (roentgenographs). However, a combination of methods will potentially yield more information and, in certain instances, do so more accurately than one method alone. Although some of these methods lend themselves primarily to experimental work on animals, nevertheless they do contribute to our fundamental knowledge of the subject and, with limitations, are of value in the human. Only a few methods and selected examples of their use are presented. Since this report is limited primarily to methods, generally findings will not be included. Additional historical and methodologic details can be found in articles by Sarnat and Gans,[34] Baer and Ackerman,[2] and Hall.[13] Every student of growth will delight in becoming acquainted with the seminal work of Thompson.[47]

What follows serves as a brief, general introduction for consideration of (1) some of the various methods, and their subtleties, and (2) those methods used personally in the studies to measure the nuances of craniofaciodental growth. In planning experiments to determine changes in size and shape with time, as accurately as possible, various approaches were considered and used, both direct and indirect (see Table 36.1).

METHODS USED

Anthropometry

The earliest studies of the human form can be traced to the beginnings of anthropometry by ancient Egyptians and Greeks. Examination of skeletal remains (skull, pelvis, long bones) and those of human growth received special impetus in the 19th century. Camper, Morton, Broca, and Topinard are a few of the outstanding early[15] and later[9,10] contributors to this science.

Anthropometry can be performed on either the living or dried subject specimen. In spite of the accuracy of the anthropometry apparatus, exact

Table 36.1 Approximate Information Obtained from Various Methods Used Personally to Study Postnatal Craniofaciodental Growth. Sarnat BG. (1997) Some methods of assessing postnatal craniofaciodental growth: A retrospective of personal research. *Cleft Palate Craniofac J* 34: 159–172

Method	Growth				Type of Study	Limitations
	Site	Amount	Rate	Direction		
Osteometry; skeletal remains	0	X	X	X	Cross-sectional	Sometimes material of unknown history; posthumous distortion
Living	0	X	X	X	Longitudinal	Soft tissues restrict accurate measurement
Impressions and casts	0	XX	XX	XX	Cross-sectional and longitudinal	Soft tissues restrict accuracy of impression
Serial photographs	0	X	X	X	Longitudinal	Two-dimensional study of three-dimensional process
Vital markers*	XXXX	XXXX	XXXX	XX	Longitudinal	Toxicity; method requires refinement
Implant markers*,†	XX	XXX	XX	XX	Longitudinal	Local reaction to implants; requires reoperation

(*Continued*)

Table 36.1 (*Continued*)

Method	Growth				Type of Study	Limitations
	Site	Amount	Rate	Direction		
Histological (see vital markers, metaphysial bands, and autoradiographs); serial cephalometric radiographs	0	XXX	XX	XX	Longitudinal	Must obtain stable landmarks; two-dimensional information not entirely accurate; radiation exposure
Serial cephalometric radiographs and implant markers	XXX	XXX	XXX	XXX	Longitudinal	Two-dimensional information not entirely accurate; radiation exposure
Radiographs and metaphysial bands‡	XXX	XXX	XXX	XXX	Longitudinal	Record of toxic process; rate of growth not normal; radiation exposure
Autoradiographs	XXX	0	0	0	Cross-sectional	Primarily of qualitative value
Elliptical Fourier functions	XXX	XXX	XXX	XXX	Cross-sectional and longitudinal	Curve-fitting approach, requiring special software; only as accurate as initial source of date

0 — gives no information; X — shows trends; XX — relatively accurate; XXX — grossly accurate; XXXX — microscopically accurate. Can be used to measure: *apposition and resorption, †sutural growth, ‡endochondral growth.

measurements of growth are extremely difficult to obtain. When anthropometry is performed on the living, the measuring instruments must be placed on the soft tissue overlying the bony landmarks, thereby precluding precise accuracy of measurements. However, this does show trends of the rates, total amounts, and relative directions of growth in the same person. This longitudinal approach is a dynamic one, in the sense that serial measurements can be made on the same growing individual, and the actual amount of growth can thus be evaluated.

Dried bones and superimposed dried bones have been used frequently to study regions of growth. Anthropometry of the dried specimen brings with it the disadvantages of the static cross-sectional type of study. Here, measurements are made on a large number of bones of varying ages and frequently unknown histories. By comparison of measurements of progressively older samples, growth information is deduced.

There are many anthropometric reports on the orbit of various animals.[32] In one particular report,[24] linear measurements were made to the nearest 0.1 mm with a sliding Helios dial-reading needlepointed caliper (Fig. 36.1). The measurements were anteroposterior (width, horizontal), superoinferior (height, vertical), and lateromedial (depth). For the last measurement, a transverse bar (not reported previously) was adapted to the caliper. Orbital volumes were determined after various experimental conditions were implemented.

Impressions and Casts

Duplication of various parts of the body (skull, face, orbit, eye, maxillary sinus, teeth and dental arches, and extremities) is possible by taking impressions with plaster of Paris, hydrocolloid, Thiokol rubber, low-fusing metal, stone, or other materials. Individual or sectional impressions may be necessary, depending on the size, shape, and contour of the particular part that is to be duplicated. The impression serves as the negative, and by filling it with a material such as plaster of Paris an accurate positive or duplication of the part can be obtained. These models will be permanent records and can be compared with models made at a later stage to evaluate both normal and abnormal growth and development.

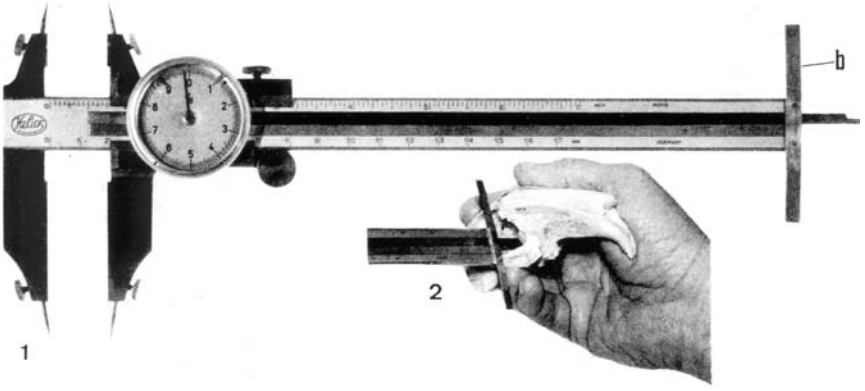

Fig. 36.1 (A) Sliding Helios metric dial-reading, needlepoint caliper model 2RTUR15068C (Neise) with a transverse bar, b, at the end, adapted by us to facilitate depth measurement of the orbit. (B) Caliper and transverse bar in position against the supraorbital process and zygomatic arch to measure the depth of the orbit. (From Ref. 24.)

Orbit

Various methods of determining orbital volume have been reported, including linear measurements.[24,44] Other direct methods require the sealing of openings, which immediately introduces a possible source of error. An accurate determination is precluded in the use of rapeseed, sand, or liquid substances, because the orbital entrance is not represented by a single plane. Low-fusing metal has been used to determine the volume of the maxillary sinus and could be used to develop permanent orbital imprints.[28,29] However, the orbit would be altered in removal of the imprints because of undercut surfaces and rigidity of the metal. Indirect methods, such as the roentgenographic one, are less accurate (Fig. 36.2).[26] Thus, the method of a direct imprint with an elastic rubber base material seemed to offer the most advantages and the least disadvantages.

Orbital imprints

This procedure, which had not been reported previously,[31] was developed in rabbits to determine volumetric changes in the orbit after specific

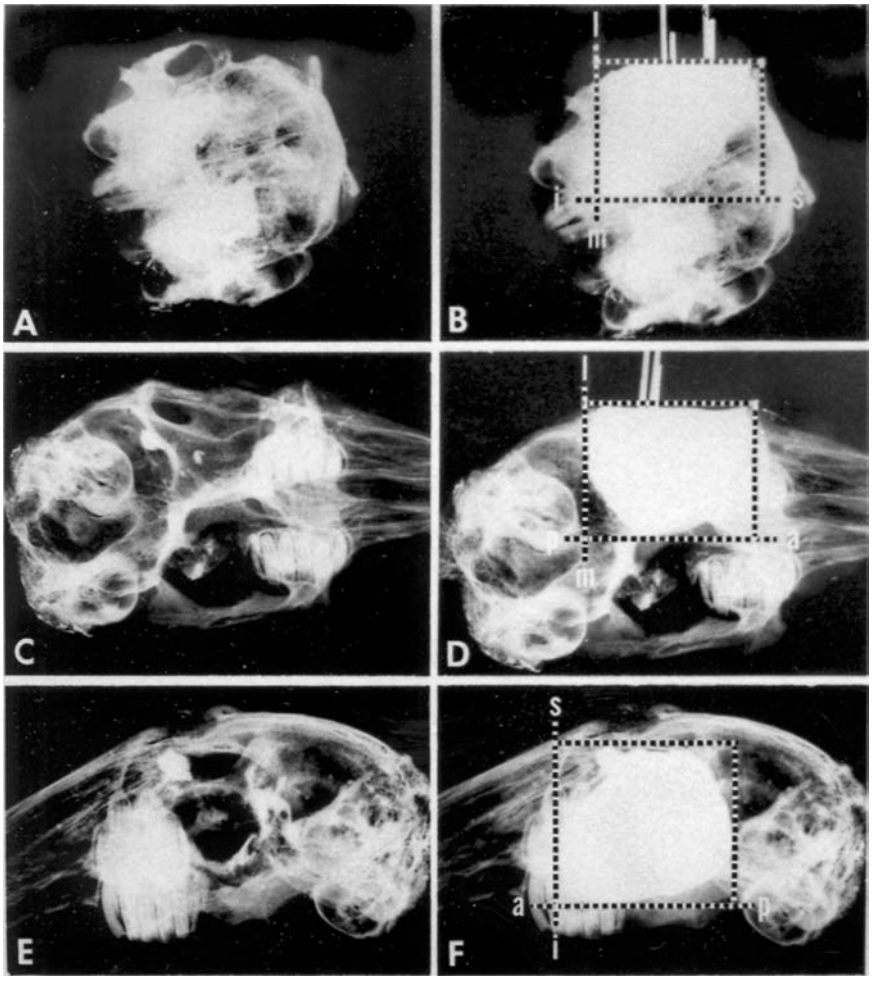

Fig. 36.2 Roentgenographs of the 180-day-old rabbit skull in Fig. 36.1, without and with the imprint in position in the left orbit. Posteroanterior (**A**), superoinferior (**C**), and lateromedial (**E**) views without the imprint in place. Posteroanterior (**B**), superoinferior (**D**), and lateromedial (**F**) views with the radiopaque rubber base elastic imprint in position. Orbital boundaries are more readily defined with the imprint in position. Note the irregular shape of the two-dimensional radiopaque imprint image. Parallel planes (lines) were erected to obtain the greatest measurements in the anteroposterior (ap), superoinferior (si), and lateromedial (lm) dimensions. (From Ref. 26.)

experimentation.[32,42] The openings of the orbital walls and rims were sealed with a semisoft wax. Undercut areas in the depth of the orbit were not modified. Templates of double-thickness hard base-plate wax were warmed and pressed into place to create an imprint of the orbital borders. The borders were lubricated with liquid petrolatum and the templates chilled to facilitate removal. A paper clip was inserted through the template, with the portion of the clip in the orbital cavity bent to a right angle.

An elastic rubber base imprint material (Permlastic-Kerr), which is easily handled at room temperature, was used to make imprints of the orbit (Fig. 36.3). This imprint material has the following advantages: it produces good detail accurately (including undercuts), sets at room temperature, is elastic for a long period of time, is dimensionally and heat-stable, resists weathering and oxidation, can be inserted readily and removed without damage to either the imprint or the anatomic specimen, and is radiopaque. Advantage was taken of this material to determine orbital volume from X-ray studies of imprints in place in the orbits (Fig. 36.3).[26]

The light-bodied elastic rubber base imprint material was prepared by mixing equal parts of the base material and catalyst for about 1 min. This was poured into the orbital cavity. The template was then positioned and affixed to the skull with rubber bands to prevent shifting during the setting of the imprint material. After the material had set, the wax template was broken loose from the imprint and paper clip. The orbital imprint was then removed by gripping the protruding portion of the paper clip. From the net weight and specific gravity of the imprints, the orbital volumes were determined.

Eye

This study describes a method of immediate, permanent duplication of the enucleated rabbit eye so that accurate linear and volumetric measurements can be made at any time with no change in the form of the model. No such report was found in the literature.[12]

The following describes a split-impression technique for producing a permanent model of a fresh eye. Sectional impressions of the freshly enucleated rabbit eye were made, one half of Thiokol rubber and the other half of a silicone material. The eye was removed after separating the two

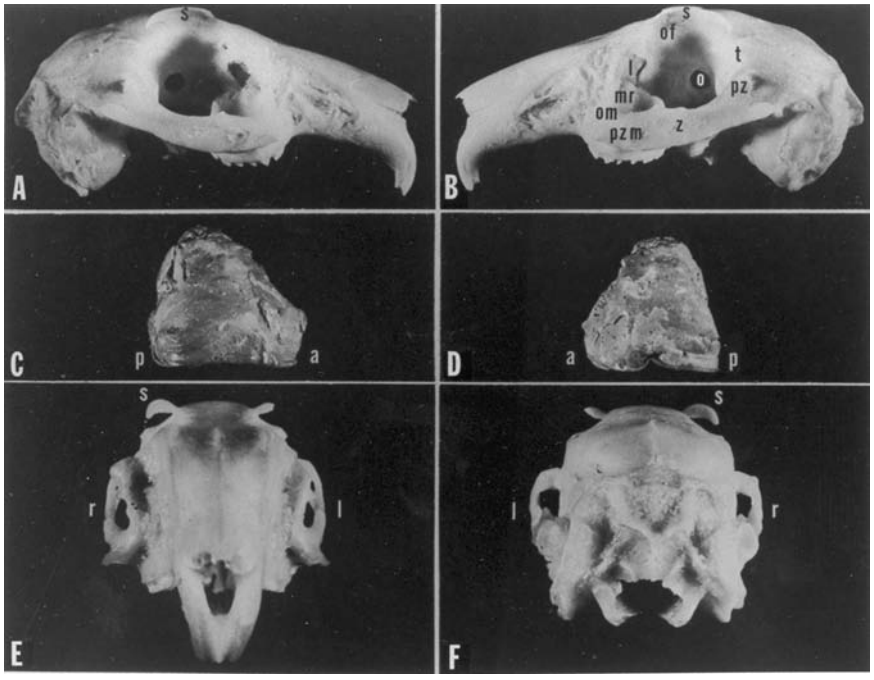

Fig. 36.3 Photographs of the skull and superior view of elastic rubber base orbital imprints of Dutch rabbit No. 4. After 10 injections at about weekly intervals, a total of 1.6 ml of silicone had been instilled into the anterior chamber of the right eye. The rabbit was euthanized at 15 weeks of age. (**A**) Right orbit (volume 3.9 ml) of the injected eye. It is 8.3% larger than the left orbit. (**B**) Left orbit (volume 3.6 ml) of the noninjected eye. I — lacrimal bone; mr — molar root region; o — optic foramen; of — orbital part of the frontal bone; om — orbital process of the maxilla; pz — zygomatic process of the squamosal; pzm — zygomatic process of the maxilla; s — supraorbital process of the frontal bone; t — temporal fossa; z — zygomatic arch. (**C**) Imprint of the right orbit. Note that it is larger than the imprint in **D**. (**D**) Imprint of the left orbit (a — anterior; p — posterior). (**E**) Anterior view of the skull. Note that the supraorbital process (s) is larger and higher on the right side (r). (**F**) Posterior view of the skull. (From Ref. 42.)

impressions, each of one half of the eye. The impressions were replaced, and through a previously prepared opening a mixture of powdered stone and water was poured into the cavity. After the stone hardened, the impressions were separated and the permanent model of the eye was removed. Several permanent models were made from the one set of

impressions. Volume could be determined by either displacement of fluid by the model or from the specific gravity and weight of the model. Measurements of height, width, and depth could also be made. These measurements could be repeated at any time. This method is accurate, with minimal distortion of the eye after enucleation to determine volumetric and linear measurements.[12]

Maxillary sinus

This procedure was developed to measure changes in maxillary sinus volume one year after surgical experimentation (see Chap. 16). The adult dog was selected for this experiment, because it was readily available and had a maxillary sinus of sufficient size to facilitate the contemplated casting procedure. Change of the volume of the maxillary sinus in the adult dog was studied by comparing the volumes of the left and right maxillary sinuses after extraction of the teeth adjacent to the left maxillary sinus.[29]

Dental arches

A rare case of complete anodontia and ectodermal dysplasia was studied from 2 to 16 years of age.[33] This presented an unusual opportunity to study facial and jaw growth in a patient with total absence of all tooth buds and teeth, primary and secondary (see Chap. 27). In addition to a serial cephalometric roentgenographic study, five sets of full upper and lower dentures were designed, constructed, and delivered during this time. Each successive denture was larger and contained more and larger teeth to accommodate the progressive increase in the growth of the jaws (Fig. 27.1).

A maxillary growth deficiency to deal with is that of the patient with cleft lip and palate, especially bilateral. The severity of the growth arrest of the middle third of the face may be dependent on the time, type (Brophy in particular), and frequency of the surgical procedures. In the past, successive and larger maxillary prostheses with more and larger teeth were constructed and adapted to the deficient maxillary region. These serial prostheses were studied to determine the deficiencies of growth.[35] With current surgical techniques, the above method of corrective treatment is outdated.

Serial photographs

The effects of disease on the skull[33,38] and other parts of the body have been recorded readily by means of photographs and serial photographs. These should always be taken under standard controlled conditions, with the subject placed against a graduated grid to allow a comparison with subsequent measurements. This well-known method has been reported in detail by Farkas.[10]

Vital markers

The use of a variety of vital markers has added substantially to our knowledge of bone growth. These include alizarin red S and yellow phosphorus (see Chaps. 25 and 26).

Alizarin red S

Alizarin is one of the principal tinctorial agents found in the madder root (juice of alizari) and is available in synthetic form.[7,43] In contrast to the diffuse effects of prolonged madder feeding, the selective, sharp, vital staining of calcifying substances may be obtained by a single intraperitoneal or intravenous injection of a 2% isotonic solution of alizarin red S (color index 1034, Coleman & Bell Company, Norwood, Ohio). Injections of alizarin have been used to determine the rate of calcification of bone, dentin, and cementum under both normal and experimental conditions. They have been used in studies of calcification under other circumstances, such as healing of fractures, kidney casts, salivary gland and gall stones, calcified plaques of the atheromatous aorta, and calcified scars. The eggshell and the shell of the turtle are also stained by alizarin red S, and probably the otolith, a stone of the inner ear.[18,43] This dye would also be of value in the study of the effects of outer space on the calcification process. There are many different alizarin dyes, mostly used commercially.

For microscopic studies, ground sections are prepared, since the red staining effects are lost by the action of the acid used in preparing decalcified sections. After gross dissection, the desired plane is obtained by

the use of a saw. The specimen is kept wet and is ground to the desired thinness, either by hand or by means of a motor-driven carborundum stone. The section is then cleansed, dehydrated, cleared in xylene, and mounted.

Ground sections (25–50 μm thick) show sharp red lines that may be studied with a dissecting microscope under reflected light. Under higher magnification and strong transmitted illumination, the red lines (5–20 μm in width) are readily counted, and the distance between them can be accurately measured with a micrometer.

The use of alizarin red S or any vital stain in the study of growth of bone has both advantages and disadvantages (Table 36.1). After one injection of the dye, several red lines may be found in a ground section of bone. This can be a result of either deposition of the dye at the same time in several areas of active calcification, or the improper plane of a section of a bone. Because resorption may lead to the removal of stained bone, vital staining will give incomplete data on the pattern of bone formation. This is not true in dentin apposition, since it is laid down one cone within the other and is ordinarily not subject to resorption.

Other agents, such as the procion dyes, tetracycline, fluorochrome, lead acetate, trypan blue, and sodium fluoride, have been shown to be of value, with their advantages and disadvantages. One or more different vital markers have been used consecutively in the same animal.[2]

Hibernation

Developing teeth reflect and record metabolic changes promptly, accurately, and permanently.[39,40] During hibernation, there is an extreme depression of general metabolism. In this investigation, we sought to determine the effect of hibernation on the rate of dentin apposition in the 13-lined ground squirrel.[36] Experimental animals of unknown age were used. They were kept in the laboratory for 2 months and fed the standard rat ration. Hibernation was induced by withholding food and water for 2 days and then placing the animals in a dark, constant-temperature room (2–5°C). The rate of dentin apposition was determined by intraperitoneal injections of a 2% solution of alizarin red S, a calcium-specific vital stain (100 mg/kg), at the beginning and at the end of the experiment. The dye was deposited in the dentin that was in the process of forming and mineralizing at the time of injection and

appeared as a sharp red line in the ground section of the dentin (Fig. 25.1, Chap. 25). This experiment in depressing growth was probably done prior to our development of a program for outer space.

Yellow phosphorus

This interesting vital marker of endochondral bone formation and dental development has not been popularly used (see Chap. 26).

Implant markers (and serial roentgenographs)

The use of this method and that of vital stains has contributed considerably to our knowledge of bone growth. Two or more implants within a single bone have been used to develop its growth pattern. Implants placed on either side of a suture furnish information on sutural growth (see "Multiple bones," below).

Single bones (apposition and resorption)

Implants as reference markers were used in the direct gross study of the growth of bones as early as 1742 by Duhamel[8] (Table 36.2). Hunter[17] inserted two pellets along the length of the shaft of the tarsus of a young pig and measured the distance between the pellets. When the tarsus was fully grown, he found that the distance between the pellets had remained exactly the same, and that the bone had increased in length at the ends (see Fig. 35.1). Thus, this experiment demonstrated that there was no interstitial growth of bone. Implantation of gold, silver, dental silver amalgam, stainless steel, vitallium, or tantalum in the form of screws, pegs, pins, clips, or wires within a single bone have been used for the study of the total amount of bone growth by measuring the increase in the distance between the implants and the outer borders of the bone (Sarnat 1968). Humphry,[16] by placing wire loops around the ramus of the pig mandible, demonstrated that there was resorption of bone on the anterior border and deposition of bone on the posterior border of the ramus (see Fig. 2.2). However, this direct method of study does not yield serial data without reoperation of the animal.

Table 36.2 Brief Historical Review of Implant Markers Used in the Longitudinal Study of Postnatal Bone Growth*

Investigator	Year	Material Used	Bone Studied	Animal
Gross (Direct) Studies				
Hales	1727	Holes	Tibia	Chicken
Duhamel	1742	Silver sylets	Long bone	Pigeon, dog
Hunter	1771	Lead shot	Tibia, tarsometatarsal	Pig, chicken
Humphry	1863	Wires	Mandible	Pig
Gudden	1874	Holes	Parietal, frontal	Rabbit
Wolff	1885	Metal	Frontal, nasal	Rabbit
Giblin and Alley	1942	Wax	Parietal, frontal, etc.	Dog
Roy and Sarnat	1956	Stainless steel wire, black silk suture	Rib	Rabbit
Gross (Direct) and/or Serial Radiographic (Indirect) Studies				
Dubreuil	1913	Metal	Tibia	Rabbit
Gatewood and Mullen	1927	Shot	Femur	Rabbit
Troitzky	1932	Silver wires	Skull	Dog
Levine	1948	Dental silver amalgam	Frontal, nasal	Rabbit
Gans and Sarnat	1951	Dental silver amalgam	Various facial	Monkey
Sissons	1953	Metal	Femur	Rabbit
Selman and Sarnat	1955	Dental silver amalgam	Frontal, Nasal	Rabbit
Robinson and Sarnat	1955	Dental silver amalgam	Mandible	Pig
Björk	1955	Tantalum	Various facial	Human
Elgoyhen *et al.*	1972	Tantalum	Various facial	Monkey
Sarnat and Selman	1978	Dental silver amalgam	Nasal	Rabbit
Sarnat and McNabb	1981	Tantalum	Plastron	Turtle

*Modified from Sarnat 1968. (Copyright © 1968, *Am J Phys Anthropol*, by permission of Wiley-Liss, a division of John Wiley and Sons, Inc.)

We employed dental silver amalgam implants to serve both as direct gross and indirect radiopaque markers for measurement. In general, after the animals had been anesthetized, usually with sodium pentobarbital, and the surface for the implantation surgically prepared and exposed, an inverted cone dental bur, mounted in a hand piece, was used to create an undercut 1 mm cavity in the desired bone. Dental amalgam was freshly prepared, and packed into the cavity. It was used because of its plasticity, tolerance by tissues, and radiopacity. An indentation was made in the center of each implant with the point of the caliper, and the appropriate gross measurements made.

Mandible: Surgical procedure

Young Hampshire pigs were selected for study of the growth pattern of the mandible, a single bone, grossly and roentgenographically (see Chap. 2 for details and Fig. 2.4).

Nasal bone

The growth pattern of another single bone, the nasal bone region, was studied in the young rabbit (see Chap. 13 for details and Figs. 13.2, 13.3).

Rib (endochondral)

Roy and Sarnat,[30] by direct measurements, determined the actual and relative amounts of gross endochondral bone growth in length at the costochondral junction of the third, fifth, and seventh ribs in growing rabbits by means of wire and silk suture markers placed on each side of the costochondral growth site.

Multiple bones — sutural (apposition)

Frontonasal suture and multiple facial sutures

Metallic implants (direct measurements). Dental silver amalgam was inserted into prepared cavities in the frontal and nasal bones. The distances between

the paired implants and between the implant and the suture were measured directly and roentgenographically. (See Chap. 12A for details and Figs. 12A.1, 12A.2; and Chap. 15, Fig. 15.1.)

Multiple turtle shell sutures

Growth of the turtle shell with multiple sutures (the turtle is the only animal with sutural growth outside the skull) has been used as a substitute model for a comparison study of the cranium.[37] Increase in the size of the turtle shell may be related to increase in the size of its contents, as increases in the size of both the cranium and the orbit are related, at least in part, to increases in the size of their contents.

Two tantalum implants (1.2×0.37 mm) were placed into each of the left and right hyo- and hypoplastron bones, for a total of eight implants.[37]

Dorsoventral roentgenographs were taken, beginning at 8 weeks of age and thereafter at about 6-week intervals for the first 18 months, at about 12-week intervals for the next 6 months, and in certain turtles, only once at the end of the last 12 months (3 years of age). From roentgenographs of the turtles at 14 different time periods, those taken at 233, 317, 433, 606, 786, and 1154 days of age were selected for detailed study. On the roentgenograph, the distance between the pair of implants within each bone and across the sutures were recorded to the nearest 0.1 mm (Fig. 33.1).

Histology

See vital markers, metaphysial bands (Chap. 31), and autoroentgenographs (Fig. 11.3).

Serial cephalometric roentgenographs

Roentgenography is a relatively reliable, indirect method of studying growth of bones. In 1912, Tandler[46] suggested the use of X-ray films in anthropometry of the skull. In 1931, Broadbent[5] and Hofrath[14] simultaneously but independently described a technique of cephalometric roentgenography. A refinement in the cross-sectional method was made by the use

of roentgenographs and the superimposition of serial cephalometric-roentgenographic tracings over various supposedly stable, bony landmarks to obtain the pattern of growth. Brodie[6] was the first to apply Broadbent's method to a longitudinal growth study of human males from the third month to the eighth year of life. The accuracy of the method depends on standardization of the technique. However, selection of a stable anatomic base for superimposing the roentgenographic tracings is the key to reliable findings, since any shift of the area used as a baseline distorts the true direction of growth.

This method eliminated the most serious deficiencies of the anthropologic technique. It permits a dynamic study of the growing child, i.e. the increase in size and the change in shape of the same growing bone (e.g. the mandible) or a group of bones forming a complex (e.g. the middle third of the face and the cranium). It reveals the rate, the amount, and the relative direction of bone growth. However, it does not reveal either the sites or the mode of growth of bones. Other disadvantages, including the fact that two-dimensional information was being interpreted from a three-dimensional process, were pointed out by Gans and Sarnat.[11] In addition, Moyers and Bookstein[23] reported that conventional cephalometrics fails to capture the curving of form and its changes and thus misrepresents growth.

Serial cephalometric roentgenographs and implant markers (see "Implant markers")

Use of a combination of serial roentgenographs and radiopaque implants is a more accurate and reliable approach for a dynamic longitudinal study of the growth of bone(s) (Tables 36.1, 36.2). This method has been used in the turtle, rabbit, pig, monkey, and human[4,11,27,37,45] (Table 36.2). The serial roentgenographs demonstrate the increase in size and the change in proportion with time. In addition, a stable base for superimposing the serial roentgenographic tracings is obtained by inserting two or more radiopaque implants. Thus, the ensuing growth can be more accurately determined and measured by superimposing serial roentgenographic tracings over the images of the metallic implants. Measurements between implants and the outer borders of an individual bone are valid only after

verification that, with growth of the bone, the implants remained stable within bone tissue and also were not extruded into the surrounding soft tissues. To avoid foreshortening, implants must lie in a plane parallel to the X-ray film and perpendicular to the X-ray beam. This approach is particularly useful in studying the growth pattern of the mandible, nasal bone, or other single bones if they are clearly outlined on the roentgenograph.[27,41]

Another advantage of this combined method is the ability to measure the amount of new bone formation and resorption that occurred from one period to another without reoperating on the animal. There is also no interference with the normal diet, such as occurs in madder-fed animals. A disadvantage is that the roentgenograph demonstrates the sum total of apposition and resorption at that particular time without the detailed intervening changes as are shown with vital markers and histologic sections.

Roentgenographs and metaphysial bands

In addition to sutures (see Chaps. 12A and 33), another type of joint, the synchondrosis (spheno-occipital and sphenoethmoidal), is found in the skull at its base (see Chap. 31, Fig. 31.1). In this instance, the bones are joined by cartilage rather than by connective tissue. Transverse lines of increased radiodensity in growing long bones at the site of endochondral bone formation after addition of yellow phosphorus to the diet were described by Phemister.[25] Adams and Sarnat[1] were the first to describe these lines of roentgenographs of the skull, where growth of the base occurs by endochondral bone formation at the synchondroses.

Autoroentgenographs (cartilaginous nasal septum) (see Chap. 11)

An autoroentgenograph (Fig. 11.3) is obtained by placing the tissues of a subject injected with a radioactive substance in close contact with a photographic emulsion for a suitable exposure period. Alpha, beta, or gamma rays from the radioactive material affect the silver bromide crystals of a photographic emulsion in a manner similar to that of light. After development and fixation of the film, darkened areas will be found that correspond to the distribution of the radioactive material. Application of this principle was reported as early as 1904.[3]

Radioisotopes have already yielded considerable fundamental information previously unobtainable on the growth and development of animals. A radioactive isotope of an element will behave in exactly the same manner biologically and chemically as the stable isotopes of the same element as long as the radiations from the radioactive isotope are not sufficiently intense to produce pathologic changes. The minute amount necessary to be detectable does not interfere with physiologic processes. Thus, radioactive phosphorus-deposed bone will behave like ordinary phosphorus. Some other radioisotopes used are sodium, calcium, strontium, fluorine, chlorine, iodine, carbon, plutonium, uranium, americium, and gallium.

Cartilaginous nasal septum

Autoroentgenographic studies with tritiated thymidine were undertaken to determine normal levels of proliferative activity in the young rabbit's cartilaginous nasal septum.[22]

Fourier descriptors

Because the majority of morphologic structures encountered in biology are irregular in form, conventional metrics composed of distances, angles, and ratios are inefficient shape descriptors. To circumvent this drawback in the application of morphometrics to describe two-dimensional shapes, an alternative procedure based on Fourier analysis was developed and applied to the turtle carapace.[19] At this juncture, a brief discussion on the Fourier method is in order. The Fourier function used is a convergent series that contains both cosine and sine terms. The cosine terms describe symmetric relationships, and the sine terms describe asymmetric relationships of the morphology with respect to the coordinate system (polar coordinates are used here). One advantage of using the Fourier series is that the separate terms are mathematically independent of each other (the property of orthogonality). Once size differences were controlled for, the presence of shape changes with age could be demonstrated. This study showed that small systematic differences in the phase angle are associated with increase in carapace

asymmetry. The differences were not visually apparent in the original data. These results reinforce the need for precise shape descriptors that are capable of measuring a large percentage of the informational content that is present in all biologic forms.

Analysis of changes in morphologic shape using Fourier descriptors has been limited to two-dimensional boundary representations. The shape of the rabbit eye orbit is a three-dimensional structure that cannot be readily described in two-dimensional space.[20,21] Orbital specimens were placed in a specially constructed headholder and photographed in *norma lateralis* and *norma verticalis*. The left eye orbit was carefully traced onto acetate sheets, and 36 points located in each view and digitized. Comparisons of the infant, juvenile, and adult groups displayed consistent shape changes in the eye orbit. This study represents the first extension of the elliptical Fourier functions to three dimensions: namely, modeling a morphologic boundary as a curve in three-dimensional space.

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CHAPTER 37

Cartilage and Cartilage Implants*

INTRODUCTION

Studies on the transplantation of tissues have contributed not only to our knowledge in this field but also to a better understanding of such phenomena as metaplasia, neoplasia, cellular differentiation, tissue individuality, and the endocrinopathies. Consequently, information related to cartilage and cartilage implants is of more than a passing interest to those who are not necessarily surgeons.

The clinical value of cartilage implants has been well established and much has been written about the successful use of such implants in plastic and reconstructive surgery. However, opinions differ in regard to which type of cartilage to implant. In addition, the subsequent fate of the various types of cartilage implants is not completely understood. It seems timely, therefore, to review and summarize the fundamental properties of cartilage and cartilage implants and to correlate them with the clinical observations that have been made. In this way it is hoped that there will be a better understanding of some of the controversial issues, that the limitations of our present knowledge will be appreciated, and that a foundation will be laid for further basic and clinical research.

*Excerpted from a historical review: Sarnat BG, Laskin DM. (1954) Cartilage and cartilage implants. *Int Abstr Surg Surg Gynecol Obstet* **99**: 521–541.

BASIC CONSIDERATIONS OF CARTILAGE

Cartilage represents a modified form of connective tissue. Like other connective tissues, it is composed of cells and an intercellular substance consisting of fibers and ground substance. It is the physical character of the ground substance which imparts to cartilage its firm consistency. According to the nature and microscopic appearance of its fibrillar elements, cartilage has been classified into three main types, namely hyaline, elastic, and fibrous. Of the three, hyaline cartilage has the widest distribution throughout the body and is most extensively used in plastic and reconstructive surgery. Since much of the basic information concerning hyaline cartilage can be applied to the other types, it will be considered primarily, with only a brief discussion on the modifications found in the elastic and fibrous varieties.

HYALINE CARTILAGE

Gross Morphology

Hyaline cartilage is a firm yet flexible tissue which can be readily cut with a knife. It derives its name from the Greek word "*hyalos*," meaning glass. The term has been applied to this form of cartilage because of its translucent, bluish white, glassy appearance in the fresh state. Its surface is covered by a firmly attached, relatively thin fibrous tissue layer, the perichondrium, except at articular surfaces.

Distribution and Function

The sites of distribution of hyaline cartilage may be classified according to whether they are transitory or permanent. In the young individual, transitory cartilage forms the important growth centers at the epiphysial plates of the long bones and the carpal and tarsal bones, at the base of the skull, the head of the mandibular condyles, in the vertebrae, sternum, clavicles, hyoid bone, scapulae, and pelvis. With cessation of growth, the cartilage in these areas is replaced by bone.

Permanent hyaline cartilage forms the covering of all articular surfaces except those of the temporomandibular joint and clavicle. In addition to

its role in the growth of these regions, it also provides a firm smooth surface for joint movements with a minimum of friction and wear. Its elastic properties, moreover, enable it to absorb the shock of pressure changes in these joints.[15]

The 12 pairs of costal cartilages are the largest regional collection of permanent hyaline cartilage in the body. Of these, the sixth, seventh, and eighth are the biggest. The costal cartilages not only serve as the principal sites of growth for the ribs, but also contribute to the general elasticity of the thorax. Moreover, their articulation with the sternum allows the free movement of the chest during respiration. The xyphoid portion of the sternum is also cartilaginous but may sometimes become partially calcified or ossified in older individuals.

Permanent hyaline cartilage also plays an important role as a supporting tissue, as in the external nose, nasal septum, larynx (except for the epiglottis and corniculate cartilages, which are entirely elastic cartilage, and the arytenoid cartilage, which is elastic at its apex), the trachea, and the large bronchi. The nasal cartilages and septum, in addition to their supportive functions, are also important in the growth of the nose.

Histologic Appearance

The cellular elements of cartilage, i.e. the chondrocytes, vary in size and shape, depending upon their location. The chondrocytes located just beneath the perichondrium are usually small and somewhat flattened, while those nearer the center are larger and more spherical. The cells have a centrally placed, ovoid nucleus with one or more nucleoli. The cytoplasm is finely granulated and contains glycogen, fat droplets, mitochondria, centrosomes, and a Golgi apparatus.[116,169,177]

The chondrocytes lie in lacunae within the intercellular substance. Normally the cells completely fill these spaces, but in the routine preparation of a specimen for histologic examination loss of fat and water may cause the cytoplasm to shrink. In the peripheral layers of the cartilage, the cells are separated from each other by varying amounts of intercellular substance. Toward the center of the cartilage, as the older cells divide, they come to lie in groups of 2–8 with little matrix between them. Such clusters of chondrocytes are termed “cell nests” or “isogenous groups.”

The matrix of hyaline cartilage presents a homogeneous appearance throughout, except for distinct zones known as cartilage capsules, which immediately surround the lacunae. These areas contain a greater number of intercellular fibrils[161] and are characterized by a higher refractive index and a more intense stainability with basic dyes than the remaining matrix. The homogeneous nature of the intercellular substance of hyaline cartilage is a result of a masking of the contained collagenous fibrils due to the similarity between their index of refraction and that of the ground substance. The presence of such fibrils, however, can be demonstrated by the use of special silver stains or by pretreatment of the decalcified tissue with trypsin, collagenase, or dilute alkali.

Cartilage is supplied with neither blood vessels, lymphatics, nor nerves.[177] It is generally agreed that the so-called canaliculi, which have been described as permeating the matrix and linking the lacunae, actually represent artefacts.[26,40] The occasional vessels seen are believed usually to be merely coursing through the tissue and to have no intimate relationship to its nutrition.[69] Some,[67,81] however, feel that in the epiphyses they are directly concerned with supplying nutriment to the cartilage.

The perichondrium surrounding the cartilage is composed in its outermost portion of a layer of dense, collagenous connective tissue. The inner layer is more cellular. In that part adjacent to the cartilage, when growth is occurring the mesenchymal cells show a gradual differentiation into chondroblasts. These cells are arranged in a plane parallel to the surface of the cartilage. The perichondrium is well supplied with blood vessels, lymphatics, and nerves.

Histogenesis

The cartilaginous anlage of the human skeleton appears in the embryo at about the fifth week *in utero*.[10] This cartilage is formed by differentiation from the mesenchymal tissue. Normally the mesenchymal cells are stellate or spindle-shaped, with a finely granulated cytoplasm containing a few fat droplets. The intercellular substance is jellylike and amorphous in character. The earliest change noted in an area of developing cartilage is a condensation of the mesenchyme accompanied by the transformation of the mesenchymal cells to a more spherical shape (precartilage). Within these

closely packed cells there is a clumping of the granules and the formation of large, fat globules.[39,50] At about the same time, the matrix becomes quite homogeneous and firm. Although it contains numerous fibrils, these are masked by the changing ground substance. With continued matrix formation the cells become widely separated from one another. The developing cartilage, in fixed preparations, stains acidophilic at first but soon acquires its characteristic basophilia.

The mesenchymal tissue immediately surrounding the developing cartilage gives rise to the perichondrium. In the outermost regions of this layer, the mesenchymal cells develop into fibroblasts, and coarse, collagenous fibers appear in the intercellular substance. The cells in the area approximating the cartilage remain relatively undifferentiated. They thus retain their ability to give rise to new cartilage tissue.

While some believe that the cartilage matrix is a product of cellular secretion,[40,116] others feel that it represents a primary change in the intercellular substance, possibly under the chemical influence of the developing chondroblasts.[26,154] *In vitro* studies on the reconstitution of collagen fibers have yielded findings which may be applicable to a reconciliation of those divergent ideas. It has been shown, for example, that collagen dissolved in dilute acetic acid will again form characteristic fibers upon the addition of sodium chloride or following neutralization of the solution.[63] As a result of such observations, it has been postulated that in fibrogenesis the cells secrete precursor protein substances, which, when brought into contact with certain ions or other factors within the intercellular fluids, become aggregated into a more highly organized form such as fiber. It is possible that a similar situation may exist in cartilage whereby the cells and the intercellular fluids would contribute equally to matrix formation.

The intercellular substance of cartilage is composed primarily of collagen, chondroalbumoid, and condromucoid.[70,192] The collagen is similar to that found in most other connective tissues.[135] When cartilage is boiled in water and acid, its collagen is transformed into gelatin, which, unlike collagen, is highly soluble and easily broken down by proteolytic enzymes. Chondroalbumoid is present in relatively small amounts in cartilage. It resembles collagen in many of its properties, especially its resistance to proteolytic enzymes. Chondromucoid, a glycoprotein, makes up approximately 40% of the ground substance.[123] Upon hydrolysis it yields a protein

and condroitin sulfate,[120] a complex mucopolysaccharide consisting of sulfuric acid, and N-acetyl galactosamine.[119] Chondroitin sulfate normally exists in the ground substance in a highly polymerized state.[25,135]

In addition to its colloidal and inorganic components, adult cartilage matrix, like that of most soft tissues, contains approximately 65–75% water. Fetal cartilage contains as high as 85% water.[82] The exact water content of cartilage varies with the state of the colloids and electrolytes present within the matrix.[85] These electrolytes (sodium, chlorides, potassium, calcium, magnesium, sulfates, and phosphates) have been chemically assayed.[47,109] There is about 7% ash in young cartilage and 6% in adult tissue.[70] The pH of cartilage is approximately 7.4.[53,150]

Histochemical studies have contributed much to our knowledge of the sites of localization of various substances shown by chemical methods to be present in cartilage. Among the substances investigated have been glycogen, lipids, glycoproteins, nucleoproteins,[53] calcium phosphate, chondroitin sulfate,[182] hyaluronic acid, and various enzymes, including alkaline phosphatase, phosphorylase, succinic dehydrogenase,[53] and citric acid dehydrogenase.[53]

Glycogen was first demonstrated histochemically in cartilage cells by Rouget in 1859.[160] Since that time many investigators[53,59,72] have confirmed this finding. In the chondroblasts and young chondrocytes, only a few glycogen granules can be found. As the cells mature, multiply, and increase in size, the granules become larger and more numerous. With continued aging, however, there is again a gradual depletion of intracellular glycogen.[2]

The greatest glycogen content is found in the enlarged vesicular cells of the growing epiphysial cartilage plate. Prior to provisional calcification, however, these cells quickly lose this glycogen. A similar occurrence has been observed in the chondrocytes of the intermediate zone of costal cartilage prior to calcification.[2] Disappearance of glycogen concomitant with the calcification of cartilage matrix has led to the suggestion that it may play an active role in the calcification process.[72,80] It has thus been postulated that glycogen serves as a substrate for the enzyme phosphorylase.[64,72] The action of this enzyme upon glycogen results in the formation of glucose-I-phosphate. This substance, in turn, can be acted on by the enzyme phosphatase, serving as one of the mechanisms for producing an increased

local concentration of phosphate ions.[155] Another substrate for phosphatase may be phosphocholine, which is formed from lecithin by the action of a lecithinase also found in cartilage.[97] As the concentration of phosphate ions exceeds the solubility product of calcium phosphate, calcification of the matrix takes place. Both phosphorylase[41,64] and phosphatase[52,61,156] have been demonstrated in cartilage.

Lipid distribution in cartilage cells has been determined in several histochemical studies.[53,124,169] The presence of fine fat droplets can be shown in the cytoplasm of young chondrocytes, and as these cells mature the amount of fat increases. There is general agreement among investigators, however, that the presence of fat globules in the chondrocytes is not indicative of a degenerative process as it is ordinarily considered in other tissues.

Metachromasia is readily exhibited by cartilage matrix.[194] This refers to the peculiar property of certain tissues, when stained with a specific group of dyes (toluidine blue, methylene blue), to show a color other than that of the original dye. It has been suggested that metachromasia depends upon the highly aggregated state of the dye molecules.[121] This condition results from the adsorption of the dye by certain molecular structures within the tissues which are also highly aggregated. It was originally believed that the dyes reacted specifically with high molecular weight esters of sulfuric acid, such as the chondroitin sulfate found in cartilage matrix.[102] Others[11] have shown, however, that acid colloidal substances containing phosphate and carboxyl groups will also exhibit metachromasia. The significance of the metachromatic staining reaction appears to lie, therefore, in its relationship to the state of polymerization of the tissue mucoproteins rather than to their specific chemical composition. The metachromasia of the ground substance of cartilage indicates that it is probably in a relatively high state of aggregation. Since in cartilage there appears to be no substance other than chondroitin sulfate which can exhibit metachromasia, this method has been used for the histochemical assay of such material. The results obtained have shown good correlation with the data obtained by chemical methods.[181]

The carbohydrate–protein complexes of rabbit costal cartilage have been investigated by means of the periodic acid – leucofuchsin procedure.[2] This reaction depends upon the oxidation of adjacent hydroxyl groups in

the two- and three-carbon positions of the sugar moieties by periodic acid. The polyaldehydes thus produced form insoluble red compounds when combined with fuchsin-sulfite (Schiff's reagent). The intensity of the staining reaction has been presumed to be related to the state of aggregation of the ground substance, which is composed principally of mucoproteins.[55]

In young animals the ground substance of the costal cartilage appears to be most highly aggregated in the peripheral and intermediate zones. In older animals, the intermediate zone shows the most intense staining at its internal and external borders. At the same time, the rest of the zone is undergoing calcification. It is possible that the depolymerization of the substance in this area, as indicated by the high degree of staining at its margins, predisposes the region to calcification.

The areas stained by the periodic acid – leucofuchsin procedure generally parallel those exhibiting metachromasia with toluidine blue,[2] thus suggesting that both reactions might represent an interaction with the chondroitin sulfate, to changes in the state of aggregation of the ground substance, or decreased staining in older cartilage could possibly be related to a loss of chondroitin sulfate, to changes in the state of aggregation of the ground substance, or to a combination of the two factors.

Physiology

Nutrition

Since cartilage is avascular, the cells must depend upon the diffusion of tissue fluids from the perichondrium for their source of food and oxygen and the removal of metabolic end products. The physical state of the matrix thus has a profound effect upon the metabolism of the chondrocytes. As the cartilage becomes thicker in a growing individual, the rapid interchange of materials with the more central zones becomes more difficult. The increased condensation of the ground substance associated with aging of the tissue also impairs diffusion. Consequently, there may be a diminished viability of many of the chondrocytes, which accounts for the central degeneration that is commonly found in adult cartilage.

Metabolism

Only carbohydrate metabolism has been extensively studied in cartilage.[33,43,77,92,94,158] The rate was found to be among the lowest of all tissues. This was partially attributed to the avascularity and relative acellularity of cartilage. It has also been demonstrated, when cell counts are considered, that while the glycolytic activity of the chondrocytes is similar to that of most other cells, the oxygen consumption is only 1/50–1/100 as great.[33] Cartilage thus differs from most other tissues in possessing a very low metabolic rate and exhibiting a predominately anaerobic metabolism. The rate of anaerobic glycolysis remains constant throughout life. Respiration, however, decreases with age.[158]

There is direct evidence for the existence in hyaline cartilage of practically all of the enzymes involved in the usual mechanisms of glycolysis.[4,65] The presence of glycogen,[41,53,72] lactic acid,[33] and adenosine triphosphate (ATP)[3] has also been demonstrated. The aerobic enzymes in cartilage have not been as thoroughly investigated and the intermediate stages of respiration are still unknown. Both lactate[111] and pyruvate[77] can be metabolized, but as indicated by manometric determinations, the process is very slow in comparison to that in most other tissues. Succinic and citric acid dehydrogenases have been observed histochemically.[53] Dehydrogenetic activity has also been studied manometrically.[159] The presence of cytochrome[11] and cytochrome oxidase,[33] however, has not been demonstrated. Hills[77] has speculated on the possible function of the dehydrogenases in cartilage in the absence of any oxidase.

Growth

Cartilage increases in size by both appositional and interstitial growth. Appositional growth depends upon the division of the chondrogenic cells in the innermost layers of the perichondrium accompanied by the formation of additional intercellular matrix. Interstitial growth occurs by an increase in intercellular substance accompanying the mitotic division of chondrocytes already contained within lacunae in the cartilage matrix. Only in fetal and young cartilage, when the matrix is relatively plastic, can interstitial growth occur. In mature cartilage cell division is rare, and

because of the firm nature of the matrix, no interstitial increase in size is possible. When cellular division does occur in fully differentiated chondrocytes, it is usually by amitosis.[48]

Repair

The independent regeneration of cartilage following injury is extremely limited.[17] Instead, the defect usually becomes filled by granulation tissue proliferating from the perichondrium. If the perichondrium has been destroyed, the regenerating cells are derived from the surrounding connective tissue. In the healing of costal cartilage, it has been demonstrated that these regenerating cells undergo differentiation into chondroblasts and the interstitial substance gradually becomes cartilaginous.[66] The new tissue may at first have the appearance of fibrocartilage, but later it becomes hyaline in character.[115] The defect is thus ultimately completely repaired with new cartilage.

The healing of defects in articular cartilage has been thoroughly investigated.[16,17,168] The results indicate that even in this location, where normally no perichondrium is present, cartilage can still be repaired. The new cartilage is formed by differentiation of the connective tissue derived from the joint capsule or, in deep wounds, from the subarticular marrow spaces. In many cases, however, the healing is incomplete, and in instances of large defects, repair may be by scar formation only.

Ectopic cartilage formation

The multipotentiality of the undifferentiated mesenchymal cells found throughout the body makes it possible for ectopic cartilage formation to occur in many places. Thus, cartilage has been found in the penis, uterus, kidney, tonsil, salivary gland, tongue, and periodontal membrane. It also occurs in healing fractures,[164] on amputation stumps, and in pseudarthroses.[165] The differentiation of cartilage in these latter areas has been attributed to the presence of functional pressures.[60] Hyaline cartilage, being nonvascular, and of firm character, is capable of withstanding stress more readily than ordinary fibrous connective tissue. It has thus been suggested that a decreased blood supply may be the stimulus for ectopic

cartilage formation in such regions. Some substantiation of this idea has been derived from the observation of chondrogenesis through transparent chambers in the rabbit ear.[39] In these studies cartilage was found to develop only in areas of slow or moderate circulation.

There have been many attempts to produce ectopic cartilage experimentally. The intramuscular injection of 40% ethyl alcohol, monobasic calcium phosphate, autogenous, homogenous, and heterogenous bone extracts, calcium chloride, and quinine hydrochloride have all been used successfully.[9,20,74,96,178] The transplantation of fascia to the urinary bladder[129,130] and muscle traumatization have also given rise to ectopic cartilage. It is unfortunate, however, that most of these investigations have been confined to the rabbit, since this animal seems especially prone to ectopic cartilage formation.[74]

Age changes

The morphological and chemical changes associated with the aging of human costal cartilage have been extensively investigated.[6,73,108] Hass[73] found that from infancy until the fourth decade of life there is a continual increase in the amount of chondroitin sulfate in costal cartilage, proportionate to the increase in the quantity of matrix. Beyond this point, the chondroitin sulfate content declines despite any further matrix formation. Loewi,[108] on the other hand, using somewhat different analytical methods, found the chondroitin sulfate content to be highest at birth and thereafter to vary inversely with age. He thought that the decreased amount of chondroitin sulfate in aging costal cartilage is probably a result of its depolymerization and subsequent elution. Concomitant with this change in the ground substance, there is an increased deposition of calcium within the axial zones of the tissue. Loewi suggested that the depolymerization of the chondroitin sulfate, by increasing the number of reactive groups available for acceptance of calcium ions, may be one of the factors responsible for this calcification process.

In addition to calcification, aging costal cartilage exhibits yellow pigmentation and fibrillation of the matrix in the central areas. The chondrocytes located in these regions show signs of diminished viability. Chrondrogenesis in the perichondrium greatly decreases. With further

increase in age all these changes become more progressive. The chondroitin sulfate content falls to less than half the maximal value. The calcium deposits increase in density, and areas of calcified cartilage are resorbed and replaced with bone. The pigmentation becomes brown and more diffuse. The areas of fibrillation in the matrix become more prominent and some show further signs of disintegration. The character of the tissue is firm and brittle. Hass concluded from his investigations that most of the changes observed were dependent upon the depletion of chondroitin sulfate, which he in turn related to a decreased capacity of the chondrocytes to resynthesize this material. He found no explanation for the presence of pigmentation. Since no significant variation occurred in either the lipid or iron content of costal cartilage throughout life, it was thought that these substances bore no relationship to any of the morphological or chemical changes observed.

Pathology

Degeneration

Cartilage is susceptible to most of the degenerative changes affecting other tissues.[86] Thus, the matrix may be involved in generalized amyloidosis, or show mucinous degeneration. Irregular calcification of the cartilage matrix may also occur.[49] The frequency with which this change is found, especially in the ribs and cartilages of the respiratory passages, warrants its consideration as a normal aging process. In some instances, such as in the laryngeal cartilages, calcified areas may be replaced by bone. In gout, urates are deposited within the cartilage matrix. Grossly, these areas appear as whitish plaques in which, microscopically, the urate crystals can be demonstrated.

The chondrocytes may exhibit cloudy swelling (albuminous degeneration) and hydropic degeneration. Fatty degeneration has also been described. As pointed out earlier, however, the presence of many fat droplets or globules within the chondrocytes is considered a normal finding and so the diagnosis of fatty degeneration becomes a relative matter. Therefore, the use of this criterion as an indication of degenerative change in cartilage is not entirely reliable.

Asbestos degeneration is a condition peculiar to cartilage. It is found particularly in the central portions of the ribs and in the articular cartilages of old individuals. It is characterized by a gradual softening of the matrix with the appearance within the ground substance of fibrillar structures which have none of the properties normally attributed to collagen. These probably represent unmasked collagenous fibrils which have undergone degradation. The chondrocytes in such areas show large accumulations of fat and may eventually undergo complete necrosis. Macroscopically, the earliest changes in the matrix appear as glistening white spots, In more advanced degeneration, the cut cartilage exhibits translucent yellow or yellow–brown local or diffuse areas. In the most advanced stages, softening of the matrix may proceed to such an extent that fluid-filled spaces resembling cysts may develop. Areas of asbestos degeneration occasionally show calcification, or even bone formation in instances in which the connective tissue of the perichondrium has invaded the softened regions.

Ochronosis is a rare condition in which brown or black pigmentation occurs in all the cartilages in the body. The discoloration is frequently visible through the skin. Most cases are due to a congenital disturbance in protein metabolism associated with alcaptenuria. An exogenous form due to chronic phenol poisoning by absorption of the drug from dressings has also been reported.

Inflammation

In a firm avascular structure such as cartilage, in which exudation and cellular migration are not possible, inflammation does not occur. The degeneration and necrosis usually observed in cartilage are actually secondary to involvement of the perichondrium. Thus, "chondritis" and perichondritis should be considered as a single phenomenon. Syphilis and tuberculosis are the most common causes of perichondritis of the laryngeal and costal cartilages and the nasal septum (saddle nose).[38,151,190] Perichondritis in these areas has also been related to typhoid and paratyphoid fever, gonorrhea, and many other specific and nonspecific infections.[12,83] Ultraviolet and x-ray therapy as well as physical trauma have also been implicated as predisposing to perichondrial inflammation.

The perichondrium may become infected either by direct extension or via hematogenous or lymphatic routes. Since it is the sole source for nutrition of the underlying cartilage, either the eventual decrease in perichondrial circulation associated with inflammation, or elevation of the perichondrium by purulent exudate or caseous material indirectly results in cartilaginous degeneration and necrosis. This dependence of cartilage upon a peripheral circulation accounts for its poor resistance to infection. Small areas of devitalized tissue may become resorbed. Sylven[183] has shown histochemically that this is preceded by a loss of chondroitin sulfate from the matrix. In extensive necrosis the cartilage may be sequestrated or liquefied.

Abnormal growth and development

Cartilage may be affected by hereditary diseases, certain endocrine dysfunctions, vitamin deficiencies, and general dietary restrictions. Toxic doses of certain metals will also affect it. Since the growing epiphysial plate is cartilaginous, these various disturbances will exert a profound effect upon the skeletal development of an individual.

Chondrodystrophia fetalis (achondroplasia) is a hereditary dysfunction of cartilage which is transmitted as a simple dominant Mendelian factor. It is characterized by a failure of the epiphysial and articular cartilages to attain their normal degree of interstitial growth. The result is a dwarf exhibiting short limbs, and lack of development of the middle third of the face (spheno-occipital and sphenoethmoidal synchondroses), with concomitant deep saddling of the nose, relative bulging of the forehead (dish face), and a relative mandibular prognathism. Since the important growth site of the mandible, i.e. the condyle, also contains cartilage, the last finding seems paradoxical. An explanation may be found in the fact that the condylar cartilage is covered by connective tissue and thus grows mainly by apposition, which is not impaired in fetal chondrodystrophy.

Hyperpituitarism in a growing individual produces a generalized skeletal overgrowth known as gigantism. The epiphysial cartilages, cranial synchondroses, and mandibular condyles are stimulated to an increased rate and longer duration of activity than normal. The epiphysial and sutural changes, though exaggerated, maintain their regular sequence.

In acromegaly (adult hyperpituitarism) the skeletal changes are more disproportionate, since the cartilaginous epiphyses and cranial synchondroses are no longer present. Other areas of cartilage in the body, however, still respond to the growth stimulus. Thus, the increase in the size of the hands and feet is partially attributable to proliferation of the articular cartilages, the enlargement of the nose is due to growth of the septal and the upper and lower lateral cartilages, while the increased anteroposterior dimension of the chest results particularly from growth at the costochondral junctions. Condylar growth contributes to the mandibular prognathism as a result of either the stimulation of persistent areas of cartilage in the condyle, or the differentiation of new cartilage in its fibrous covering.

Hypogonadism may also lead to gigantism. In such instances, cartilage, especially that in the epiphysial plates, continues to grow far beyond the normal period. Hypergonadism, hypopituitarism, and hypothyroidism all retard cartilaginous growth.[175]

In vitamin A deficiency the normal growth, maturation, and degeneration of epiphysial cartilage essential for endochondral ossification are retarded. Remodeling resorption of bone ceases, but apposition continues until inanition supervenes.[195] Soft tissue growth, especially in the central nervous system, may also proceed for some time. In experimental studies, such disproportionate growth has resulted in pathological compression of the brain, spinal cord, and nerve roots by the adjacent bone.[117,118] In hypervitaminosis A there is acceleration of epiphysial growth beyond the normal rate.[195]

Deficiencies in the total vitamin B complex have been shown experimentally to produce a retardation in cartilaginous growth.[174] Similar but less severe changes have been noted in mice deficient only in pantothenic acid[98] or in pyridoxine.[173] Riboflavin deficiency retards cartilage growth the least, but produces more marked degenerative changes than are seen in any of the other B complex deficiencies.[99] The production of a vitamin B complex deficiency in pregnant rats has resulted in impeded growth and skeletal deformities in the offspring.[189] This was partially attributed to disturbances in the formation of the cartilaginous skeleton and to a decreased endochondral ossification.

Vitamin C is also essential for the proper growth and development of cartilage. In children suffering from scurvy, the proliferation of cartilage is

retarded and irregular, and the newly formed tissue contains less collagen than normal. The epiphysial zones of preparatory calcification are generally widened. They are visible in the roentgenograph and serve as a diagnostic feature of the disease. Fractures of the ribs in the costochondral region or in the metaphysis of the tubular bones are not uncommon. These regions are weakened by the limited apposition of trabecular bone.[69]

Vitamin D is not only important for the proper calcification of bones but it also plays a significant role in their growth. A prerequisite for the orderly resorption and replacement of the epiphysial cartilage is the provisional calcification of the metaphysial end. In rickets, failure of this zone to calcify results in diminished or halted endochondral bone formation and extreme thickening of the epiphysial cartilages.[44] This epiphysial thickening or beading is most evident at the wrists, ankles, and costochondral junctions (rachitic rosary). It may be demonstrated roentgenographically in all the epiphyses. The reduced cartilaginous growth not only produces a shortness of the extremities, but also results in extreme facial disharmony by its effect upon the mandibular condyles and the synchondroses of the base of the skull. Delayed eruption and malpositioning of the teeth also occur, since the normal intermaxillary space needed for eruption is dependent upon condylar growth.

Undernourishment has been shown to produce changes in developing cartilage. Animals fed on a diet restricted in calories but adequately balanced exhibit a atrophy of the chondrocytes and diminished cartilaginous growth.[176] Upon refeeding, growth is quickly resumed, at first at an intensified rate, but later at the original, normal level. In prolonged dietary restriction, although the rate of growth is retarded, the total growth period is increased and regressive changes in the cartilage are less severe.[166]

The ingestion of toxic doses of lead,[34] phosphorus,[1] or bismuth[35] can also produce pathologic change, in endochondral ossification (long bones and the base of the skull). The microscopic picture is similar in each instance, being characterized by a failure of the primary cartilage-containing trabeculae at the metaphyses to become resorbed and replaced by new bone. It is these areas of densely packed trabeculae, rather than the deposition of the metals themselves, which produce the radiopaque lines visible in the roentgenographs of the long bones and the base of the skull. Although these changes may be due to the direct effect of the metal

involved, they are more likely a part of the general toxic reaction. When ingestion or absorption of the metal ceases, normal endochondral growth is resumed. The radiopaque zones no longer increase in width, but remain as osseous disks after the epiphyses grow away from them (lines of arrested growth). In accord with the period of toxicity, there may or may not be a grossly noticeable retardation in growth.

Neoplasms

Although neoplastic growths have been described as originating from costal cartilage,[79] most often cartilaginous tumors arise within or on the surfaces of the adjacent bone. While many consider that such tumors develop from pre-existing cartilage or cartilage rests, others believe that the site of origin is in the multipotential mesenchymal cells of the neighboring connective tissue.[191]

The benign cartilage tumors include the chondroma, osteochondroma, myxochondroma, and chondroblastoma. The highly malignant chondrosarcoma may develop as a primary neoplasm but it often occurs as the result of the malignant change of a chondroma or osteochondroma.[101]

Effects of irradiation

The hyaline cartilage of the epiphysial plate is readily affected by irradiation. Doses of X-rays even less than those necessary to produce an erythema of the skin will result in an altered histologic pattern.[21] In experimental studies, pyknosis, swelling, and disorientation of the chondrocytes have been observed in 1–2 weeks after exposure to as little as 300–600 roentgens. These early changes were noted in the lowly differentiated cells of the proliferating zone just beneath the germinal layer of the epiphysial plate. When larger doses of irradiation were given, the more differentiated cells were also disturbed.[54] The least effect was seen in the germinal layer, which exhibited minimal degenerative changes. The matrix also revealed structural defects as characterized by altered stainability, diminished opacity, and fibrillation. The net result of these changes was an extreme retardation in growth of the affected bones. After relatively small doses of irradiation

there was eventually an almost complete return to normal morphology and development.[78] There was, however, no compensation for lost growth. With higher doses, the abnormalities persisted for longer periods, but even in such cases there was some evidence of spotty regeneration through proliferation of the chondrocytes in the highly resistant germinal layer.[21,30]

There are conflicting reports regarding tie effect of irradiation upon articular hyaline cartilage. In some investigations[13,54] there were little or no changes noted in these areas, despite extreme disturbances in the epiphysial regions. In another study, however, slight-to-moderate degenerative changes were observed.[153] It is possible that these degenerative changes were secondary to disturbed joint function in limbs altered by lack of epiphysial growth, rather than primarily due to the X-ray effect. In any case, it appears that articular cartilage is somewhat more resistant to irradiation than epiphysial cartilage.

The hyaline cartilage of the ribs and respiratory passages is also much less radiosensitive than that of the epiphysial plates. So long as these areas are protected by the overlying tissues from bacterial contamination, they can tolerate large amounts of radiation without extreme gross change. If the cartilage becomes exposed by either infection or trauma, however, the subsequent perichondritis is usually accompanied by extensive necrosis and sequestration.

ELASTIC CARTILAGE AND FIBROCARTILAGE

With few exceptions,[7,8,33,112,123,124,136,172,184,193] most of the investigations of elastic cartilage and fibrocartilage have been limited to anatomic and histologic details. Very little is known, therefore, about the chemistry and physiology of these tissues.

Elastic cartilage is found in the external ear, eustachian tube, epiglottis, corniculate and cuneiform cartilages, at the apex of the arytenoid cartilage, and in the midline of the thyroid cartilage. Grossly, it differs from hyaline cartilage, in having a yellowish color, greater opacity, and a higher degree of elasticity. Like hyaline cartilage, it is nonvascular. Microscopically, it is characterized primarily by a dense network of interlacing elastic fibers running throughout the matrix. These fibers account for the flexibility of

the tissue. Because of this property, elastic cartilage can withstand considerable bending force without fracturing.

Fibrocartilage is a nonvascular, tendonlike tissue. It is found in the intervertebral disks, pubic symphysis, glenoid and cotyloid ligaments, and the ligamentum teres femoris. The interarticular menisci of many joints (sternoclavicular, acromioclavicular, temporomandibular, knee, and wrist) are also composed of fibrocartilage. Histologically, fibrocartilage consists of rows of ovoid chondrocytes surrounded by small amounts of hyaline-like matrix, lying between long, parallel bundles of thick, collagenous fibers. It has been considered by some as a transitional form between dense connective tissue and cartilage. It does not have a distinct perichondrium, but rather the intercellular collagenous fibers merge with the surrounding connective tissue of the joint capsule or ligament. The matrix of fibrocartilage is softer than that of either hyaline or elastic cartilage. Thus, while the tissue is very strong, it is still highly flexible and compressible. It is therefore well suited to the function of moderating pressure changes within joints, while still allowing freedom of movement.

CARTILAGE IMPLANTS

Brief Historical Review

Bert[19] in 1865 was apparently the first to report the study of transplanted cartilage. In this experiment skinned, amputated rat tails which were implanted subcutaneously in the abdominal wall of the same and different rats for as long as five months were studied. Subsequently the fate of the cartilage implant, with and without perichondrium, was studied.[51,152,200] Other phases considered experimentally were the growth and fate of fetal cartilages,[62,95,200] and the reactions at the recipient site to autogenous, homogenous, and heterogenous cartilage implants.[51,95,103–106,200] Carrel[36] in 1912 transplanted dog cartilage which had been stored from 24 to 28 h at 1–7°C and believed that the cartilage remained alive. He also found that the morphology of cartilage of adult dogs and chick fetuses was not modified after a few months in cold storage.

The clinical use of autogenous cartilage in man was first reported by Koenig[96] in 1896. In this instance an immediate skin flap including

one-half of the thyroid cartilage was utilized to cover a tracheal defect. Mangoldt[113] in 1899 reported the subcutaneous transplantation of autogenous rib cartilage in a child, first under the chin and eight months later to a tracheal defect. Soon thereafter the use of costal cartilage for dorsal support of the nose was reported.[114,128] Tuffier[185] in 1910 stored cartilage from an amputated limb of one patient in an icebox and used it five days later in another patient. Morestin[126] in 1915 reported the successful use of homogenous cartilage implants.

Classification

A human cartilage graft may be strictly defined as one in which the viable tissue is completely detached from its bed and tissue fluid supply and transferred to a different bed in another part of the body, where it must establish a new and independent tissue fluid supply to maintain its viability permanently. Generally, however, the term "cartilage graft" includes and has been used to describe any type of implanted cartilage, regardless of its donor source, or its physical or biological state.

Cartilage implants may be classified according to donor source, donor site, and physical state. From a clinical point of view three principal types of cartilage implants have been used: (1) living autogenous cartilage (a true graft), (2) dead preserved homogenous cartilage (an implant), and (3) dead preserved heterogenous cartilage (an implant)[167] (Table 37.1).

Donor source

Autogenous cartilage grafts

Viable cartilage transferred from one site to another in the same individual is known as an autograft. The perichondrium is not essential for the transplantation of viable cartilage. It has been utilized in autografts, however, (1) to suture the graft to its bed, (2) to hinge a graft for angulation, and (3) to produce a curvature of that surface of the cartilage which retains the perichondrium. To decrease the possibility of warpage after transplantation, autogenous cartilage has on occasion been boiled.[131] This procedure destroys the vitality of the cells and transforms the collagen of

Table 37.1 Comparison of the Fate of Autogenous, Homogenous, and Heterogenous Cartilage Implants and Cartilage.[1] Sarnat BG, Laskin DM. (1954) Cartilage and cartilage implants. Collective Reviews Section, *International Abstr Surg, Gynecol Obstet* 99: 521–541

Type of Cartilage Implant	Gross		Histologic		Histochemical Changes		Metabolism	Susceptibility to Infection	Host Reaction
	Decrease[2] in Size	Warpage After Implantation	Viable-Appearing Cells	Resorption	Matrix[3]	Cells[4]			
Autogenous (fresh)	0	May occur	Yes	0	++	++	+	++	0 to +
Autogenous (boiled)	+++	No	No	+++	++++	++++	0	+++	+++
Homogenous (fresh)	++	May occur	Variable	++			+ to 0	+++	++
Homogenous (preserved)	+	No	No	+			0	+++	+
Heterogenous (preserved bovine)	++++	No	No	++++	++++		0	+++	++++
Cartilage (fresh)	0		Yes	0	0 to + (with age)	0 to + (with age)	++	+	

[1] Based primarily upon reports of experimental work on animals and human beings.

[2] Although children's cartilage increases in size, the reports vary as to whether children's autogenous cartilage grafts increase in size.

[3] Depolymerization of ground substance (0 to ++++).

[4] Depletion of glycogen (0 to ++++).

the matrix into gelatin, which, unlike collagen, is highly soluble and easily broken down by proteolytic enzymes.

A graft consisting of one tissue such as cartilage is known as a simple graft. Grafts composed of more than one tissue are called composite grafts. Immediate composite autografts of cartilage covered on two sides with skin have been successfully transplanted from the external ear and from the ala of the nose.[28,84,91]

Homogenous cartilage implants

Cartilage transferred from one individual to another of the same species is known as a homogenous cartilage implant. This may be immediate (fresh) or delayed (stored or preserved). For instance, cartilage which has been taken from the maternal ear and transferred immediately to the child for construction of an ear would be considered to be an immediate homogenous cartilage implant.

This should be distinguished from a more frequent source of human homogenous cartilage (delayed) which has been stored in a bank. Thus, costal cartilage may be obtained under aseptic conditions from a young, healthy adult immediately after accidental death. The cartilage is stripped of its perichondrium because of the inflammatory reaction it might elicit when implanted, and preserved under refrigeration in a chemical solution until used. In the past, cartilage has been preserved in formalin or alcohol. More recently, aqueous solutions of merthiolate diluted with normal saline solution (merthosaline)[29,149,180] have been used. It is recommended that the solutions be changed and that cultures be made not only of the solutions but also of the preserved cartilage at periodic intervals to determine the presence of any bacterial contamination. The cartilage should be thoroughly rinsed of the preservative solution in normal saline solution before being implanted, lest a chemical, inflammatory response be provoked at the recipient site. Recently, on an experimental basis, homogenous cartilage has been stored after rapid freezing and drying and subsequently implanted.[93]

The preserved homogenous cartilage implant has the following advantages over the fresh autograph: (1) an additional surgical procedure

on the patient is not necessary to obtain the cartilage, (2) adequate amounts of cartilage are available (shape, size, and quality), (3) the cartilage can be trimmed to the desired form preoperatively and is not subject to warpage or curling, and (4) the operative and postoperative care requires less time, and (5) there is less postoperative discomfort. Autografts, however, seem to be better tolerated and less subject to resorption and infection.

Heterogenous cartilage implants

Preserved homogenous cartilage is not always readily available. Consequently, preserved heterogenous cartilage (heat-sterilized in boiling water and stored in merthosaline), i.e. cartilage obtained from a different species, has been utilized. Bovine cartilage has been the most frequently transferred to humans. It is readily available in the desired size and amount. However, variable clinical results, mostly unsatisfactory have been obtained.[56,58,132,179,188] Recently whale cartilage has been used.[167] Experimentally, it has been found that heterogenous cartilage elicits a tissue reaction and may be extruded or resorbed.[106] Fischer[51] observed that heterogenous cartilage transplanted from dogs, ducks, frogs, guinea pigs, rats, and humans to the chicken's comb invariably perished and was resorbed. In one instance he observed proliferation, for a few weeks, of a human infant's cartilage transplanted within several hours after death to the comb of a chicken.

Donor sites

In addition to the various sources of cartilage, various sites of a donor have been utilized. The donor site is selected on the basis of the requirements, namely: amount, particular characteristics, and availability of the cartilage. Hyaline cartilage, particularly costal, has been used most commonly. Cartilage has also been taken from the external ear (elastic), nasal septum and ala, and knee joint (semilunar). The cartilage of epiphyses and joint surfaces including half and whole joints has also been transplanted. Most of this work has been on an experimental basis and in a limited way clinically.[22,125,130,134]

Physical state

Cartilage can be classified not only in terms of donor source and donor site but also according to its physical state. Thus, when cartilage is implanted, whether it be autogenous, homogenous, or heterogenous, a single piece is usually trimmed to conform to a previously prepared pattern. Sometimes two or more pieces may be required. In addition, cartilage has been purposely cut (diced) into small pieces, because it can be more readily inserted and adapted to a desired form. In some instances the diced cartilage has been introduced into a fenestrated metallic form, which can then be buried subcutaneously. Several months later the duplicate structure is removed from the form and transplanted to the desired site.[139,140,197,198] Cartilage flakes have also been utilized.[23]

Clinical Uses of Cartilage Implants

Because of its bulk, firm consistency, and relative inertness, cartilage has been of great value in plastic and reconstructive surgery. It has been used to fill depressions and build prominences in the following deformities: (1) in congenital anomalies in which certain structures are partially or totally absent or deficient, (2) in arrested growth, (3) in inactive inflammatory lesions to replace loss of structure, and (4) in traumatic lesions, either accidental or purposeful (surgical treatment of cancer) (Table 37.2). Thus, cartilage is used as a substitute or replacement for absent, deficient, lost, or displaced tissue, particularly when bulk and support are essential. There are many reports of various sites (principally the face) to which cartilage has been transplanted.

Definition of a Successful Implant

From a clinical point of view, the definition of a successful cartilage implant would be one which has maintained the desired correction and is tolerated during the lifetime of the patient. Viability *per se* is not paramount. Consequently, implanted preserved cartilage which is metabolically inactive cannot be considered as a graft which has "taken" (as in a skin graft) but only as an implant which is a tolerated, relatively inert

Table 37.2 Sites to Which Cartilage has been Transplanted Clinically and Experimentally. Sarnat BG, Laskin DM. (1954) Cartilage and cartilage implants. *International Abstr Surg, Gynecol Obstet* 99: 521–541

Cranium
Eyelid
Orbit (floor, rim)
Zygoma
External, ear, and mastoid area
Nose (dorsum, ala, tip, columella)
Jaws
1. Mandile (alveolar process, chin, body, ramus)
2. Maxilla
Palate
Retropharynx
Trachea and bronchi
Thorax
Abdominal wall (recurrent hernias)
Sacrum (spina bifida)
Joints (temporomandibular, hip, phalangeal)
Penis
Uterine tubes (maintain patency)

foreign body. Can transplanted fresh human homogenous cartilage be considered as a "take" from a biological point of view or rather as a clinical persistence? The similarities of cartilage and cornea (nonvascularity, low metabolism, relative acellularity) have often been compared. However, the statement that cartilage and cornea survive as vital homografts in the human being must be examined more carefully. In a recent review concerning the fate of the corneal homotransplant, it was concluded that the host cells tended to invade and replace the cells of the grafted donor material and that the stroma of the transplant tended to maintain its own integrity.[187] There is a need for critical evidence to determine whether the biological survival (or "take") of transplanted human homogenous cartilage does occur.

Even though a portion or all of an implant might either degenerate, or undergo resorption and be replaced with fibrous tissue or bone, the implant would still constitute a satisfactory filling material if the clinical

result is the one desired. On the other hand, many clinically successful implants would not be considered so if based upon the maintenance of their original characteristics on a gross, histologic, histochemical, and metabolic basis. Thus, the practical value of an implant need not correspond with its biologic fate.

Factors Influencing Successful Implantation of Cartilage

The factors which influence the successful implantation of cartilage are many. In addition to careful surgical technique, they may be classified generally into (1) the state of the implant, and (2) the state of the host area and host. The ultimate fate of a cartilage implant will also depend upon its source (autogenous, homogenous, or heterogenous), its viability (fresh, boiled, stored, preserved), its physical state, the inflammatory reaction it provokes from the host (immunological,[1] foreign body,[2] bacterial,[3] chemical[4]), and the general health of the recipient.

The central portion of a thin autogenous cartilage graft survives better after transplantation than the central portion of a thick cartilage graft, since the latter is further removed from its source of nourishment.[103,130] A rule which has been applied to autogenous cartilage grafts is: "The smaller the graft the better its chances of complete survival after transplantation."[140] Thus, the expectation might be for diced autogenous cartilage grafts to have an excellent opportunity for survival except possibly for the trauma incident to the cutting of the cartilage into smaller pieces and the time required for vascularization of the fibrous tissue between the pieces.

In regard to the survival of bovine cartilage implants in the human, it has been stated that the amount of antigen liberated to provoke resorption of the implant is related to the cartilage surface area.[56] Thus, diced bovine cartilage is resorbed more readily than a block implant, which may have the same mass but considerably less surface area. In addition, it was found that each successive bovine cartilage implant in the same human volunteer showed a greater degree of resorption than the preceding one. From this is was concluded that an antigen–antibody reaction elicited the resorptive response on the part of the host.

It is important that both the cartilage and the recipient area be free of infection. Usually an implant cannot tolerate infection. Nevertheless, there

are reports of cartilage insertion through regions which harbor bacteria (mouth, nose) with successful retention.

Another factor which may aid successful implantation is an adequate bed and covering of the implant in terms of thickness of the tissue, blood supply, and tissue fluids. A thin, scarred atrophic covering is not sufficient and may lead to exposure and extrusion of the implant. It is also important that the recipient site and the cartilage implant be well adapted to each other, with no "dead" space, and that they be relatively freed of motion, trauma, or undue pressure, particularly during the early period of implantation. The cartilaginous end of a rib bone graft used to reconstruct the false joint, ramus, and body of a mandible tolerates motion and trauma.[32] Cartilage implanted to maintain a false joint after resection of the condyle and ramus for ankylosis is also subjected to some trauma and motion.

There is considerable difference in the degree of host reaction to autogenous, homogenous, or heterogenous implants. The metabolism which is characteristic of the particular tissue in general and the specific metabolism of the tissue at the time of implantation is important.

Usually, homogenous and heterogenous implants fail to survive, partially because of their inability to withstand the complicated biologic response of the host. Loeb[106] indicated that this host reaction is due primarily to variations between the chemical constitution of certain substances elaborated by the implant, which he termed "individuality differentials," and the tissue fluids of the recipient animal. In an autogenous environment, these factors produce no abnormal reaction. In homogenous surroundings, however, they not only act as toxins which result in the local tissue reaction but they apparently also stimulate the formation of immune bodies which intensify this response. Loeb demonstrated that tissues with the most active metabolism produced these materials in the greatest quantity.

The metabolism of viable cartilage grafts is exceedingly low.[93] The response of the host provoked by these grafts is therefore minimal in comparison with that of more energetic tissues. This offers a partial explanation for the acceptance of these implants by the host. In regard to viable cartilage transplants, homogenous cartilage and heterogenous cartilage provoke the greatest reaction from the host.[170] Because a preserved cartilage

implant exhibits no metabolic activity, it is tolerated presumably as a relatively inert, organic foreign body. However, as an animal tissue, though nonvital, it is affected by the host and subject to resorption and replacement by fibrous tissue. Thus, although satisfactory clinical results have been obtained, the fate of preserved cartilage cannot be termed a biological survival but rather a clinical persistence.

Cartilage and its perichondrium react unequally and differently to new surroundings. Cartilage with its low metabolism is relatively nonreactive as compared to perichondrium, which has a higher metabolism and greater individuality differentials. Consequently, all soft tissue, including muscle, fascia, and perichondrium, should be removed from the implant before transplantation because, in particular, the soft tissues of one individual transplanted to another give rise to considerable reaction.

Fate of Implanted Cartilage

Experimental studies as to the fate of fetal, young, and adult implanted cartilage are not all in agreement.[19,42,45,51,103,130,134,137,147,148,152,157,163,196,200] This may be a result of a wide variety of experimental conditions with few attempts to duplicate procedures so as to be able to accept or reject earlier reports. Thus, a number of different experimental animals (both unborn and born) have been used as donors, and cartilage with and without perichondrium has been transferred to animals of the same or different species either subcutaneously, in the anterior chamber of the eye, the comb of the chicken, or to joints. Cartilage from ribs, joints, epiphyses, and ears has been transplanted for widely varying periods. The methods of study have principally been gross and histologic. Recently, metabolic[87,93] and histochemical[2] means have been employed.

Gross findings

All cartilage implants that are retained, regardless of whether they are autogenous, homogenous, or heterogenous, are encapsulated by fibrous tissue. The fibrous tissue reaction, however, seems to vary with the type of human cartilage implant.[31] A fresh autotransplant becomes firmly united with its adjacent tissue. A fresh homogenous cartilage transplant becomes

attached to the host tissues but not nearly as firmly as autocartilage. Chemically preserved cartilage becomes enveloped in a capsule of the host tissues and is relatively loosely attached. Gross examination of autogenous and homogenous cartilage in dogs up to 1.5 years after implantation showed that the transplants were firmly attached to the soft tissues and that they retained their cartilaginous appearance and springlike physical qualities.[197,199] Peer and Walker[147] stated that human cartilage grafts are joined to the host cartilage by fibrous tissue and not by a cartilage union. Young[196–199] found, in dogs, that costal cartilage transplanted to defects in articular surfaces of joints healed with a fibrous tissue union. Interestingly, however, he also found that when several pieces of rib cartilage transplanted into the joint were examined there was a cartilage union.[196]

Shape

Generally, cartilage implants maintain their shape. The autograft, however, has a tendency to warp or curl, particularly toward the side where the perichondrium remains. Because removal of the perichondrium did not always obviate this difficulty, fresh autogenous cartilage has been immersed in a container of merthiolate and placed in boiling water for 10 min. This procedure apparently decreased the tendency of fresh cartilage to curl. However, the physical and chemical state as well as the viability were altered.[2,93]

Variations in size

Increase in size. The question of growth of cartilage grafts is an important one in plastic surgery. Fischer[51] transplanted embryonic cartilage of a chick to the comb of an adult chicken and found the cartilage to develop and grow for a few months, after which it was "transformed." He also found that the fewer the soft tissues that were transplanted with the cartilage the better it grew. Zahn[200] implanted epiphysial and rib cartilage from live fetal rabbits and cats immediately after removal into the anterior chamber of the rabbit's eye and also subcutaneously, and found doubling of the size of the cartilage within a few weeks. Similar findings had been reported by Leopold.[95] He also found that cartilage transplanted from a

six-month-old rabbit under similar experimental conditions either remained the same or was resorbed.

Dupertuis[45] demonstrated the growth of implanted autogenous and homogenous cartilage (auricular and costal) in young rabbits by direct measurements. Clinically, Peer[142] also found, by direct measurement in a 2-year study of 15 autogenous cartilage grafts (with and without perichondrium) in young human beings, a definite increase in size in the septal and auricular but not the costal cartilage grafts. Thus, Peer[142] concluded that autogenous cartilage grafts should be used in children so that the growth of the transplanted cartilage may keep pace with the regional growth. Dupertuis,[46] in a clinical study of four patients, was also able to measure the growth of young human autogenous rib cartilage grafts (without perichondrium) over a period of 4–6 years. However, in a more recent study of young human autogenous cartilage grafts for a period of years, Peer[142] found no increase in size and was inclined to believe that his earlier observations had been erroneous.

Constancy in size. In the correction of deformities in the adult which require filling in defects or building prominences, an amount of cartilage is used to give the desired result. Permanency of the result is important. Therefore, cartilage which maintains constancy in size is preferred. It is generally accepted that a fresh piece of autogenous cartilage best meets this requirement (Table 37.1). In this regard the perichondrium apparently does not play an important role.

Zahn found that there was no increase in the size of rib autogenous cartilage implanted subcutaneously in adult dogs and rabbits. Young[199] also found, in dogs, that autogenous and homogenous cartilage implants did not lose in weight or volume up to as long as 1.5 years. Whether the cartilage was transplanted with or without the perichondrium seemed to make no difference. Loeb and Siebert,[107] however, stated that there was a greater tissue reaction to, and more eventual resorption of, homogenous cartilage than in autogenous cartilage transplants.

Decrease in size. All other than autogenous cartilage transplants are more subject to a decrease in size. Although there may be an actual decrease in size or partial replacement of the implant, the clinical result may not be

significantly affected. The use of fresh maternal ear cartilage for the construction of the child's ear has been disappointing, because of its change in size and configuration. This may be a result of resorption and fibrous tissue replacement and/or loss of original elasticity because of pressure effects of the overlying tissue. Clinical[56,132] and experimental[106] studies demonstrated that heterogenous cartilage is subject to extreme resorption. Preserved cadaver implants are invaded by fibrous tissue, usually over long periods of time, but occasionally they are resorbed rather suddenly.[144] Living homogenous cartilage is not superior to preserved cadaver cartilage implants in human beings.[143]

Histologic findings

Early studies of the fate of cartilage implants in animals were not in accord,[19,130,200] particularly in regard to results of transplantation of joints and epiphyses. Some reports stressed the importance of the perichondrium for survival of a costal cartilage graft.[51] More recently, Young[197,199] found that if microscopically the presence of normal cartilaginous architecture is a criterion of viability, both autogenous and homogenous cartilage implants in the dog are viable up to 18 months, and that the presence or absence of perichondrium does not alter the findings.

Experimental studies on the guinea pig demonstrated variable cellular responses to different types of cartilage implants. Thus, autogenous cartilage grafts elicited no lymphocytic response.[103,104] In homogenous cartilage transplants, however, a lymphocytic infiltration was noted in the surrounding fibrous tissue at the end of the first week, which continued to increase until the fourth week, after which time it remained constant. It was also found that the lymphocytic and connective tissue response to homogenous cartilage was dependent upon the metabolism of the living tissue.[170] Homogenous cartilage killed by heating elicited no reaction. Both living and dead heterogenous cartilage, however, did provoke a reaction.

Gillies[57] was apparently the first to report histologic studies of human autogenous and homogenous cartilage transplants. Histologic studies of human rib autogenous cartilage 23 years after transplantation revealed what appeared to be a normal cellular and matrix structure.[141] Similar examination of a diced human rib autogenous cartilage graft 3 years after

transplantation revealed no evidence of degenerative changes, invasion, or resorption.[139]

Histologic study of fresh human homogenous cartilage 45 months after transplantation showed normal-appearing cartilage cells and a complete absence of invasion or resorption.[140] However, as examination of other implants buried for a shorter period of time showed invasion, partial resorption of the matrix, and degeneration of the cartilage cells, it was concluded that living homogenous cartilage was not a consistently reliable grafting material. The impression is that in human beings fresh homogenous cartilage is inferior to both fresh autogenous cartilage and preserved homogenous cartilage.[143]

Experimental studies with septal and rib homogenous cartilage preserved in 50% alcohol and buried in human tissue from 9 months to 2 years demonstrated that it was tolerated as a dead foreign body and that histologically the implant was progressively invaded and replaced by fibrous tissue although the bulk of it was still present after 2 years. Some specimens 14 months and 2 years after transplantation showed areas of either calcification or early bone formation.[138]

In all of these studies it would be important to compare the histologic section of the cartilage after a period of implantation not only with a section of normal cartilage but also with a section of the same cartilage just prior to transplantation. One must also remember that findings of animal experimentation cannot and should not be interpreted as being strictly comparable with those on human beings. In addition to species differences, the experimental conditions may be different. For example, cartilage may not behave the same when implanted in the abdominal wall as when implanted subcutaneously in the nose, where the bed may be scarred and relatively nonvascular and the covering atrophic and thin.

Histochemical findings

Histochemical investigations on implanted boiled and nonboiled autoenous cartilage in the rabbit[2] have revealed alterations in the physicochemical state of these tissues that were not demonstrable by the ordinary histologic techniques. When stained by the periodic acid – leucofuchsin procedure for the visualization of carbohydrate–protein complexes, the

previously boiled cartilage implants showed evidence of a rapid dissolution of these components from the ground substance in the peripheral zones. Similar changes, but to a much lesser degree, occurred in the untreated autografts. Accompanying the rapid depolymerization of the matrix in the boiled cartilage transplants was the deposition of calcium phosphate. The degradation of the cartilage matrix as a result of boiling increased its susceptibility, *in vitro*, to such enzymes as collagenase and hyaluronidase. Since the connective tissue cells of the host may be capable of liberating similar mucolytic enzymes, it is possible that cartilage treated in such a manner will be more readily resorbed following implantation.

Comparison of fresh costal cartilage with cartilage autografts revealed similarities in the distribution of carbohydrate–protein complexes and metachromatic substances, phosphate, and/or carbonate and glycogen.

Nutrition and metabolism

The nutrition for cartilage grafts is obtained by diffusion from the tissue fluids of the host. Although in most instances the normal diffusion pattern should be quickly re-established after transplantation, there may still be a short period of hypoxia. The small oxygen requirements and predominantly anaerobic carbohydrate metabolism of cartilage, however, probably allow most of the chondrocytes to survive this interval. Once the graft has been adapted to its new environment, any further variation in the passage of substances into the graft will be governed by changes in the physical state of the matrix. The amount of intercellular fluid reaching the cartilage, on the other hand, will be determined by the type of surrounding host tissue. Thus, the nature of the recipient bed can also have a distinct influence upon the continued viability of a cartilage graft.

The carbohydrate metabolism (respiration and anaerobic glycolysis) of fresh rabbit costal cartilage autografts, and fresh and preserved (merthosaline, freeze-dried) homogenous cartilage, has been investigated.[93] The metabolic activity of the fresh autografts and homogenous cartilage declined to about one-half that of normal rabbit costal cartilage during the first 7 days after transplantation. No further variation was noted in the subsequent 150-day period of observation. Cartilage preserved for 7 days in merthosaline or by freeze-drying exhibited only about

one-fifth the normal rate of carbohydrate metabolism. When the cartilage was preserved for longer periods, the metabolism was completely terminated in most instances. After implantation, no further significant change in metabolic activity was noted. Merthosaline exerted its deleterious effect by the combination of the mercury ions with essential reactive groups in the intracellular enzymes. These investigations indicated that, in the rabbit, fresh autogenous and homogenous costal cartilage remained viable for as long as 150 days after implantation. They also revealed that a difference existed between the state of viability of these implants and fresh costal cartilage. This has not been demonstrated by ordinary histologic methods.

The vitality of cartilage and cartilage grafts was studied by the use of radioactive phosphorus. A comparison of the uptake of radioactive phosphorus (as determined with a Geiger counter) in cartilage and autogenous cartilage grafts (without perichondrium) in dogs revealed that after 4 days the uptake was 65% of normal and had increased to about 90% by the 10th day.[87] This method could be utilized for further study in comparing the uptake of radioactive material in different types of cartilage implants under variable conditions.

SUMMARY

Cartilage is a nonvascular, relatively acellular type of connective tissue of firm consistency and comparatively low metabolic activity. It forms the most important growth centers of the skeleton, provides smooth surfaces for joint movements, and contributes support and elasticity to many structures of the body. It is subject to most pathologic changes.

Cartilage implants have been used with clinical success in plastic and reconstructive surgery. When this tissue is transferred from one part of the body to another in the same individual and retains its viability, it is known as an autograft. Viable cartilage transferred from one individual to another of the same species is known as a homogenous cartilage implant. Because of the vascular and cellular reactions elicited in the host, these implants may fail to retain their vitality and be gradually resorbed and replaced with fibrous connective tissue. Preserved homogenous cartilage implants (nonvital) are tolerated by the host. They remain as relatively nonreactive foreign bodies which also undergo resorption and replacement at a variable

rate. Since the invading connective tissue, if not too extensive, may maintain the cosmetic result, one should distinguish between clinical success and actual persistence of the implant. Preserved heterogenous cartilage implants (bovine, whale), on the other hand, are less satisfactory because of the high incidence of early complete resorption. Of the various types of cartilage clinically employed, fresh autogenous cartilage and merthosaline-preserved homogenous cartilage are perhaps the two most successful, the former remaining as a viable graft and the latter as a tolerated nonvital implant (Table 37.1).

Although experimental studies have shed considerable light on the clinical problems related to cartilage and cartilage implants, the findings on lower animals should not always be interpreted as being strictly applicable to humans. Continued, well-controlled research, particularly on human subjects, is imperative before many of the existing questions can be answered.

Cartilage is probably one of the least complex tissues. When its basic properties have been thoroughly investigated, the information gained may not only help solve some of the general problems of tissue transplantation, but also aid in a better understanding of many of the physiologic and pathologic processes found in the more complex tissues and organs.

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PART VII

PUBLIC HEALTH ASPECTS

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The Teeth as Recorders of Systemic Disease*

This clinical investigation is based on a dental analysis of 60 nonluetic patients with enamel hypoplasia. These were selected from a group of more than 1,000 persons. In addition, a medical history stressing the infancy and childhood periods was obtained from each patient. More than 300 extracted teeth with enamel hypoplasia were studied grossly (see Chap. 30, Fig. 30.1).

Enamel hypoplasia is a dental manifestation of a constitutional disturbance that affects the enamel increments of the deciduous and permanent teeth forming during the disease period, and indelibly indicates the time of occurrence and duration (see Chap. 24, Fig. 24.1). This record, which is comparable to the lines of arrested growth in long bones, can be readily studied on roentgenographic, clinical, and histologic bases.

A chronologic analysis showed that two-thirds of the enamel hypoplasia occurred during the infancy period (from birth to about the end of the first year), about one-third during the early-childhood period (about 13–34 months) and less than 2% during the late-childhood period (about 35–80 months).

No specific etiology was found. Exanthematous diseases are not so frequent a cause of enamel hypoplasia as was heretofore commonly believed. Possible etiologic factors are rickets, hypoparathyroidism, and fluorosis,

*Excerpted from: Sarnat BG, Schour I. (1941,1942) Enamel hypoplasia (chronologic enamel aplasia) in relation to systemic disease: a chronologic, morphologic and etiologic classification. *J Am Dent Assoc* **28**: 1989–2000; **29**: 67–75.

but hypoplasia cannot be predicted with any reliability, even in the most severe forms of these diseases. In more than 50% of the cases studied, no etiologic factors could be determined.

Except in fluorosis, enamel hypoplasia is not restricted to certain geographic localities, but is as ubiquitous as is disease.

Because of its high incidence (5–18%) and because not all the etiologic factors are known as yet, this public health problem necessitates further study.

Rickets

See Chapter 30.

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Congenital Syphilis

See Chapter 29.

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Sickle Cell Anemia*

Roentgenographic studies of the jaws were made in 22 African-American patients with proven sickle cell anemia. Significant findings, characterized by a generalized osteoporosis, were made in the dental roentgenographs of 18 patients of this group, but were observed in the roentgenographs of the long bones of 3 patients and of the skull in 1 patient. Since sickle cell anemia is a systemic disease, dental roentgenographs should be taken in addition to those of long bones, the skull, and vertebrae. Although an unusual degree of osteoporosis as shown in the dental roentgenograph may not necessarily be pathognomonic for sickle cell anemia, it should be considered in the differential diagnosis.

In an article some 50 years later, this thesis is wholly supported. [White SC *et al.* (2000) Digital analysis of trabecular pattern in jaws of patients with sickle cell anemia. *Dentomaxilofac Radiol* **29**: 119–124.]

*Excerpted from: Robinson IB, Sarnat BG. (1952) Roentgen studies of the maxillae and mandible in sickle-cell anemia. *Radiology* **58**: 517–523. (This was the first report of the roentgenographic findings on the jaws in sickle cell anemia.)

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Oral and Facial Cancer*

Oral and Facial Cancer is the first and only book at this time to deal with the subject matter in this manner. It is of course not feasible to include the contents of the book but the foreword and prefaces will suffice. The first edition was translated into Portuguese and published in Brazil.

FOREWORD†

Doctors Sarnat and Schour have written a book on oral and facial cancer. Why?

Cancer is a leading cause of death. The insidiousness and treachery of its attack has fired the American public with a zealous desire to conquer this disease. Research in this field has been tremendously augmented in the last four years. A vigorous and dramatically effective attack should not be postponed until the cure for advanced cancer is discovered. The cure for early cancer, in many cases, is known and well established, and if applied widely will decrease the ravages and lethality of the disease by one-half.

*Excerpted from: Sarnat BG, Schour I. (1950) *Oral and Facial Cancer*. The Year Book Publishers, Chicago. 304 pages, 236 illustrations on 118 figures, 12 color illustrations on 2 plates.

Excerpted from: Sarnat BG, Schour I. *Cancer Da Face E Da Boca*. Transl. into Portuguese by Cl. Mello. Editoria Cientifica, Rio de Janiero.

†Foreword to: Sarnat BG, Schour I. (1950) *Oral and Facial Cancer*. The Year Book Publishers, Chicago.

Thus, if the public is educated to consult both the physician and the dentist at reasonably frequent intervals, and if both the physician and the dentist have been taught to recognize early cancer and are kept alerted to it, great progress will be made.

It was with this latter objective in mind that Congress appropriated funds to the National Cancer Institute to help improve the teaching of cancer in both medical and dental schools. Dental schools were included for a very important reason. Fifteen percent of all cancers occur in the region of the head and the neck, and approximately six percent start in the oral cavity. Forty percent of all cancers of the head and neck are seen first by the dentist.

Nevertheless, a text on oral and facial cancer for the teaching of students and for ready reference by general practitioners was not available, particularly one which was dedicated to the early recognition and treatment of cancer in the oral and facial regions.

That is why Doctors Sarnat and Schour wrote this excellent text. Every new development and concept in the field of diagnosis and treatment requires its textbook. Hence, this book represents a new period and a pioneering accomplishment in the professional field of cancer education. Many lives will be saved from a cancer death as a result of the skilful and attractive pedagogic technics the authors have employed to attain the dedicatory aim of their book.

Andrew C. Ivy

PREFACE TO THE FIRST EDITION

Cancer is the second greatest cause of death in the United States. This fact has led to the concerted efforts of the agencies of the health professions to conquer this most tragic illness. In the division of responsibility in waging war against cancer, the health professions have a particular and common challenge in cancer. This challenge is the early recognition of oral and facial cancer, which lies within the special field of competence of the dentist as well as of the physician. The dentist's responsibility rests not merely on the diagnosis and treatment of dental disorders. He shares with the

physician the responsibility for the prevention and diagnosis of oral disease, of both local and systemic origin.

This book is dedicated to the early recognition and treatment of cancer of the oral cavity and to meeting the growing demand for a guidebook and survey of the field of oral and facial cancer and related conditions. The text is organized for ready reference in the general practitioner's office and for use in teaching. It may be read in its entire sequence or may be used for information on special aspects by referring to individual chapters. Selected case histories are presented to illustrate the characteristics of various types of tumors.

In order to deal with the problem of oral and facial cancer comprehensively and in its proper relation to the health and to the diseases of the oral cavity and face, consideration is given to such correlative aspects as public health, research, anatomy and physiology, and differential diagnosis. A selected bibliography is appended for those seeking a more detailed discussion.

The material has been obtained from so many sources that individual acknowledgment has not been possible in every instance. Grateful acknowledgment is due to authors who have given permission to reprint certain selections and illustrations from their works. In addition, material has been taken freely from the literature prepared by the American Cancer Society and the Tumor Committee of the Connecticut State Dental Society and from textbooks on cancer by Ackerman and Regato, Cutler and Buschke, and Blair, Moore, and Byars. The photographs are those of patients seen primarily in private practice, at the University of Illinois clinics and at Cook County Hospital. Preference was given to illustrations of early lesions.

We wish to acknowledge our gratitude to Dr. Harry Sicher, whose aid was invaluable in the preparation of this text. We also wish to thank, for their assistance in the preparation of most of the illustrations, Mrs. Helen Kutuzov for the line drawings and Mr. William M. Winn for the photographs. A grant from the Gertrude Everett Memorial Fund made some of the illustrations possible.

Bernard G. Sarnat
Isaac Schour

PREFACE‡

The cordial reception given the first edition of this book by the dental, medical, and allied professions, both in practice and in the schools, has led to this second edition. The same general purpose was kept in mind in preparing this edition as in writing the first edition; namely, to present the essentials of oral and facial cancer in an easily read style and to include representative, but selected, illustrations and diagrams. This work was not intended to be an exhaustive treatise but rather to serve only as an introduction to the subject. The text was reorganized to give further emphasis to the logical sequence of diagnosis and treatment. A number of new illustrations have been added and others redone. In order to meet repeated requests from teachers and lecturers, 35 mm slides of the illustrations of this text have been made available; these can be secured through Clay-Adams Inc., 141 Fast 25th Street, New York 10, New York, USA.

The recent translation of this text into Portuguese is a welcome step in advancing professional cancer education.

We are grateful to many colleagues for their valuable suggestions and to Dr. C.I. Mohammed for his devoted assistance.

Bernard G. Sarnat
Isaac Schour

‡Preface to: Sarnat BG, Schour I. (1957) *Essentials of Oral and Facial Cancer*, 2nd ed. The Year Book Publishers, Chicago. 297 pages, 240 illustrations on 122 figures (18 in color).

Oral Occupational Disease*

Our purpose in this report is to present a summary and analysis of the available information on a public health issue — oral occupational disease. The occupational hazards, and exposures coincident with industrial activities, present a special challenge to the medical profession to maintain the health of the worker.

Ramazzini[1] (1633–1714), "the father of industrial hygiene," was the first to advocate the inclusion of the patient's occupation in each medical history. In 1690 he warned painters against wiping brushes on their lips, and yet recently the lives of a number of workers were lost because, in disregard of this simple precaution, they used their lips to moisten and point the brushes in painting luminous watch dials.

There are a limited number of reports and reviews on oral occupational diseases. Many of the available references are statements of a descriptive rather than analytic nature. Direct investigations of carefully controlled cases are not common. There are several excellent textbooks on occupational disease which present occasional references to oral lesions.

Relatively few oral manifestations are included in the compilation of occupational disease symptoms in the 1941 Standard Bodyparts Adjustment Guide prepared for insurance companies.

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*Excerpted from: Schour I, Sarnat BG. (1942) Oral manifestations of occupational origin. *Oral Occupational Disease. JAMA* 1197–1207. (Remarkably, there is no mention of asbestos in this 1942 report.)

REFERENCE

1. Ramazzini B. (1940) *Diseases of Workers*; the Latin text of *De Morbis Artificum* (1713), revised with translations and notes by W.C. Wright. University of Chicago Press.

Becoming a Plastic Surgeon* — Yesterday (BGS)

INTRODUCTION

> The contrast in the plastic surgery training of the authors is startling. In the 1940's Dr. Sarnat had the unusual opportunity to spend three years full-time with the Blair, Brown, Byars plastic surgery program. This was not only in their private practice but also at Barnes Hospital and Washington University Department of Surgery in St. Louis. At that time it was undoubtedly one of the foremost programs — if not the foremost — in the world. The training offered superb exposure to a wide variety of well-performed surgical procedures. It was surgery, surgery, surgery. There was no didactic plan. Very little, if any, significant literature was available. The journal *Plastic and Reconstructive Surgery* did not exist. There were no fellow trainees to discuss problems with. So, although it was a superb surgical training program at its time, there is no comparison with the great strides made over the past several decades. It was Blair who played the singular role in founding the American Board of Plastic Surgery.

May I share some selected memories? How to begin? Where to begin? Reminiscence is the essence of senescence: I will try to deal primarily with the former.

*Excerpted from: Sarnat BG. (2003) As I remember: becoming a plastic surgeon and my three years (1943 to 1946) with the Vilray P. Blair Group. *Plast Reconstr Surg* **111**(3): 1262–1275.

No previous reports[1–4] relate to three years of continuous direct professional and personal experiences as a full-time assistant to both Dr. Vilray P. Blair and Dr. Louis T. Byars in the practice of plastic and reconstructive surgery in St. Louis.

Robert H. Ivy,[5] in the first paragraph of a 1955 article, expressed my feelings very well: "Professional men, if they live long enough, reach a stage when they are no longer able to report much on current practice and must rely for their contributions on events and personalities of bygone days. A suitable term for such individuals is 'Links-with-the-Past.' These may therefore be defined as persons of more or less advanced years. Still in contact with current activities of their profession, but who have enjoyed close association with prominent personalities and significant events of the past, and are privileged to recall to the present generation some of these bygone happenings and individuals so that they will not be forgotten."

I was 9-years old in 1921, when I first learned of Dr. Truman W. Brophy. My 19-year-old brother was a first-year dental student at Chicago College of Dental Surgery at Harrison and Wood Streets on the west side of Chicago. Dr. Brophy was the founder and principal owner of the dental college, a proprietary school, which was later affiliated with Loyola University, no doubt as a result of the Gies report[6] on dental education of 1926.

As a curious youngster and a reasonably good student, I studied along with my brother as he learned anatomy, biochemistry, physiology, microbiology, etc. During the next few years he would talk about his famous professor, who not only had dental, medical, law, and many other degrees, but was also a world-renowned surgeon with patients coming from everywhere because of his reputation in the repair of cleft lips and palates.

When I saw the distinguished, bewhiskered Dr. Brophy and all of his many degrees in my brother's 1925 class graduation picture, I was full of awe. My brother stressed that I should try to emulate Dr. Brophy. Little did I, as an impressionable, somewhat naive nine-year-old, realize what a lofty goal he had set.

In grammar and high school, science and biology, in particular, interested me. During this period I was intrigued by several experiences.

My goal was to go to medical school and, subsequently, to dental school. However, as an undergraduate I took an honors research course in

physiology and became so enamored that I seriously considered enrolling in the doctoral program.

After finishing medical school in 1936 at the University of Chicago, I interned at Los Angeles County Hospital. In 1937, oral and plastic surgeons had both the M.D. and D.D.S. degrees. As I continued to pursue this goal, I researched dental schools and studied the 1926 William Gies report on the state of dental education in the United States.[6] This did for dentistry what the Abraham Flexner report of 1910 did for academic medicine.[7] However, my interest was in the biological and not the technical aspects of dentistry.

I already knew of Dr. Isaac Schour (S.B. and Ph.D. in anatomy, University of Chicago) at the University of Illinois College of Dentistry, who was deeply involved in, and at the forefront of, biological dental research. So, after taking the California Medical State Board, I returned to Chicago in August of 1937. Interviews at the University of Illinois College of Dentistry with both Dean Frederick B. Noves (a wonderful gentleman) and Dr. Isaac Schour, professor and head of the Department of Histology, led to immediate and very warm responses when I stated my interests and goals. I was awarded a faculty position in Histology while simultaneously enrolled as a first-year dental student, given full credit for all biological courses taken at the University of Chicago School of Medicine, and also enrolled in the graduate school at the University of Illinois. The university paid my tuition and all of my expenses for instruments and materials; I received no other compensation. To obtain some extra money, I made house calls as a physician for the Chicago Relief Administration for $1.50. Thus, I became involved in a very busy and ambitious full-time program.

In the morning, I would be taking courses with the first-year dental students. In the afternoon, I would be assisting in and teaching Histology. The students were confused. Who was this fellow, Sarnat, a student with us in the morning and our teacher in the afternoon? The word soon got around that I was unusual as an advanced student with a medical degree. I was wearing both hats.

During my three-year period in the dental school, I began my research program in earnest. My interest was in bones and teeth. I initiated collaborative studies at Rush Medical College and at the University of Chicago School of Medicine, dealing with the effects of yellow phosphorus on

growing bones (tibia, base of the skull) and teeth, and the decelerating effects of hibernation on growing teeth, in particular. I used a calcium-specific vital stain to measure the degree of hibernation. This, of course, could relate to our program in outer space, which probably had not as yet been undertaken. In addition, I began a long-term study of the teeth as recorders of systemic disease. This work resulted in my winning, in 1939, both the highly coveted Joseph A. Capps Award, offered by the Institute of Medicine of Chicago, and the Frederick B. Noves Award, offered by the University of Illinois College of Dentistry.

On reflection, the most important part of my three years at the dental school was my relationship with Dr. Isaac Schour. He was the ideal role model and mentor: his values, his ethics, his scholarship, his philosophy were what I tried to emulate. I chose wisely. I would be in the research laboratory during all of my free time, which sometimes meant 24-hour days, 7 days a week. I was a very busy fellow. What I treasured most was Saturday afternoons, when only the two of us were in the laboratory and we would organize and write up our research material and discuss other, more expansive matters. We developed a close relationship. So, after three very busy, 12-month work years I received an M.S. in Histology in June and a D.D.S. in August of 1940.

In looking for definitive training in oral and plastic surgery, I soon recognized that little was available. Mayo Clinic offered a residency in oral and plastic surgery and laryngology; the training was limited to above the clavicles. Gordon New, M.D., D.D.S., was chairman, and Drs. Figi, Havens, and Erich were on the staff. I applied; they did not accept me. In 1940 I received approval for the one-year residency at the Cook County Hospital in Chicago in oral (and plastic) surgery. The attending staff was composed of two M.D., D.D.S. oral and plastic surgeons. W.H.G. Logan (developer of the Logan bow and son-in-law of Truman W. Brophy), who had been chief of the Dental Surgery Department during World War I, appeared infrequently; Joseph Schaeffer came regularly and performed cleft lip and palate, nasal plastic, skin grafting, and some flap surgery. He was inspiring, challenging, and colorful, but somewhat eccentric. Nevertheless, it was a good year. When I finished my residency, Dr. Logan invited me to assist in and teach Biology at what was then Loyola School of Dentistry. In July of 1941, through Isaac Schour's wife, Esther, a social work supervisor at the Jewish Social Service Bureau, I met one of her key supervisees, Rhoda Gerard. The relationship

developed rapidly, and we were officially engaged at Thanksgiving and married at Christmas. That was more than 68 years ago.

In early 1942, I first learned that an American Board of Plastic Surgery had been formed. To become eligible to take the board, two years of general surgery followed by two years of general plastic surgery were necessary. So now, after having been awarded S.B., M.D., M.S., and D.D.S. degrees, and after one year of internship and another year of residency, I came home to my new bride and discussed my need for at least four years of additional training. She immediately responded by saying, "Let's go for it." With this impetus, I began looking for a general surgery residency. I was most fortunate in being accepted by Dr. Marshall Davison, an outstanding and highly regarded Chicago general surgeon and another wonderful role model, as his first assistant at the University Hospital in Chicago. Since the board would accept one year of research in lieu of one year of general surgery, my requirement would be fulfilled with one year of a general surgery residency. Now my quandary was: Where do I obtain the two years of plastic-surgical training? Other than the Mayo Clinic and the Cook County residency, I knew of no other programs than that in maxillofacial surgery at King's County Hospital in Brooklyn, under the supervision of Dr. Walter Coakley. I also wrote to Dr. Varstad Kazanjian in Boston, Dr. John Staige Davis in Baltimore, Dr. Ferris Smith in Grand Rapids, Michigan, and Dr. Vilray P. Blair in St. Louis. Coakley placed me on the waiting list. Kazanjian said that his nephew was with him, Davis had nothing to offer, and I did not hear from either Smith or Blair.

One day my general-surgical chief, Dr. Davison, invited me to a luncheon to be held on January 6, 1943, for Dr. Blair, who was going to be in Chicago. In addition, Drs. Sumner Koch, Michael Mason, and Loyal Davis attended. Who was I in the presence of such a galaxy of stars! Nevertheless, after reviewing my curriculum vitae and meeting me, Dr. Blair asked me to sign an agreement dated December 31, 1942 (Fig. A.1). What a wonderful surprise! The famous Dr. Blair, who had been head of the section of oral and plastic surgery in the United States Army and consultant in maxillofacial surgery with the American Expeditionary Forces during World War I, had accepted me to be his first assistant for two years, and even with salary. I was ecstatic to think that I would be privileged to learn at the feet of the world giants in plastic surgery. I would now

DR. VILRAY P. BLAIR
DR. JAMES BARRETT BROWN
DR. LOUIS T. BYARS
DR. FRANK McDOWELL

400 METROPOLITAN BUILDING
GRAND AVENUE AND OLIVE STREET
ST. LOUIS, MISSOURI

MEMORANDUM OF AGREEMENT CONSUMMATED DECEMBER 31, 1942

I, Dr. Bernard Sarnat, agree to give my full time as an assistant working with Dr. Vilray P. Blair and Dr. Louis T. Byars for the remuneration of $200.00 per month until at least I have completed the two years of the minimum still required before I am eligible to appear before the American Board of Plastic Surgery.

V. P. Blair

V.P. Blair, M.D.
L.T. Byars, M.D.

Fig. A.1

like to share some of my professional and personal experiences with the Vilray P. Blair Group.

There were the three famous B's of music, and there were also the three famous B's of plastic surgery — Blair, Brown, and Byars.

The office of the Vilray P. Blair Group was located in the Metropolitan Building Suite 400 at Grand and Olive Streets in St. Louis. It was large, spacious, and plainly furnished. The waiting room seated 40 persons comfortably. There were several examining rooms and several offices for personnel.

DR. VILRAY P. BLAIR
DR. JAMES BARRET BROWN
DR. LOUIS T. BYARS
DR. FRANK McDOWELL
DR. BERNARD G. SARNAT

400 METROPOLITAN BUILDING GRAND AVENUE AND OLIVE STREET ST. LOUIS, MISSOURI

Fig. A.2 New office stationery, 1943. As a surgeon on the staff, my name was now included on the stationery for the period 1943–1946.

The surgical staff included: Vilray P. Blair; James B. Brown, who was in the military service (Valley Forge Hospital) but returned from time to time; Louis T. (Bill) Byars; Frank McDowell; and now the new addition, Bernard G. Sarnat (Fig. A.2). Two full-time registered nurses completed the professional staff. I soon learned that there were two separate and independent administrative staffs. I was certainly not aware of the schism in the office until I arrived, and I never did learn of the cause. Della O. Cooper was the financial secretary exclusively for Drs. Blair and Byars, and Mr. Hance exclusively for Drs. Brown and McDowell. Miss Fahrni was Dr. Blair's full-time secretary, and Estelle Hillerich was part-time office and part-time American Board of Plastic Surgery secretary. Gertrude Hance (sister of Mr. Hance) was the full-time photographer, artist, tattooist, and prosthetist. A handyman ran errands and performed other services. Office hours usually began at about 2 P.M. (following a morning of surgery) and sometimes lasted until 6 or 7 P.M. During the busy summer we would see as many as 100 patients, who came from far and near. Some had very complex problems (Blair and Byars enjoyed the challenge); others not so complex. Every socioeconomic class and age group was represented. No one was ever turned away.

Dr. Blair, then 72-years old, was performing surgery only 3 days a week. In the afternoon, Miss Fahrni and I would accompany him to see new patients. He would dictate the history and examination and his plan for the surgical procedure the next day. I would bring this information to surgery. Frequently, partway through the operation, I would be lost. Blair, with his nimble, genius mind, had thought of a new and better approach. I was responsible for the postoperative care for all of Dr. Blair's and some of Dr. Byars' patients.

Della O. Cooper managed the office for Dr. Blair until 1950 and was in charge of making appointments. After he had seen a new patient, she set

the surgical fees and arranged for hospital admission, temporary housing, and other matters. In addition, Cooper conducted a rather active business in the delivery of radium needles and radon gold seeds to various outside medical consumers. She signed all of her memos "D.O.C." At one time Dr. Ellis Fischel, a prominent head and neck surgeon and radiation oncologist, had his office with Dr. Blair. Blair apparently inherited his radiation company, which eventually was turned over to Cooper.

When the very busy summer practice slowed down, particularly during the winter, we turned to other medical matters. One day Dr. Blair called in Miss Fahrni and asked her to gather the last 100 records of patients with partial and total nasal reconstructions with pedicle flaps. I assisted over many afternoons in reviewing and organizing this material with Dr. Blair. He submitted the manuscript to Dr. Loyal Davis, then editor of *Surgery, Gynecology, and Obstetrics*. I well remember a telephone call from Dr. Davis asking Dr. Blair for a title other than "Hits, Strikes, and Outs." Dr. Blair was adamant and his title remained intact.[8]

This was without question the finest plastic surgery training program at that time. Yet, even by 1947, there were only nine formal residencies in plastic surgery. Needless to say, the more than 100 present-day plastic surgery residency programs are far superior in both breadth and depth.

VILRAY P. BLAIR (1871–1955)

Several excellent reports give many details about the life of Vilray P. Blair. I shall try to limit my comments to how I remember him principally in the years I was his first assistant, from 1943 through 1946.[2–4] He was a fairly tall (certainly compared with me), rather stooped, formidable-appearing gentleman with a shock of gray hair. Although he was soft-spoken, his voice was commanding. He was a man of the utmost integrity.

At Dr. Blair's request, Dr. Davison permitted me to leave for St. Louis in May of 1943. Rhoda and I were greeted most warmly soon after we arrived for a Sunday afternoon tea at Dr. Blair's home, where we met his wife, Kathryn, and members of the family.

Blair would often telephone me at home at usual, and sometimes unusual, hours for various reasons. Sometimes he would wonder about the postoperative condition of a patient. Other times, at 6 A.M., we would

visit a convent, where he rendered general medical care to the nuns, and from there we would go to Mass, which he attended every morning before surgery. Some trips were to a special horse farm, where Blair would carefully inspect the tails, looking for the optimum horsehair for surgical sutures. From time to time we would travel to the Veterans Administration Hospital at Jefferson Barracks, near St. Louis, to do surgery.

Most of us are predictable in our actions. This was not usually true of Blair, and therein lay his genius.

VILRAY P. BLAIR AND THE AMERICAN BOARD OF PLASTIC SURGERY

The American Association of Oral Surgeons, a forerunner of the American Board of Plastic Surgery, was formed in 1924 by three double-degree (M.D., D.D.S.) men in Chicago, representing the heads of the oral and plastic surgery departments in the three dental schools (Brophy, Chicago College of Dental Surgery; Gilmer, Northwestern University Dental School; and Moorehead, University of Illinois College of Dentistry). For several years, those with a general-surgical background but without a dental degree were not admitted. These included Vilray Blair, John Staige Davis, and Ferris Smith. The rules were subsequently modified, and they were admitted.

Blair, single-handedly, was the predominant driving force that established the board. His concept was that a plastic surgeon should have at least two years of general-surgical experience before going into the specialty. A second concept was to bring the various plastic surgery subspecialties under one umbrella (oral surgery, otolaryngology, ophthalmology, head and neck surgery, hand surgery, genitourinary surgery, esthetic surgery, etc.).

Blair traveled the country in the 1930's and would hold dinner meetings assessing the status of plastic surgery in the United States and who might be grandfathered in, in the formation of the board. Grandfathered in Los Angeles were Otto Bames, William Kiskadden, and Emil Tholen. Not accepted were Balsinger, Felsen, Gaynor, McGee, Smith (he sued the board), and Updegraff. In Chicago, Koch, Logan, Mason, Merrifield, Moorehead, and Louis Schultz, Sr., were grandfathered in. Not included were Salinger, Schaeffer, Schultz, Jr., and Thorek.

When it came time to elect the first officers of the newly formed American Board of Plastic Surgery, Blair was the unanimous choice as president. However, he demurred, saying that he would be more effective as secretary. He championed John Staige Davis as president.

JAMES B. BROWN (1899–1971)

Dr. James B. Brown joined Dr. Blair in practice in 1925. Brown had been in the military service during most of the period 1943–1946, first in the European Theater and then at the Valley Forge Hospital in Pennsylvania. He would return periodically, more often by 1946. Although we met on several occasions, I knew him least well of those in the group. Listed as famous surgeons who trained under Brown were Cannon, Murray, Randall, Peacock, Millard, Jurkiewicz, and Hartrampf.[4] Brown died as a result of hypertension and a stroke.

LOUIS T. (BILL) BYARS (1906–1969)

Dr. Louis T. (Bill) Byars joined the Blair group in 1935, and I spent much close time with him. He was a quiet, somewhat shy, undemonstrative, unusually fine, modest, extremely capable, and gentle but firm man. Bill Byars was undoubtedly one of the most able master surgeons I have ever known. From 1943 through 1946, he carried the workload of the group, operating six days a week. His varied surgical capabilities were most remarkable, and never did I observe a surgical failure. Although he had received national recognition, I doubt that Dr. Byars was ever as fully appreciated as he deserved.

We produced several publications together,[9–12] and he wrote the foreword to a book that I coauthored.[13] Periodically, Dr. Byars invited Rhoda and me for Saturday night dinner. I treasured those evenings. With a Scotch and soda in hand, we would sit around a crackling fire and leisurely review the past week's doings at the office and hospital and the state of the specialty of plastic surgery in general. Bill married "Bam" in 1936. She was a wonderful, gracious hostess who made us feel at ease and was the sister of Dr. Brown's first wife. Their daughter, Caroline, a pretty child, was born in 1939. It was Bill (with an assist from Brad Cannon) who encouraged

Robin Anderson and Milt Edgerton to organize the Plastic Surgery Research Council, of which I was a founding member in 1955 and chairperson in 1957. When I developed a Dukes' C carcinoma of the bowel in 1961, it was Bill who gave me much-needed counseling. Tragically, he died of carcinoma of the prostate.

FRANK MCDOWELL (1911–1981)

Dr. Frank McDowell joined the group in 1939. A true scholar, Frank was somewhat withdrawn. From 1943 through 1946, he carried on the surgical practice of Dr. Brown and did considerable writing with him. Although we had a cordial relationship, I did not work as closely with Frank as I did with Drs. Blair and Byars. I did scrub in with him at times if he had an interesting or difficult surgical problem. One time, while he was scrubbing, a child being given anesthesia by a nurse anesthetist (they administered all our anesthesia) suddenly died. Frank broke his scrub, ran into the operating room, and practically went berserk. He subsequently moved to Hawaii to practice; later, under his editorship, *Plastic and Reconstructive Surgery* became an outstanding and significant journal. Sadly, he died of a carcinoma of the bowel.

BERNARD G. SARNAT (1912–)

The three years from 1943 through 1946 were busy and filled with learning. As a full-time assistant to both Drs. Blair and Byars and a member of the private practice office staff, I received appointments to both the faculty of the Department of Surgery at Washington University School of Medicine and Barnes Hospital. There was little free time for study (the journal *Plastic and Reconstructive Surgery* was born in 1946), contemplation, and a social life. I would come home tired after a long and often strenuous day.

I began organizing my 25 case reports for the American Board of Plastic Surgery during June and July of 1945. At that time, my wife was six months pregnant. We would go to the record room at Barnes Hospital on Sunday mornings, and she would help me transcribe the necessary records of patients with all manner of deformities. We wondered (although we

never shared our thoughts), will our child be born with a deformity? We were most fortunate in having a healthy, vigorous boy, who went on to Harvard College (and was a guest at Thanksgiving dinners, with thanks to Brad and Ellen Cannon and family) and Stanford Medical School.

In addition to my responsibilities as assistant to both Dr. Blair and Dr. Byars, I was appointed as plastic surgeon-in-charge at Homer Phillips and St. Louis City Charity Hospitals. Dr. H.B.G. Robinson, professor and head of Oral Pathology at Washington University School of Dentistry, and I became good friends, and he invited me to give several lectures. Dr. Barnet Levy succeeded him, and we became very close colleagues and personal friends.

In 1945 Dr. LeRoy Main, a dental radiologist and dean of St. Louis University Dental School, invited me to become a full professor and head of the Department of Oral and Plastic Surgery. I was indeed highly flattered and, of course, very pleased. I stated that I was definitely interested but with several provisos: (1) I would need Dr. Blair's permission to take on this added responsibility, (2) I would probably require approval from Washington University to be on an additional university faculty, and (3) I eventually planned to return to Chicago. Dr. Blair and Chancellor Compton gave immediate approval, and Dr. Main was not concerned about my probable return to Chicago. So I added further challenges to an already very full program.

As I was completing my two-year training program, I informed Dr. Blair about my plans to leave. He prevailed upon me to remain for another year. By this time I had developed enough of a private practice that I was earning income for the firm far beyond my salary. As time approached to depart, I mentioned that I might be interested in moving to Los Angeles. Dr. Blair communicated this to Dr. Kiskadden, a great devotee of his in Los Angeles. He was quite discouraging, saying that there were too many plastic surgeons already in Los Angeles. Consequently, the three Sarnats moved back to Chicago in 1946. I would return to St. Louis for a few days each month to honor my commitment to St. Louis University School of Dentistry. Later, in 1946, I was offered (not unexpectedly) and accepted the professorship and head of the then Department of Oral and Plastic Surgery at the University of Illinois College of Dentistry in Chicago. This position had been previously held by Dr. Frederick B. Moorehead, one of the three founding members of the American Association of Oral Surgeons — the future American Association of Plastic Surgeons. I became a diplomat

of the American Board of Plastic Surgery in 1947. I also joined Paul Greeley in the Division of Plastic Surgery of the College of Medicine at the University of Illinois.

In 1949, Blair invited me to St. Louis when he received an honorary degree from Washington University. In 1955, the very week that Vilray P. Blair died, the now-four Sarnats moved permanently from Chicago to Los Angeles (Fig. A.3). Thus, I relinquished a full professorship, head of

November 25, 1955

The Family of Dr. Vilray Papin Blair
25 Lenox
St. Louis 8, Missouri

To live a full and useful life is one of man's most cherished desires. To make major contributions to the welfare of mankind is reserved only for the elect. Thus, it was the destiny of Vilray Papin Blair, with courage, integrity and devotion, to lead the way in the development of present day plastic surgery.

It has been an inspiration and a blessing to have had the privilege to know and to work with him. There was a contagion, enthusiasm and imaginativeness about his work which inspired others, particularly younger men, to try to follow in his footsteps. Those who learned from him are forever linked by a common bond of indebtedness.

Although the absence of Vilray Papin Blair will leave a void in our lives, his thoughts, deeds and writing have influenced permanently all mankind for the better.

To you, his family, we send our deepest regrets and sympathies.

Sincerely yours,

Dr. and Mrs. Bernard G. Sarnat

Fig. A.3

department, tenure, pension, very active graduate program, and 10-year private practice of plastic surgery to start anew in Los Angeles. It is with gratitude that I am listed (the last) as a famous surgeon who trained under Vilray P. Blair, along with Webster, Padgett, Brown, Byars. McDowell, Hamm, and Fryer.[4]

BARNES HOSPITAL

Practically all surgical procedures were performed at Barnes Hospital, although from time to time we worked at the Jewish Hospital. At Barnes there were two adjoining surgical suites. Blair and Byars used the larger one, which housed two operating tables. The other suite, with one operating table, was used by McDowell and Brown. In the major suite, all walls and the ceiling had been decorated with paintings from nursery rhymes — Jack Horner, Little Miss Muffett, Jack and the Beanstalk, Tommy Tucker, etc. With this as an addition, I often wondered what emotions our patients experienced under the influences of the preoperative medication and their fears. Visiting surgeons were always intrigued. The surgical nurse, Miss McDavitt, would scrub up at about 8 A.M. and gather all of the sterile surgical equipment and dressings for the day on her central table. She would stay scrubbed and sterile all day (I never did see her go to the bathroom) and would supply the two surgeons with the necessary surgical materials. Thus there was less delay between surgical procedures.

Blair would use gauze as a mask and wear his old tennis shoes. During the scrub period, I found it particularly enjoyable because he would love to either hum or share his reminiscences with me. These were treasured times. In the early 1900's he would take the night train to Chicago to observe, the next day, Brophy and his work on cleft-lip-and-palate patients. After several years Blair was disappointed with his clinical surgical results, and by 1917 he had discarded Brophy's technique. The method required passing wires to hold the compressed maxillae together, resulting in severe deformities of the maxillae and developing teeth. This led to an excellent, detailed study by Logan and Kronfeld.[15] In searching for other methods, Blair ended with using the modified Mirault and von Langenbeck procedures. He said that he

deliberately did not publish his results until after Brophy had died in the 1920's. Blair also talked about his acquaintance with Edward Angle, the world-famous orthodontist, then practicing in St. Louis, in the early 1900's. Apparently Angle had a patient with a prognathic mandible, and he prevailed upon Blair to operate by extracting the bicuspids and the corresponding sections of the mandible. Blair said that the surgical result was a disaster, and after that episode he switched to the transramal cut. He would talk about his high esteem and his fondness for Robert Ivy, who worked closely with him in the U.S. Army during World War I. Blair invited Ivy to join him in his practice in St. Louis after the war. Ivy declined and returned to Philadelphia; however, they did coauthor a book, *The Essentials of Oral Surgery*, which was published in several editions.

The surgical schedule began at 8:30 A.M. and continued until about 2 P.M., when we would leave for the office. On Saturdays we would not go to the office, and we operated until as late as 5 P.M., especially in the summer. As I became more experienced, I was given the responsibility for the second surgical table on days that Dr. Blair did not operate, and particularly on Saturdays, when we (all three tables) would operate on as many as 25 patients. Thus, in a single day one could see the complete gamut of plastic and reconstructive surgery: toe-to-thumb transplant, hypospadias repair, forehead flap to reconstruct the nose, neck dissection, cleft lip, skin grafting of burns, rhinoplasty, facelift, etc.

Blair had told me that in the early 1900's he even did some neurosurgery. While I was there, a surgical resident's wife gave birth to a child with an exstrophy of the urinary bladder. We transplanted the ureters to the large bowel and eventually closed the defect.

Blair and Byars were most generous in sharing their knowledge, which was not true of many other plastic surgeons of that time. Any ethical surgeon was always welcome to observe. Visitors came from throughout the United States and from abroad. Earlier, after a visit with Blair's group, Jerome Webster returned to Columbia University to establish his formal residency program. Ken Pickrell, after three months of observation, initiated his residency program at Duke. Bill Longmire was on the same track but eventually chose to stay in general surgery and became chairman of

the Department of Surgery at the University of California, Los Angeles. Ralph Millard also spent some time with us. Just before, during, and just after my three-year stay, the following spent variable amounts of time in our plastic surgery service at Barnes Hospital: Robin Anderson, McCarthv De Mere, Sanford Dietrich, Milton Edgerton, Merton Hatch, Gordon Letterman, Allyn McDowell, Frank Meany, Peter Randall, and Robert Robinson.

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Becoming a Plastic Surgeon — Today (JPB)

Just as the field of plastic and reconstructive surgery has matured and changed during the last 50 years, so has the training of plastic surgeons. Dr. Sarnat's training in the 1940's was highlighted by his mentorships (with Blair, Brown, Byars, and others) and by his experiential learning. My training in the 1990's was organized by didactic lectures and specialized rotations within craniofacial, microsurgical, esthetic, hand, burns, and other subspecialties of plastic surgery.

In the 1940's Dr. Sarnat was motivated to optimize his training in medicine, dentistry and, ultimately, plastic surgery by piecing together the best available at the time. Fifty years later, I had the luxury of choosing to apply to over 89 plastic surgery residency programs committed to training young plastic surgeons. These programs all had to meet requirements for accreditation by the Accreditation Council for Graduate Medical Education. The number of plastic surgery residents and fellows increased from 9 in 1947 to 638 in 1997.

When Dr. Sarnat trained, there was no *Plastic and Reconstructive Surgery* journal and there were only a few textbooks available. During training in the 1990's, an in-depth, eight-volume textbook, *Plastic Surgery*, was referred to. The first two editions were edited by Converse and the most recent one was edited by McCarthy.[1] A more concise textbook, *Grabb and Smith's Plastic Surgery*, provided current therapy and accepted techniques for the clinical plastic surgeon.[2] Each subspecialty within plastic surgery had its own important texts, including Millard's *Cleft Craft* for

cleft-lip-and-palate surgery, Rees' *Aesthetic Plastic Surgery* for cosmetic surgery, Shaw and Hidalgo's *Microsurgery*, Stark's *Head and Neck*, and Bostwick's *Breast Reconstruction*, to name a few.[3–7] The main journal of the plastic surgery field was still *Plastic and Reconstructive Surgery*. However, this generalized publication could be supplemented by journals that appeal to almost every niche of plastic surgery: *Microsurgery*, *Journal of Craniofacial Surgery*, *Cleft Palate Craniofacial Journal*, *Journal of Reconstructive Microsurgery*, *Journal of Hand Surgery*, *Journal of Burn Care and Rehabilitation*, etc. There were also broad clinical journals, such as *Clinics in Plastic Surgery*, *Annals of Plastic Surgery*, *Seminars in Plastic Surgery*, *Aesthetic Surgery Journal*, and *Facial Plastic Surgery.* Finally, national and international meetings, as well as symposiums, were available throughout the year.

The top programs in the country in the 1990's built their reputations on their plastic surgery attending staff, their institution, and their commitment to research and education. As expected, the top programs in the country had the top surgical staff. These present-day plastic surgery greats had trained under Dr. Sarnat's peers. I was fortunate enough to be accepted into the Institute of Reconstructive Plastic Surgery at New York University by Joseph G. McCarthy, M.D. Dr. McCarthy, The Lawrence D. Bell Professor, had continued, and improved on, the long history of educational excellence begun by John Marquis Converse, M.D., in 1955.

My background leading up to my years at NYU was similar to that of most other plastic surgeons in the 1960's, '70's, '80's, and '90's. I did full general surgery training and subsequently became board-certified by the American Board of Surgery. (Currently over half of the training positions have faster tracks that allow for acceptance out of medical school and finishing in 5–6 years.) I studied Anthropology and Art at the University of Notre Dame and completed medical school at Thomas Jefferson Medical College in Philadelphia (my hometown). In the middle of my general surgery training at Pennsylvania Hospital I devoted 2 years to basic science laboratory work. It was during this time that I met and was influenced by Michael T. Longaker, M.D. He taught me the discipline of research, including the initiation of a project, the implementation of the research design, data analysis, research presentation and writing. From this experience, I feel that dedicated research time in a structured setting

is necessary during training or early in a career to maximize academic potential.

The Institute of Reconstructive Plastic Surgery was the perfect institutional setting at the time for my plastic surgery training. At Tisch Hospital residents could learn to emulate Cort Cutting's cleft-lip-and-palate care, Charlie Thorne's microtia repair, Glenn Jelk's eyelid and orbital reconstruction, Barry Zide's complex facial arteriovenous malformation reconstruction, John Seibert and Christina Ahn's innovative microsurgical techniques, or Dr. McCarthy's work. Bellevue Hospital, the county facility, was a unique "gold mine" for plastic and hand surgery cases. Weekly Halstead-like clinical rounds with the NYU attendings provided valuable learning for the residents and a great check on independent decision-making.

Dedicated rotations in hand surgery and cosmetic surgery were essential for completing the circle of plastic surgery training. Robert Beasley, M.D., was not only an excellent hand surgeon and memorable teacher of meticulous technique but also, for me, a true role model. I will always remember conversations and dinners with him and his wife, Genoveive, at exceptional New York City French restaurants. At Manhattan, Eye, Ear and Throat (The Hospital MEETH), our dedicated cosmetic surgery rotation was the best preparation for this important part of my practice. The straightforward, anatomic approach of Dan Baker was inspirational. Sherrel Aston, the figurehead and leader of this cosmetic experience, provided a lesson in running a successful practice.

My one-year fellowship in craniofacial surgery with Dr. Kawamoto was the part of my training that was most like Dr. Sarnat's mentorship learning. During this final year of training at UCLA, I was able to distill the principles that I had learned in nine years of surgical training. I learned how a master surgeon evaluates new patients, plans preoperatively and, in the operating room, definitively completes all steps without wasting movements. I was able to transport this knowledge to my first attending position at the Children's Hospital of Pittsburgh as the Director of the Craniofacial Fellowship. There I furthered my research in craniosynostosis under the tutelage of Mark Mooney, Ph.D., and my research in bone tissue engineering under the guidance of Jeffrey Hollinger, Ph.D.

Returning to UCLA as an attending and Chief of Pediatric Plastic Surgery has allowed me to continue to learn under Dr. Kawamoto. As the

Chair of Bernard G. Sarnat Craniofacial Research, I am fortunate to continue my basic science research interests in bone biology. An added benefit has been working with Dr. Sarnat. His academic energy, continued scholarly writings, and desire to further plastic surgery research is, to my knowledge, unparalleled. The Plastic Surgery Research Council, of which Dr. Sarnat is a founding member, is certainly a jewel in the plastic surgery crown. Although this research jewel of our society is sometimes not recognized, or hidden, Dr. Sarnat and I are dedicated to furthering this important society and unifying the writings of its members.

The plastic surgery programs of today have been built on the shoulders of the great surgeons of the past and their styles of teaching. These teachers were peers of Dr. Sarnat. The mentorship style of training still has its place in plastic surgery training but is typically reserved for, and is most effective in, the postgraduate years.

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