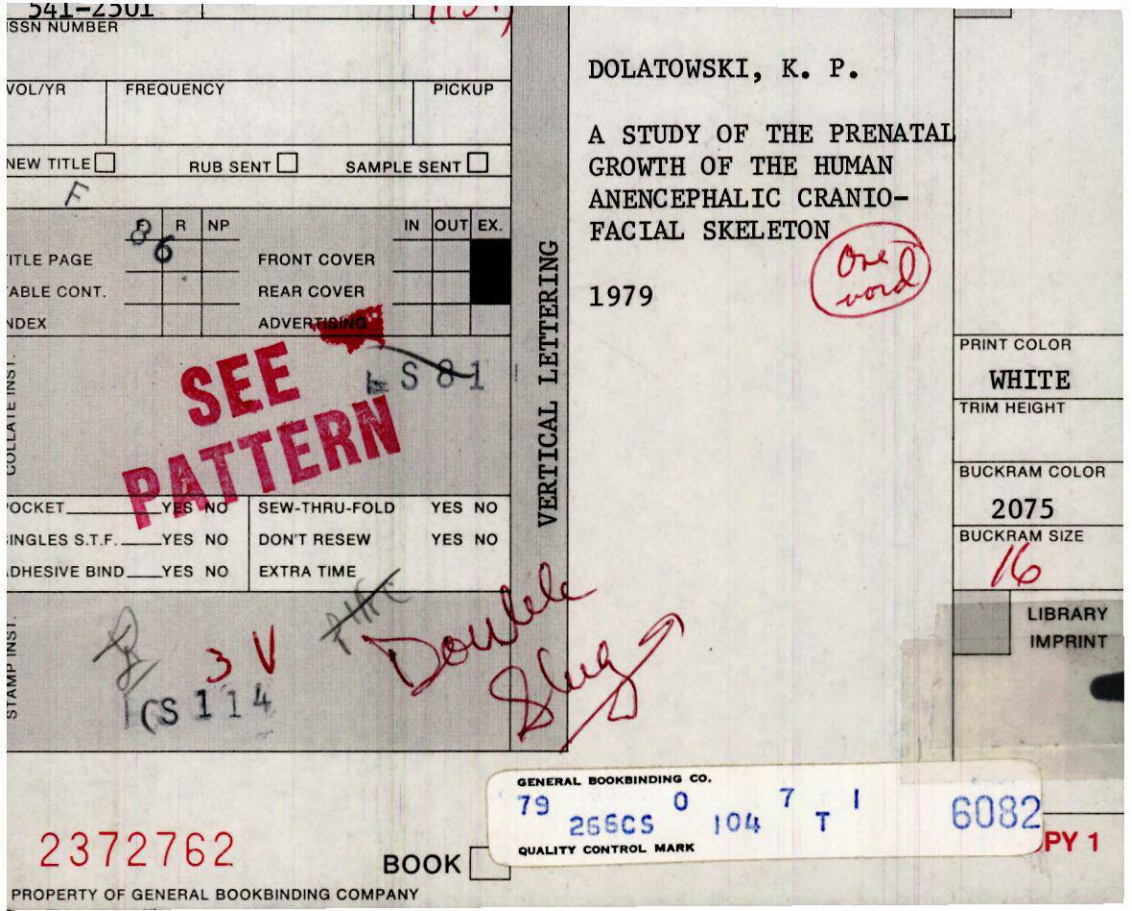

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A STUDY OF THE PRENATAL GROWTH OF THE HUMAN ANENCEPHALIC CRANIOFACIAL SKELETON

by

KENNETH PAUL DOLATOWSKI

Submitted in partial fulfillment of the requirements

for the Degree of Master of Science

Department of Orthodontics

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CASE WESTERN RESERVE UNIVERSITY

May 1979

CASE WESTERN RESERVE UNIVERSITY

GRADUATE STUDIES

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Date MAY 25, 1979

A STUDY OF THE PRENATAL GROWTH OF THE HUMAN ANENCEPHALIC CRANIOFACIAL SKELETON

Abstract

by

KENNETH PAUL DOLATOWSKI

The main objectives of this study were to investigate the remodeling patterns of the human anencephalic fetal craniofacial skeleton and to compare these patterns with those characterizing the normal prenatal and postnatal skulls. Serial sections of two anencephalic skulls of six and seven months menstrual age were analyzed for resorptive and depository surfaces. The remodeling patterns were then mapped for the entire face, calvaria, and cranial base. The anencephalic patterns were compared with normal prenatal and postnatal remodeling patterns and the similarities and differences were evaluated.

It was determined that the remodeling patterns of the anencephalic fetal skull were much the same as in the normal prenatal skull with certain areas resembling the postnatal patterns. The notable exceptions were:

1. the endocranial surface of the basioccipital part of the occipital bone, which was depository;
2. the squamous portion of the temporal bone, which displayed resorption ectocranially and deposition endocranially;

3. the medial half of the posterior wall of the orbit, which resembled the early normal prenatal pattern with resorption orbitally and deposition on the dural side;

4. the pterygoid plates, which were entirely depository;

5. the forward facing anterior margin of the buccal surface of the coronoid process, which was depository; and

6. lack of formation of the posterior margin of the foramen magnum.

There was observed an anterior and lateral constriction to the anencephalic anterior, middle, and posterior cranial fossae, increasing in severity in the order listed. The bones of the calvaria were lacking or rudimentary in size. Some of the facial bones were severely affected in morphology, size, and spatial relationships. The zygomatic bone had a superior and posterior inclination. The squamae of the frontal bone were collapsed horizontally and diverged posteriorly and laterally. This study implicates a relationship between soft tissue development and the process of remodeling and craniofacial form, with bone remodeling and craniofacial form appearing to represent a response to soft tissue development. Bone-soft tissue relationships were seen in the movement of foramina and their nerves in directions that maintain constant positional relationships. Lack of or minimum development of the neural mass resulted in minimum anterior and lateral displacement of the anterior and middle cranial fossae. The anteriorly constricted anterior cranial fossae resulted in a retruded position of the nasomaxillary complex. In the medial half of the posterior wall of the orbit, the abnormal posterior direction of growth appears to be in direct response to the rapid growth

of the bulbus oculi into a region either lacking or having a minimal extent of frontal lobe development in the anencephalic fetus.

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DEDICATED

TO

My wife, Gail, for her love,
patience, and support.

and

My mother and father, for their
love, guidance, and generosity.

and

To all my family, for their
encouragement and understanding.

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INTRODUCTION

This study deals with the remodeling changes that take place during the growth of the bones of the face and cranium of the human anencephalic fetus. Once ossification has begun and the developing bones have attained their basic form, any further increase in size is accomplished by the remodeling process involving new bone deposition on certain surfaces along with simultaneous resorption from other surfaces. Remodeling functions to constantly maintain the shape and proportions of a bone as it enlarges and to proportionately relocate the various parts of the bone as the whole bone enlarges.

The remodeling patterns occurring in the human skull from fetus to the adult have been described by Mauser et al. (1975) and Enlow (1968, 1975). The present study deals with the prenatal growth and remodeling process as determined from histologic analysis of two human anencephalic fetuses aged six and seven months menstrual age.

The major objectives were:

1. To describe the pattern and locations of the anencephalic prenatal skull remodeling fields;
2. To correlate the differences and similarities of the anencephalic prenatal remodeling process with that of normal pre- and postnatal skulls;
3. To relate the anencephalic prenatal growth process with the differential growth rates of the soft tissues of the skull.

The heads of two formalin fixed human anencephalic fetuses were completely serially sectioned. Each right half was sectioned in the sagittal plane and each left half was sectioned in the coronal plane. The relationships of the bones and the patterns of distribution of the various bone surface depository and resorptive fields were then determined histologically, mapped, and compared with normal prenatal and postnatal patterns.

REVIEW OF THE LITERATURE

Anencephaly is one of the most common of the lethal human congenital anomalies. The incidence of anencephaly in man has been estimated at one to five per thousand births among Caucasian groups (Green, 1964), and less than 0.5 per thousand in Oriental and Black races (Nakano, 1973). It occurs about four times more frequently in females (Lawrence and Weeks, 1971). The relatively high prevalence of this malformation has prompted many studies dealing with its embryology, epidemiology, etiology, and morphology. The causation is presently unknown, but its early effect is either an improper closure of the anterior neural tube (von Recklinghausen, 1886) or an opening of a previously closed neural tube (Morgagni, 1769). Anterior neural tube closure normally occurs about day 26 of gestation. An explanation advanced by Recklinghausen and supported by Feller and Steinberg (1929) and Dodds and DeAngelis (1937) suggests that failure of neural tube closure results in a severely deformed forebrain and an absence or reduction of the midbrain, medulla, cerebellum, and cervical spinal regions. The cerebrum is largely replaced by an irregular mass of hemorrhagic fibroglial tissue. Numerous explanations have been advanced to account for a possible mechanism by which the neural tube fails to close or becomes opened. These are listed in Table I.

TABLE I

THEORIES OF NEURAL TUBE CLOSURE FAILURE

OR REOPENING AFTER CLOSURE

Theory	Investigator--Year
1) Excessive cerebrospinal fluid pressure	Morgagni 1769
2) Cellular rests of the primitive knot leading to notochordal abnormalities	Feller, Sternberg 1929
3) Biochemical alteration of the mesodermal tissue	Mandrazzato 1932
4) Incomplete induction of the mesodermal tissue and an abnormal equilibrium of cerebrospinal fluid	Stroer, Van der Zwen 1939
5) Anomalous notochord	Saunders 1943
6) Cerebral vascular anomalies	Vogel, McClenahan 1952
7) Localized overgrowth of the neural tissue	Pattern 1953
8) Folic acid deficiency	Warkany, Beaudrey, Hornstein 1959
9) Effect of maternal cancer chemotherapeutic agents on fetus	Sokal, Lessmann 1960
10) Hypervitaminosis A and somite necrosis	Padilla, Fern 1965
11) Genetic	Nance 1969
12) Endocrine dysfunction	Janerich 1974
13) Residual trophoblastic material from previous pregnancy, miscarriage	Clarke 1975
14) Adherent amniotic fluid cells	Freed 1977

Only limited research has been directed to date toward the histological and histogenetic aspects of the anencephalic craniofacial skeleton. Keen (1962) dissected six anencephalic fetuses ranging from seven months gestation to full term and described the morphology of the frontal, temporal, and occipital bones. He related all morphological characteristics of the anencephalic skull to the destruction of the brain, after which any further stimulus for ossification in the cranial vault presumably becomes affected. The ossification of squamous portions of these various bones appears to have become arrested at the stage to which development had progressed at the time the neural lesion occurred. Keen believed the etiology of the disorder lies in a disturbance of the cerebrospinal fluid circulating mechanism occurring within the closed neural tube system leading to abnormal fluid pressure of an internal hydrocephalic type. Increased pressure presumably results in dilated ventricular sinuses, brain tissue destruction, and dorsal meningeal splitting. Depending on the timing of lesion appearance, the frontal bone terminates as a sharp edge forming the anterior margin of a cranial vault that is incomplete to a greater or lesser extent. The supraorbital rims have a markedly backward and laterally directed obliquity. This alignment of the orbits is the result of absence of frontal lobe development. The medial part of each orbit grows forward together with the enlarging nasal cavities. The cribriform plates are well developed in response to the normal growth of the olfactory bulbs and nerves. The lateral

expansion of the temporal bones is largely unaffected, in conjunction with the apparently normal development of the middle and inner ear components and formation of the mandibular fossae for the condylar heads of the mandible. The abnormal brain does not seem to interfere with the development of the otic vesicles and mandible. The squamous portion of each temporal bone may grow to its full extent, and it forms the side margins of the large fontanelle in the cranial vault. There are two basic morphological forms that the occipital bone may take in anencephaly. If the lesion occurs earlier, a foramen magnum is not present because the brain development is interrupted before the lower piece of the occipital squamae become united. If the lesion occurs later, the occipital squamae fuse dorsally and the upper edge of the occipital bone forms a thick, rounded margin and the posterior and lateral aspects of the vault fontanelle have sharp edges. After interruption of brain growth occurs, the base of the skull continues to expand laterally to accomodate the more or less normally developing organ of hearing and to provide mandibular fossae for articulation of a mandible of normal dimensions; the skull base expands in a forward direction in conjunction with the development of the nasomaxillary complex.

Dekabrun (1963) reported a histological study of a 24 day gestation anencephalic embryo (14 somites). Model construction of the embryo and a projection reconstruction of the nervous system from serial bromide photographs permitted an orderly assessment of histological features at specific levels of the neuraxis. Two

normal human embryos of 14 and 10 somites were similarly investigated. The number of neural folds were counted on transverse sections, and the surface area of the neural tissue was measured at corresponding levels in the three specimens. It was found that both anencephalic and normal embryos had similar numbers of neural elements and surface areas. The study lends credence to the hypothesis that the primary defect in anencephaly is non-closure of the neural tube due to a primary disturbance of the neural epithelium itself. The study also led to the conclusion that the normal development of the eyes in anencephalic fetuses relates to the closure of the anterior neurpore which proceeds from both ventral and dorsal regions. The closure of the rostral ventral portion of the neural fold allows normal eye differentiation despite non-closure of neural folds dorsally.

Marin-Padilla (1965) conducted a detailed morphological study of twelve human anencephalic fetuses of 7 to 8 months gestational age. The anomalies in the cranial base of the skull were considered to be the primary skeletal defect in these malformations, with the malformed sphenoid bone as the center of the various other defects. The principal anomalous features of the sphenoid bone consist of rudimentary lesser wings, stunted and contracted greater wings, long pterygoid processes deviated anteriorly and obliquely, a prominent and ossified rostrum, and marked reduction of the transverse diameter of the whole bone. The base of the skull was quite short, narrow, and in a kyphotic position in relation to the vertebral column. The petrous portions of the

temporal bones were stunted. The ossicles within the otic chambers, however, appeared normal. Alterations in the size, form, and duration of the neural functional matrix were suggested as the cause of changes in the cranial floor. The bones of the face showed only anomalous positions involving a slight rotation and a reduction in the transverse diameter. These facial defects were a secondary result of articulation with the much more severely abnormal sphenoid and temporal bones of the skull base. The bones of the calvaria--the frontals, the parietals, and the squamae of the temporals and the occipitals--were all present but represented only by deformed bony rudiments.

Fields, Metzner, Garol, and Kokich (1978) reported on the morphological analysis of twelve anencephalic fetuses of 26 to 40 weeks gestation age. The fetuses were classified and grouped as meroacrania, a cranial defect not involving the foramen magnum; holoacrania, a cranial defect involving the foramen magnum; and holoacrania with rachischisis, a cranial defect involving the foramen magnum and extending into the vertebral column. Their analysis of the cranial floor suggested that alterations located within the body of the sphenoid bones led to a reduced cranial floor angle with a more vertical clivus. The anteroposterior position of the lesser wings and the reduced lateral extension of the lesser and greater wings of the sphenoid constricted the anterior and middle cranial fossae, respectively. The lateral end of the petrous portion of the temporal bone was located in a more anterior position. The forward, inward, and downward rotation of

the petrous portion of the temporal bone explains the more anterior position of the glenoid fossa and the mandibular condyle. The greatest effect on the calvaria and, in specimens showing more severe defects, the sizable calvarial fontanelle was characterized by a complete exposure of the basicranium. The skeletal components of the squamous part of the cranium were markedly reduced in size. The squamous bones were oriented in a horizontal plane from anterosuperior to posteroinferior at the level of the cranial floor. The most dramatic change was the location of the interparietal portion of the occipital bone in specimens having holoacrania. The interparietal portions of the occipital bone were relocated anteriorly to approximate the frontal bone. The occipital components were rotated anterolaterally and inferiorly. The squamae of the frontal bones were collapsed horizontally and reduced in size to lie peripheral to the anterior cranial fossa forming most of the orbital roofs. Sutures were found to be narrow and smooth instead of wide and somewhat serrated. In contrast to previous reports, the morphology, size, and spatial relationships of nearly all facial bones and their fibrous articulations were described as having been morphogenetically altered to a significant extent. A primary defect in neurocranial development was believed to have resulted in adaptive secondary alterations of size and position in the contiguous skeletal components of the craniofacial complex, but anomalous shapes of the facial bones occurred that are adaptive as well. The relationship between the location of the sphenoid bones and the palatal plane influenced the size and shape of the vomer which is

angulated superiorly to make articulation with the body of the sphenoid. An increased posterior height of the vomer existed, but the vomer-maxillary articulation was normal. The zygomatic bone was severely affected in all three groups of anencephalics. The posterosuperior angulation of its frontal process and the relative position of the frontozygomatic suture suggests an adaption to the severely affected frontal bone. The zygomaticomaxillary suture was in an approximately normal position and relationship.

Normal Fetal Development

Prior to the histological study presented by Mauser, et al. (1975), studies on normal fetal skull growth were concerned primarily with the embryogenesis of the skull as a whole and the timing of appearance of ossification centers of the craniofacial bones (Tables II, III and IV).

The first systematic histological study of the prenatal growth of the human face and cranium was presented by Mauser, et al. (1975). A detailed description of the prenatal remodeling patterns of all the human fetal cranial and facial bones was presented through study of serial sections of a sample of fetal heads from 8½ weeks to 39 weeks fertilization age. Results of the study showed that most bones of the fetal skull begin to remodel at the time each individual bone reaches that stage of morphological development when its configuration approximates that of the adult, usually around 14 weeks. It was determined that the remodeling patterns of the fetal skull are similar to those characterizing the postnatal skull, but with three notable exceptions, involving

TABLE II

BONES OF INTRAMEMBRANOUS OSSIFICATION

Bones	Number of Centers	Time of Appearance (Postmenstrual)*	Investigator
Maxilla	1	6	Woo (1949)
Palatine	1	7	Woo (1949)
Premaxilla	1	7½	Chase (1942)
Frontal	1	8	Inman (1937)
Nasal	1	8	Mall (1906)
Parietal	1	8	Mall (1906)
Vomer	2	8	Fawcett (1911)
Zygoma	1	8	Mall (1906)
Lacrimal	1	12	Gray (1901)

*weeks

TABLE III

BONES OF ENDOCHONDRAL OSSIFICATION

Bone	Number of Centers	Time of Appearance (Postmenstrual)	Investigator
Ethmoid	3	Superior concha-18 weeks	Augier (1931)
		Middle concha-16 weeks	Augier (1931)
		Central center-Birth	Vidic (1971)
Inferior concha	1	18 weeks	Vidic (1901)

TABLE IV

COMPOSITE BONES OSSIFYING BOTH INTRAMEMBRANOUSLY AND ENDOCHONDRALLY

Bone	Number of Centers	Time of Appearance (Postmenstrual)	Investigator
Temporal:			
Membranous	squama	8 weeks	Mall (1906)
	tympanic ring	9 weeks	Mall (1906)
Endochondral	petromastoid 4	22 weeks	Mall (1906)
	styloid 2	Birth	Bast, Anson (1949)
Occipital:			
Membranous	interpatietal	8 weeks	Gray (1901)
Endochondral	planum nuchale	7 weeks	Harrison (1972)
	basioccipital	6 weeks	Harrison (1972)
	lateral part	8 weeks	Harrison (1972)
Sphenoid:			
Membranous	pterygoid plate	8 weeks	Keith (1948)
	great wing	8 weeks	Keith (1948)
Endochondral	presphenoid 2	9 weeks	Keith (1948)
	lesser wing 1	12 weeks	Keith (1948)
	basisphenoid 2	12 weeks	Keith (1948)
Mandible	2	6 weeks	Gray (1901)

the anterior surface of the zygoma, and the roof of the orbit. The zygoma and orbital roof undergo a state of transition from the fetal to the adult remodeling pattern during the third trimester of fetal development. The anterior surface of the premaxilla undergoes transition from the fetal pattern during the first and second postnatal years. The zygomatic bone in fetal life has mostly depository periosteal remodeling fields except for the infraorbital margin where the zygoma overlaps the maxilla. Postnatally the zygoma is surface resorptive on both anterior and orbital surfaces. The roof of the orbit is resorptive on the infraorbital side and depository on the dural side in early fetal life, but during the late fetal period a reversal occurs in which the characteristic postnatal pattern of deposition on the infraorbital side and resorption on the dural side becomes established. The labial surface of the premaxilla is depository throughout fetal life but becomes resorptive in the postnatal skull after about the first year.

Studies on Craniofacial Growth and Development

A study of abnormal anencephalic growth provides a natural experimental model to help better understand both normal and abnormal growth and development of the face and cranium. The pacemaking effects of the lack or of poor development of certain soft tissue masses of the head on the development of the craniofacial skeleton can be evaluated. The theories attempting to account for mechanisms of craniofacial growth and development and its control can also be evaluated.

Brash (1934) analyzed skull growth based on madder fed pigs. He concluded that the enlargement of the cranium can be explained by ectocranial accretion and endocranial resorption without need for any separating growth at sutural junctions. Sutural growth is presumably required only to maintain the relative position of the suture and to sustain articulations during increase in cranial size. Cranial base growth is produced by a process of cartilage replacement which results in the growth of its component bones at their ends, similar to skeletal long bone growth. Brash did not consider the relationship of cranial base growth to that of the vault or the influence of brain growth on cranial form.

Weidenreich (1941) considered the brain as the sole determinant of form in the mammalian skull. He held that the bending of the cranial base is the final step in the adaption of the skull to the upright posture.

Sicher (1947) held that both the chondrocranium and the desmocranium grow under strong genetic control. Only minor remodeling of surface configuration on internal trabecular structures of the tissue would be subject to local epigenetic factors such as the muscles, brain, and sensory organs. All the structures in the head, although genetically attuned to one another, grow without any dependent relationships to one another. Sicher ascribed equal active value to all of the osteogenic tissues provided by periosteum, cartilage, and sutures.

Scott (1953, 1956, 1957, 1958) theorized that the primary controlling factors in craniofacial growth are found only in the

cartilage and the periosteum and that sutures are passive and secondary. Scott considered the cartilaginous parts of the skull as primary centers of growth. Sutural growth can be altered by local and environmental factors. The growth of the sutures is regulated by the growth of the synchondroses together with the growth of the soft tissue structures adjacent to the skull. This allows the growth of the skull to be coordinated with the growth of the composite of other structures. The growth of the brain within its sheath of dura mater was held to be the most important factor in the separation of the bones of the cranial vault. The cranial base in its growth and morphology has a limited effect on the growth and form of the cranial vault, and Scott believed that the basicranium has little relationship to growth of the brain. The principal growth regulating element of the cranial base, he presumed, was the cartilage between the body and greater wings of the sphenoid and the spheno-occipital synchondrosis. He held that the prepituitary half of the cranial base is closely related to the development and growth of the upper facial skeleton, and that the development of the facial skeleton is influenced by the flexure of the cranial base.

Baer (1954) viewed the increase in size of the cranial vault and face as resulting from the separating growth at the sutures and synchondroses brought about by incremental additions at the margins of each center of ossification.

Ford (1956, 1958) considered cranial growth to be largely dependent on the growth of the brain, with skeletal development

conforming to the neural pattern of growth. Ford believed that facial growth is independent of brain growth and conforms to the general skeletal growth patterns shown by most other bones. He observed that individual parts of the cranial base show either the neural or general skeletal growth rates but not intermediate ones. He related the progressive flattening of the cranial floor angle that occurs during late fetal life to the forces transmitted to the chondrocranium through its articulation with the enveloping bony calvaria in response to the rapidly expanding neural mass.

Moss (1959, 1962, 1968, 1969a, 1969b, 1971b) denied any intrinsic regulatory control within cartilage or bone tissue. He based his theory on a concept of interrelated, functional cranial components, the size, position, and shape of which are determined by function. Moss elaborated on the concept of the functional matrix. Tissues, organs, and functioning spaces comprise the functional matrices relative to the bones which they enclose. Moss holds that the growth of the individual bones comprising the craniofacial skeleton is dependent on the nature of growth and the functions of this encapsulating matrix. The functional matrices provide the extrinsic influences which are the morphogenetic determinants for the form, growth, position, and maintenance of all skeletal tissues.

Young (1959) observed compensatory modifications in the size, shape, and spatial arrangement of the dura, bone, and muscle in response to increased and decreased neural mass. The cranial vault was highly influenced. With increased contents, the cranial

vault was larger and more globular and with decreased contents, it was smaller and flatter.

Enlow (1968) described the growth and remodeling patterns of the postnatal facial and cranial bones. Descriptions of these patterns will be included in later sections of the present study for comparisons with anencephalic fetal head development. The size and shape of the cranial base was believed to have become epigenetically established to accomodate an interdependent association with the developing brain. Enlow states that the cranial base itself has developed, phylogenetically, a presumably "genetic" capacity for its own growth that is at least partially separate and independent of the brain and which may develop to some extent without it during ontogenic growth. The calvaria enlarges to accomodate brain expansion by secondary (i.e., responsive) growth at the sutures with only small amounts of new deposition on the flat surfaces of both the ectocranial and endocranial surfaces to increase their thickness. The face develops in conjunction with the cranial floor and the brain, and the epigenetic control of facial development by its soft tissues is believed to accomodate its own functional association with the cranium. Enlow believes that the functional matrix concept is essentially valid and that it helps to explain a unified development and coexistence of the many separate growing parts, all developing in relation to one another. The functional matrix concept itself, however, does not explain the actual mechanism of control of the growth and development process.

Limborgh (1970), proposing that the theories of Moss, Sicher, and Scott are all inadequate, has synthesized our present knowledge into a new concept. Limborgh feels that the growth of the chondrocranium is almost exclusively governed by intrinsic genetic factors. In contrast, desmocranial growth is controlled by only limited intrinsic genetic factors but with many epigenetic factors originating from other head structures.

Latham and Scott (1970) advanced a theory of "multiple assurance" in conjunction with the process of craniofacial growth and development. This theory states that multiple processes are involved in growth, and should one or another of these processes fail (or become deleted experimentally), other means are available to accomplish a similar or comparable result.

Hoyte (1971) also supported the concept that the calvarial bones become passively carried outward by expansion of the brain mass. Sutural growth was considered by him as the major factor producing the increase in height, width, and length of the neurocranium. Only local regions of resorption exist on the endocranial side of the neurocranium and these are closely associated with the development of particular parts of the brain or cranial nerves.

In the following discussion section, the results of the present study will be used to assess the validity of some of the concepts of these major theories of craniofacial growth and development.

MATERIALS AND METHODS

Two female, formalin fixed human anencephalic fetuses aged six and seven months menstrual age were used in this study (Plates I, II and III). Menstrual age was determined according to the method of inferior extremity length of Nanagas (1931). A steel vernier caliper, which registered to 1 mm. on the major and 0.1 mm. on the minor scale, was employed for linear determinations. All linear measurements were recorded to the nearest 0.1 mm. Foot length and the length of the lower extremity were recorded. Foot length was measured from the posterior surface of the heel to the tip of the big toe. Lower extremity length consisted of the sum of the lengths of the thigh, leg, and foot height. Thigh length was measured from the top of the greater trochanter to the lateral condyle of the tibia in line with the posterior angle of the knee; leg length was measured from the lateral condyle to the most prominent part of the lateral malleolus, and foot length was measured from the external malleolus vertically to the sole of the heel. All anatomic landmarks were exposed by gross dissection. Values of the right and left sides were averaged. Lower extremity length was converted into crown-heel length using the empirical formula of Scammon and Calkins (1929): lower extremity length=0.43 crown heel length—7.0 mm. The age curves of Streeter (1920) and Scammon (1937) were used based on a study conducted by Trolle (1948).

PLATE I

Frontal view of anencephalic fetus.
Fetus No. 1 (top) and No. 2 (bottom).





PLATE II

Lateral view of anencephalic fetus.
Fetus No. 1 (top) and No. 2 (bottom).

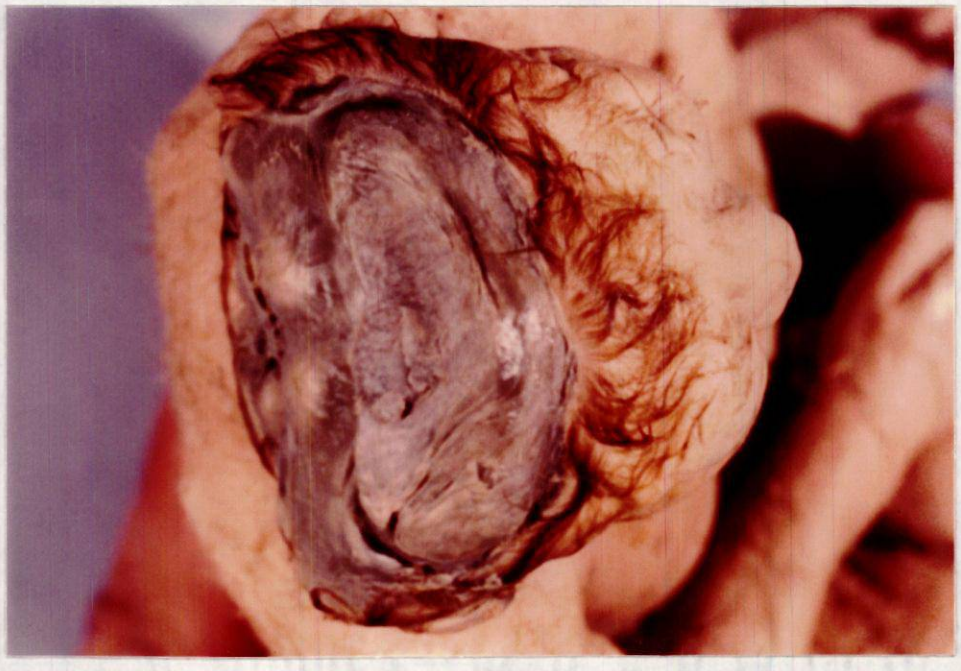

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PLATE III

Superior view of anencephalic fetus.
Fetus No. 1 (top) and No. 2 (bottom).





Trolle, using two hundred and fifty fetuses, determined that the best suited age curve, when utilizing foot length and crown-rump length, is that of Streeter (1920) and when using crown-heel length is that of Scammon (1937). Linear measurements and age determinations are listed in Table V.

The two holoacrania fetuses were radiographed in lateral and posterior-anterior directions, photographed, decapitated, and the head of each fetus was bisected in a parasagittal plane just to the left of the midline in order to include midline structures in the histological sections (Plates IV and V). The right and left halves were cut into 5 mm. thick parasagittal and coronal blocks respectively. Each block was photographed, mapped grossly, and then cut into 2 cm. x 2 cm. squares for sectioning. All were decalcified in 2.5% phosphoric acid for six days, vacuum embedded in paraffin, serially sectioned every 10 microns, and stained with hematoxylin and eosin. Using low magnification, the gross anatomical structures of each section were first oriented and a map was made of each section, including all bony and cartilagenous parts. A third anencephalic fetal head of similar age was cleared of all soft tissue and used as a reference skull to aid in the identification of individual bones observed in the histological sections. Depository and resorptive periosteal surfaces for all the bones were identified and recorded on the serial section maps using color codes. Surfaces recorded as depository presented a distinct osteogenic layer of osteoblasts. Resorptive surfaces exhibited large Howship's lacunae and/or multinuclear osteoclasts.

TABLE V

AGE DETERMINATIONS

Measurement (mm.)	Fetus No. 1		Fetus No. 2	
	Right	Left	Right	Left
Thigh Length	67.1	69.0	77.1	76.8
Leg Length	54.1	53.3	65.2	64.7
Foot Height	10.1	10.0	16.0	15.6
Lower Extremity Length	131.3	132.3	158.3	157.1
Average of Right and Left Sides of Lower Extremity	131.8		157.7	
Foot Length	47.3	45.3	54.8	58.1
Average of Foot Lengths	46.3		56.5	
Crown-Heel Length Calculated from Empirical Formula	322.8		383.0	
Age from Streeter Foot Length Curve (months postmenstrual)	6.0		6.75	
Age from Scammon Crown-Heel Curve (months postmenstrual)	6.0		7.0	

PLATE IV

Parasagittal section of the head of anencephalic fetus No. 1, cut just to the left of the midline.





PLATE V

Parasagittal section of the head of anencephalic fetus No. 2, cut just to the left of the midline.





After the complete series of sections for each skull had been analyzed, the overall depository and resorptive patterns were mapped on a dry postnatal skull using colored felt pens to indicate resorption and deposition. The two skulls were then compared for patterns of growth and remodeling in order to determine the constancy of patterns, and the nature of individual variations. Anencephalic fetal patterns were then compared with the remodeling patterns characterizing the normal prenatal and postnatal skulls as described by Mauser et al. (1975) and Enlow (1968, 1975).

OBSERVATIONS

Two separate anencephalic fetal descriptions will be given only when a disparity of pattern was observed between them.

Premaxilla

The morphology of the premaxilla and its spatial relationship to the maxilla are similar to that seen in normal fetuses. The labial and oral palatal surfaces are depository. Resorption is found on the nasal (superior) surface and at the posterior sutural surface along its interfacing with the maxilla (Plate VI and Figure 1). Bony surfaces lining the tooth crypts are resorptive (Plate VII).

Maxillary Bone

The morphology of the maxilla is similar to that seen in normal fetuses. The anterior, infraorbital, lateral, posterior, and inferior surfaces are all depository (Figures 2, 3, 4 and 5). Bony surfaces lining tooth crypts are resorptive. The frontal process of the maxilla is resorptive on the nasal mucosa side and where it bounds the nasolacrimal canal. Within the infraorbital canal, resorption occurs superior and lateral to the infraorbital nerve (Plates VIII and IX). Deposition takes place inferior and medial to the nerve. The palatine process of the maxilla is depository orally and resorptive nasally (superiorly).

PLATE VI

Sagittal section of fetus No. 2, of the junction of the premaxilla and maxilla. Left-low power (20X), right-high power (200X) of premaxillary surface of premaxillary-maxillary suture. Hematoxylin and eosin. Pr-premaxilla; M-maxillary bone; V-vomer; Z-zygomatic bone; S-sphenoid bone; T-temporal bone; C-coronoid; Co-condyle.

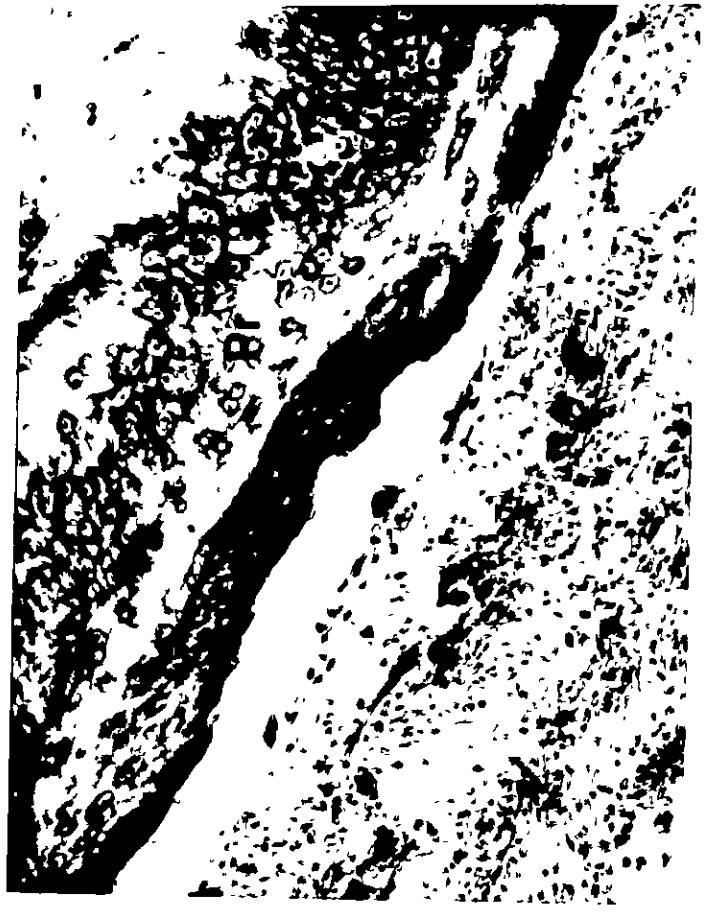
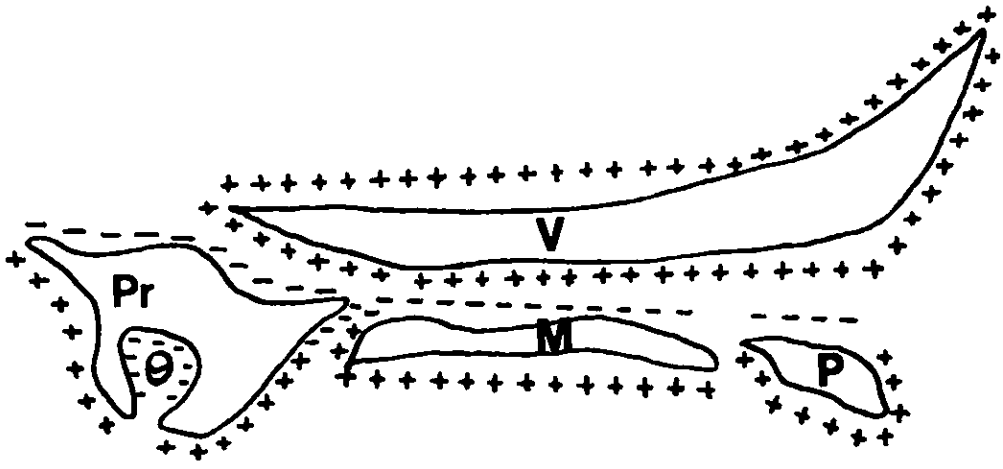
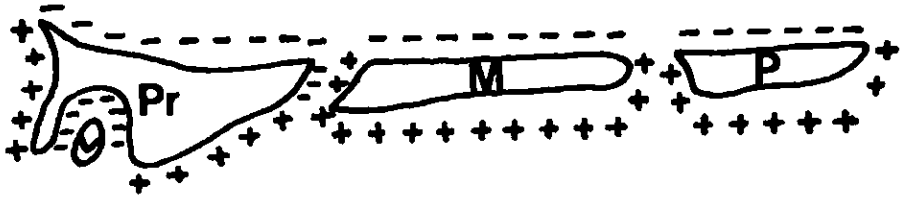




Figure 1. Sagittal sections of nasomaxillary complex of the anencephalic fetus. Top-midsagittal section through the vomer, premaxilla, maxilla and palatine bones. Middle-sagittal section more lateral than top view. Bottom-sagittal section even further laterally. V-vomer; Pr-premaxilla; M-maxilla; P-palatine bone.


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Pr
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M
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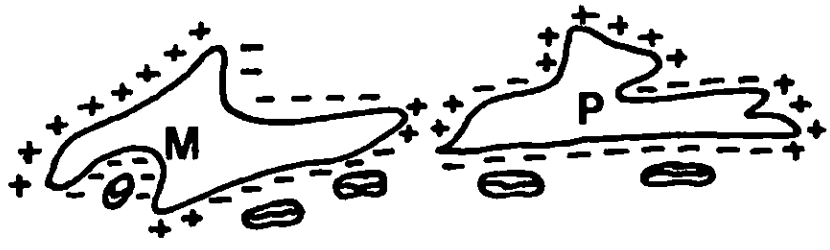

M
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PLATE VII

Sagittal section of the premaxilla of fetus No. 1 showing bony resorption adjacent to the tooth bud. Left-low power (20X); right-high power (200X). Hematoxylin and eosin.

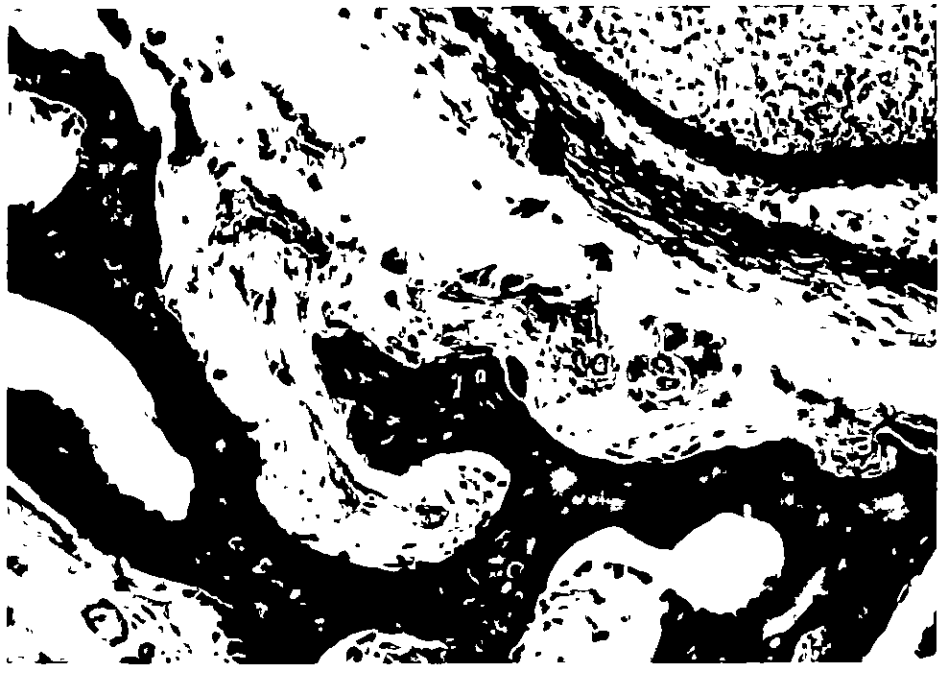
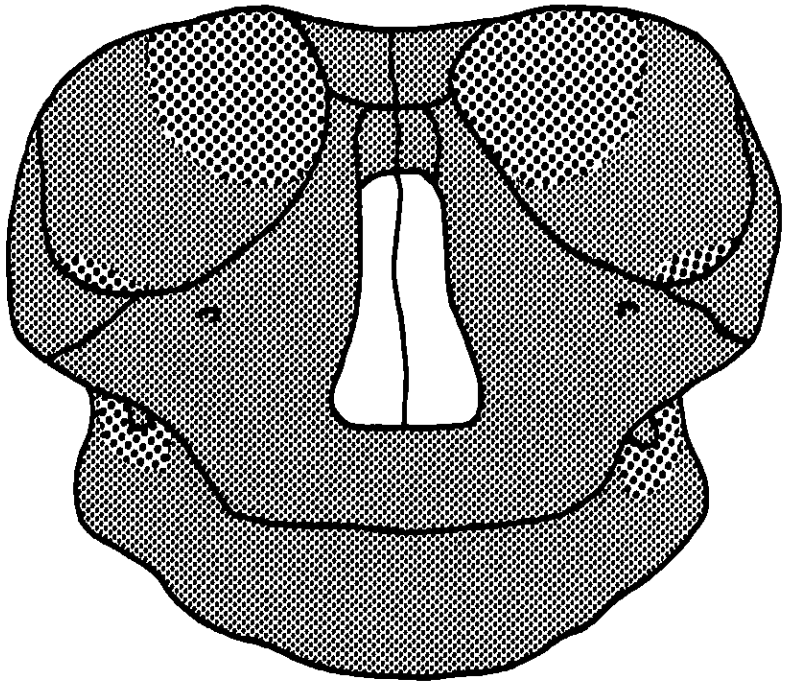
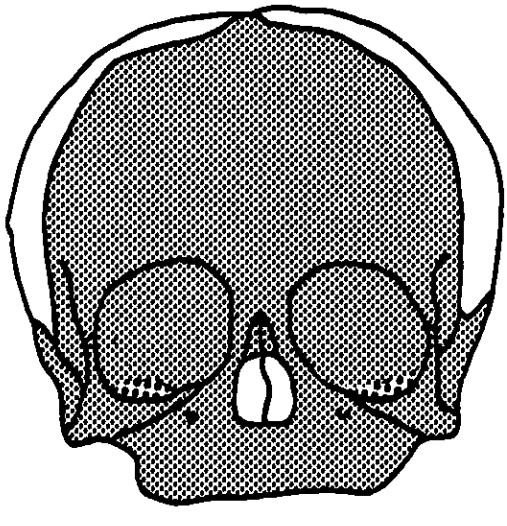




Figure 2. Frontal views. Top-anencephalic fetal skull (enlarged 2.5X) showing the overall remodeling pattern and comparing with normal fetal skull after 26 weeks gestation age, lower left and postnatal skull, lower right. Small dot stippled areas indicate deposition and large dot stippled areas indicate resorption. Note particularly the change in the orbital plate of the frontal bone. Early in normal fetal life (before 26 weeks) and in the anencephalic fetus the bone is resorptive orbitally and depository durally. After 26 weeks, the normal prenatal fetus is depository orbitally and resorptive durally coinciding with the postnatal skull. Solid white areas represent open spaces.





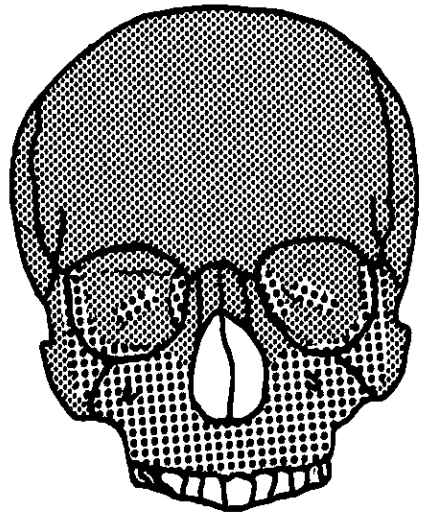


Figure 3. Lateral view of anencephalic fetus (enlarged 2X). Solid black shaded area represents cartilage.

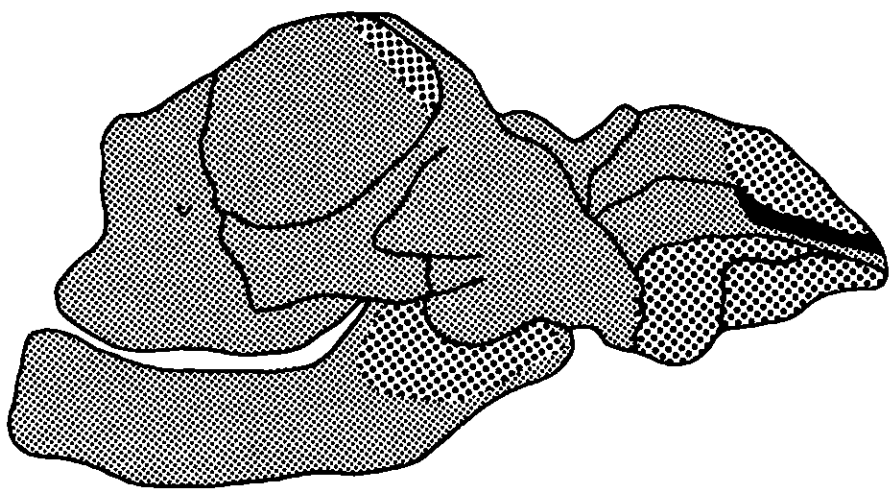


Figure 4. Superior view, roof of calvaria removed, of anencephalic fetal skull top (enlarged 2X); normal prenatal skull, lower left; normal postnatal skull, lower right. Note the lack of foramen magnum formation and the lateral and anterior constriction of the anterior cranial fossae in the anencephalic.

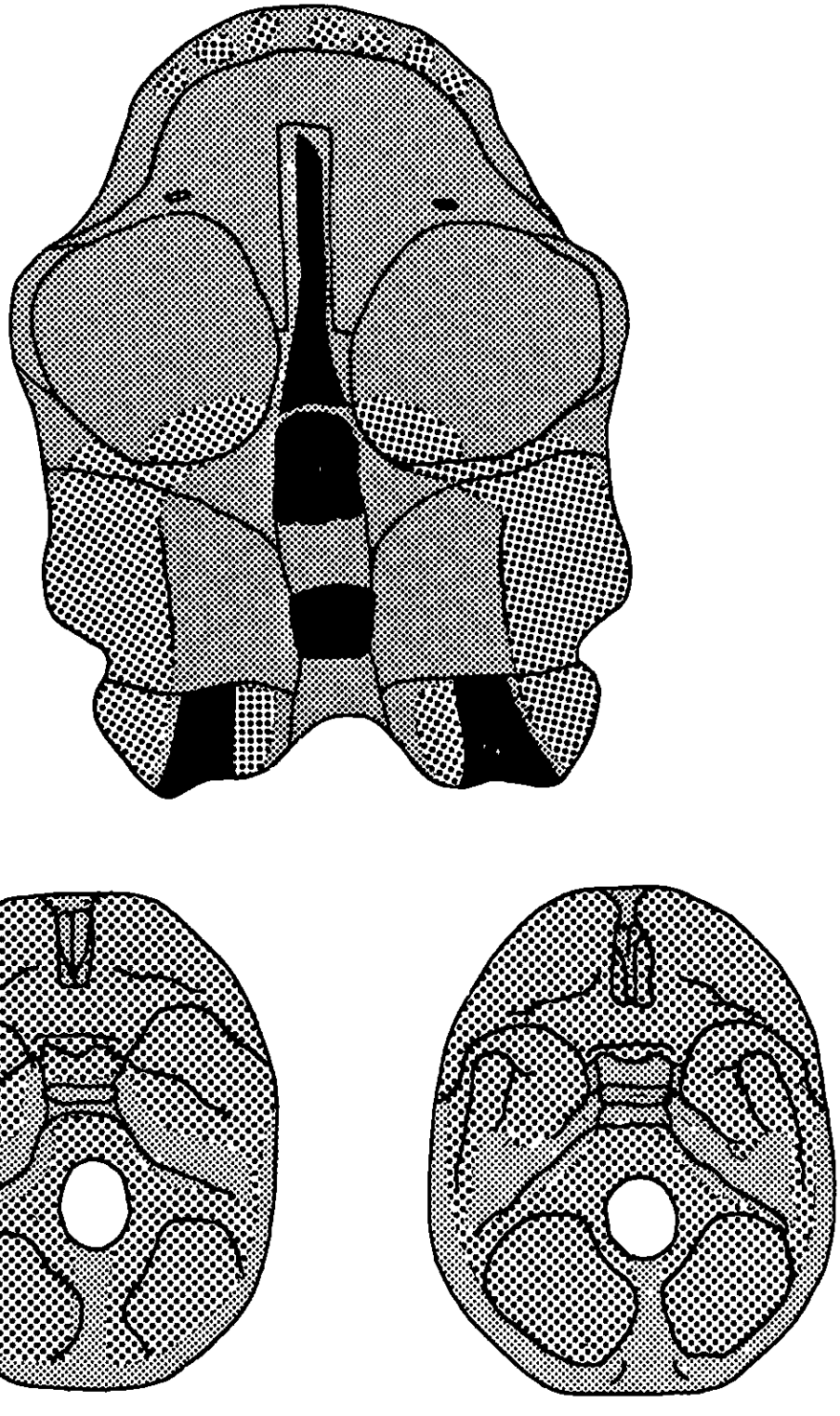


Figure 5. Inferior view of the anencephalic fetal skull, top (enlarged 1.5X); normal prenatal skull, lower left; normal postnatal skull, lower right.

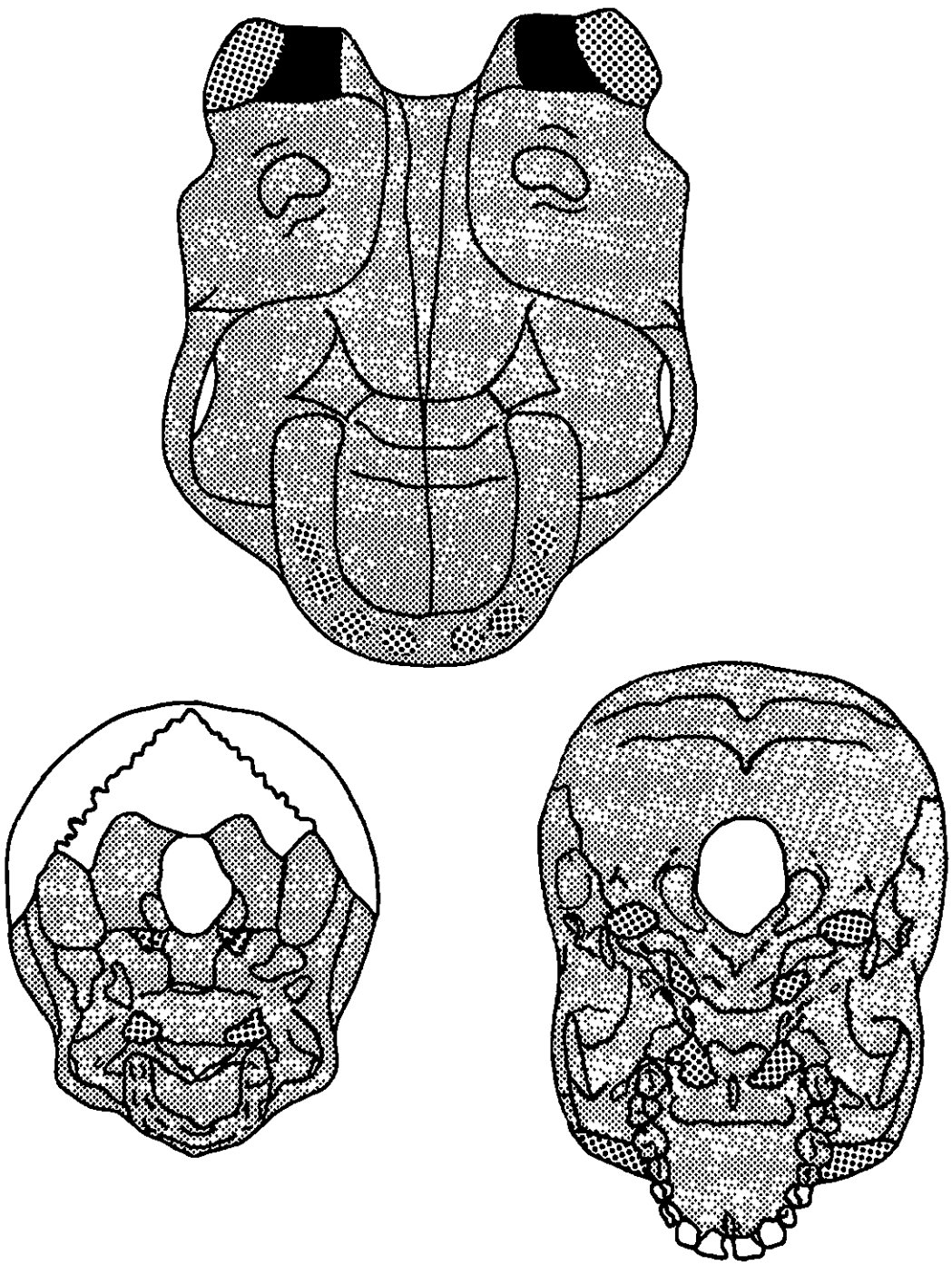


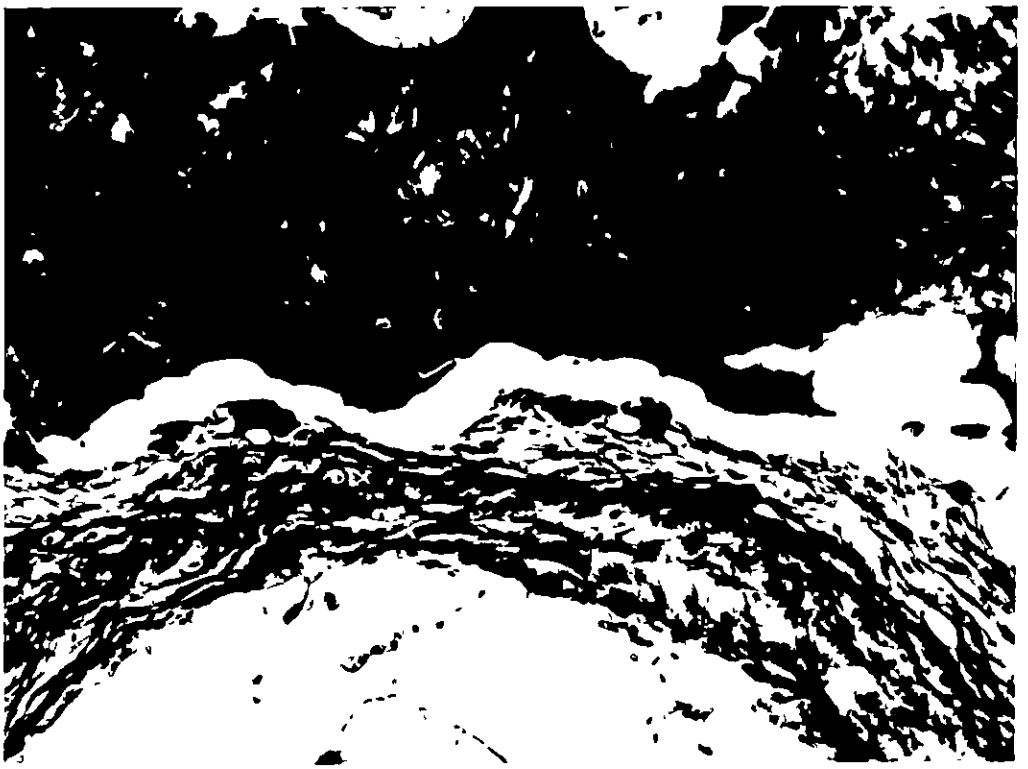
PLATE VIII

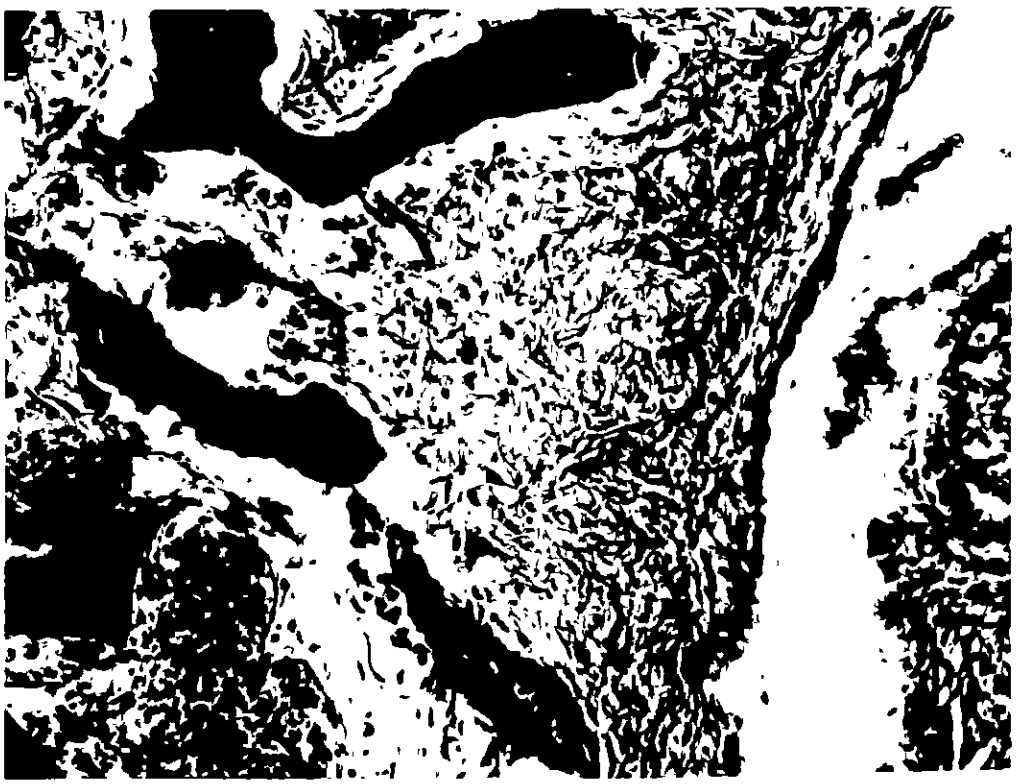
Coronal section through maxillary bone and infraorbital foramen, low power (20X). Showing foramen drift. Hematoxylin and eosin.



PLATE IX

Same view of infraorbital foramen as in Plate VIII, high power (200X). Left-superior surface resorption, right-lateral surface resorption.





Palatine Bone

The morphology of the palatine bone is similar to that seen in normal fetuses. The horizontal process of the palatine bone is depository orally and resorptive nasally (Plate X). The perpendicular plate of the palatine bone is depository laterally, anteriorly, and posteriorly. Resorption is present on the nasal side.

Lacrimal and Nasal Bones

The lacrimal bone is depository on all surfaces except where it contacts the nasolacrimal canal.

The morphology of the nasal bone is similar to that seen in normal fetuses. All external periosteal surfaces are depository, and the mucosal surface is resorptive.

Zygomatic Bone

The zygomatic bone is severely affected with respect to relative size and spatial orientation (Figures 2, 3 and 4). The frontal process of the zygomatic bone is normally directed superiorly, but in the anencephalic skull it has a posterosuperior inclination. The temporal process appeared to parallel the palatal plane, as in the normal skull. This results in the formation of an acute angle between the frontal and temporal processes of the zygomatic bone in comparison to its normal 90° angle. The zygomatic bone is resorptive where it forms the infraorbital rim overlapping the maxillary part of the orbit, and also on the medial side of the temporal process (Plates XI, XII and XIII). All other periosteal surfaces are depository.

PLATE X

Sagittal section, fetus No. 2, of the palatine, vomer junction. Left-low power (20X); right-high power (200X) showing nasal (superior) resorption, oral (inferior) deposition of the palatine bone. Hematoxylin and eosin.

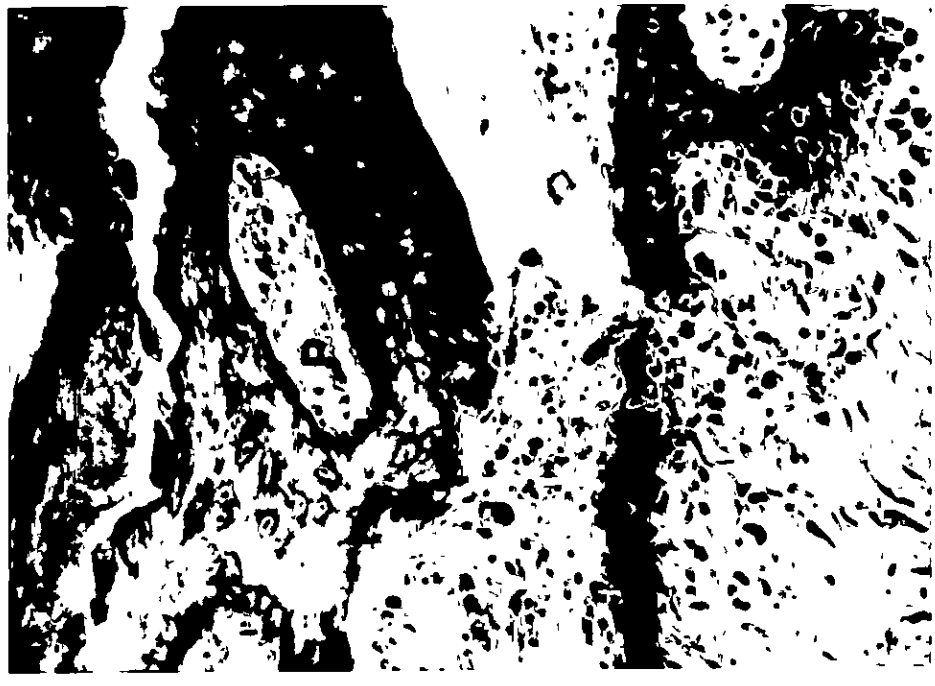




PLATE XI

Coronal section through maxillary and zygomatic bones of fetus No. 2. Left-low power (20X), right-high power (200X) showing resorption on the orbital surface of the zygomatic bone. Hematoxylin and eosin.

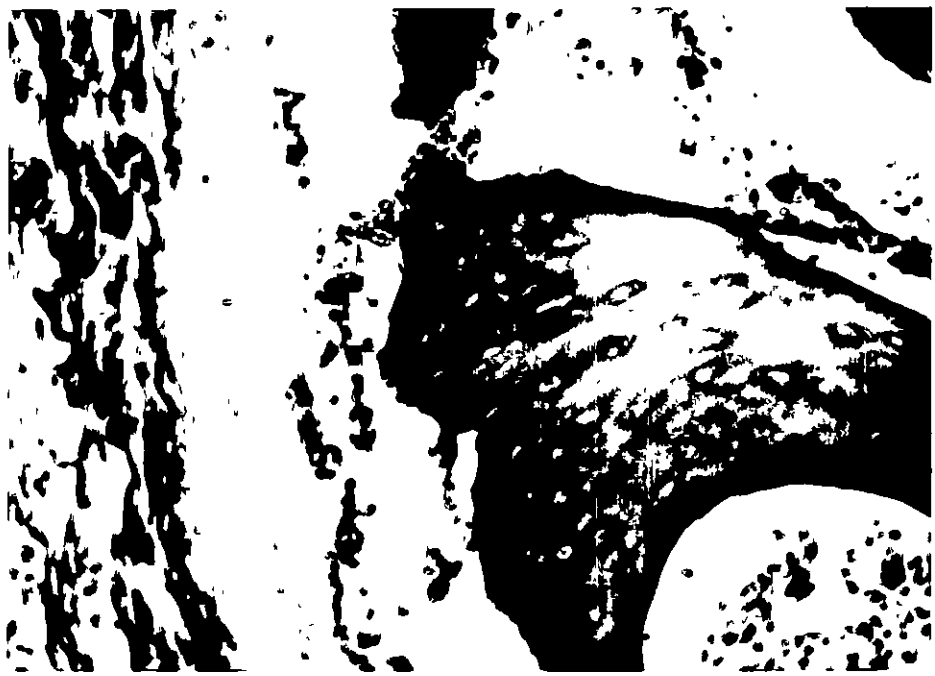




PLATE XII

Coronal section through coronoid process, temporal process of zygomatic bone of fetus No. 1. Left-low power (20X), right-high power (200X) of the temporal process showing resorption on the temporal fossa surface. Hematoxylin and eosin.





PLATE XIII

Coronal section through the coronoid process, temporal process of zygomatic bone and petrous portion of the temporal bone. Left-low power (20X), right-high power (200X) of the petrous portion of the temporal bone. Hematoxylin and eosin.





Frontal and Parietal Bones

The frontal bone is severely affected in morphology, relative size, and spatial relationship (Figures 2, 3 and 4). The squamae of the frontal bone are collapsed horizontally and rudimentary in dimensions. They diverge laterally and extend posterolaterally until approximating the squamae of the temporal bone. The frontal eminence is lacking. The superior orbital rim is directed posterolaterally. The orbital plate of the frontal bone is absent. The posterior portion of the orbit is roofed by that portion of the frontal bone that would normally form the frontal eminence. The collapsed squamae of the frontal bone form the roof of the nasal cavity. The mucosal side of this superior surface of the nasal chamber is resorptive, and the opposite, external periosteal surface is depository. The medial one-half of the posterior wall of the orbit is resorptive on the anterior (orbital) side, and depository on the posterior (endocranial) side (Figures 2, 3 and 4). The lateral one-half of the posterior wall of the orbit is depository on the anterior (orbital) side and resorptive on the endocranial side. The dural side of the squamae of the frontal bone is resorptive except in the midline where it is depository. All external periosteal surfaces are depository. The right and left parietal bones are lacking.

Vomer, Ethmoid, and Nasal Conchae

The ala and free border, making up the posterior part of the vomer, is angled more superiorly than normal from the palatal plane

to its articulation with the sphenoid bone (Figure 1). This results in an increased posterior height of the vomer. The inferior surface is depository along its articulation with the palate and also superiorly in the area supporting the cartilaginous nasal septum.

The surfaces of the inferior nasal concha show resorption superiorly and deposition inferiorly. The middle nasal concha is depository superiorly and resorptive inferiorly. The superior concha is depository superiorly and resorptive inferiorly. The lateral side of the ethmoidal labyrinth (lamina papyracea) is depository. The orbital surface of the ethmoid is depository.

Sphenoid, Temporal, and Occipital Bones

The greater wing of the sphenoid is resorptive endocranially and depository ectocranially. The pterygoid plates are entirely depository in nature and elongated in relative size. The lesser wing of the sphenoid is depository superiorly and resorptive inferiorly. The presphenoid and postsphenoid (basisphenoid) are largely cartilagenous with only a beginning of endochondral ossification.

The squamae of the temporal bone which is rudimentary, is resorptive ectocranially and depository endocranially. The medial part of the petrous ridge is depository and the approximate lateral one-half is resorptive (Plates XIV and XV). The walls of the internal acoustic meatus are largely resorptive. The ear ossicles appear to have normal morphology and spatial relationships. Cranial

PLATE XIV

Coronal section through temporal bone of fetus No. 1. Left-low power (20X), right-high power (200X). Note endocranial resorption. Hematoxylin and eosin.



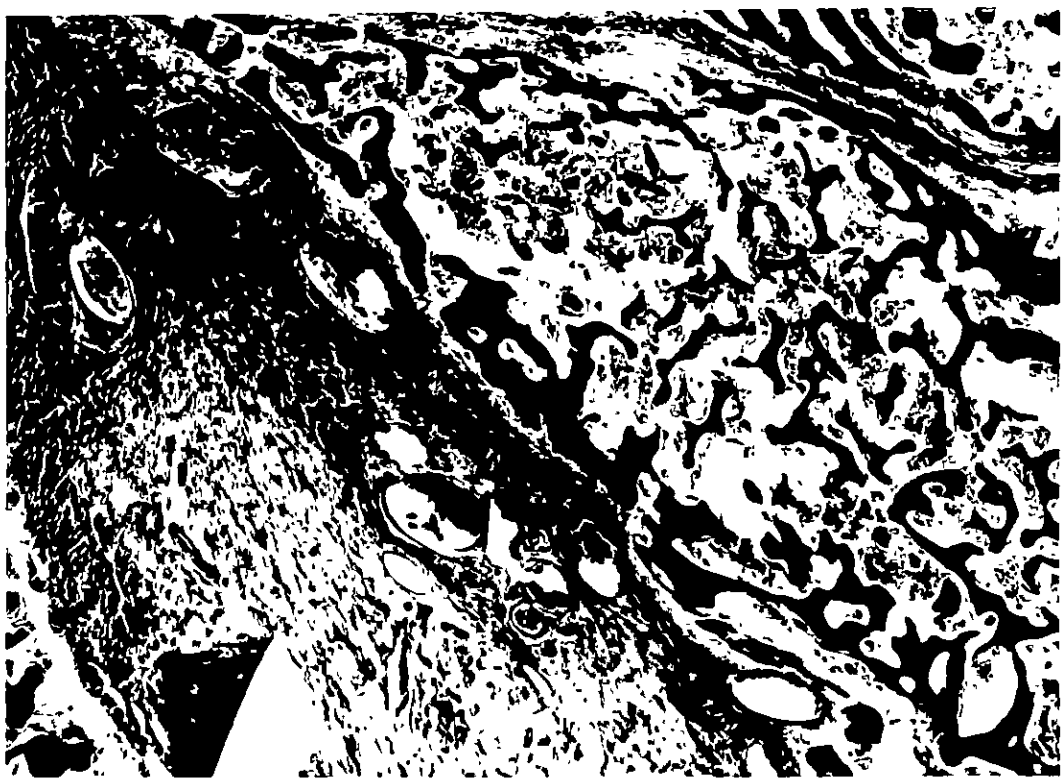
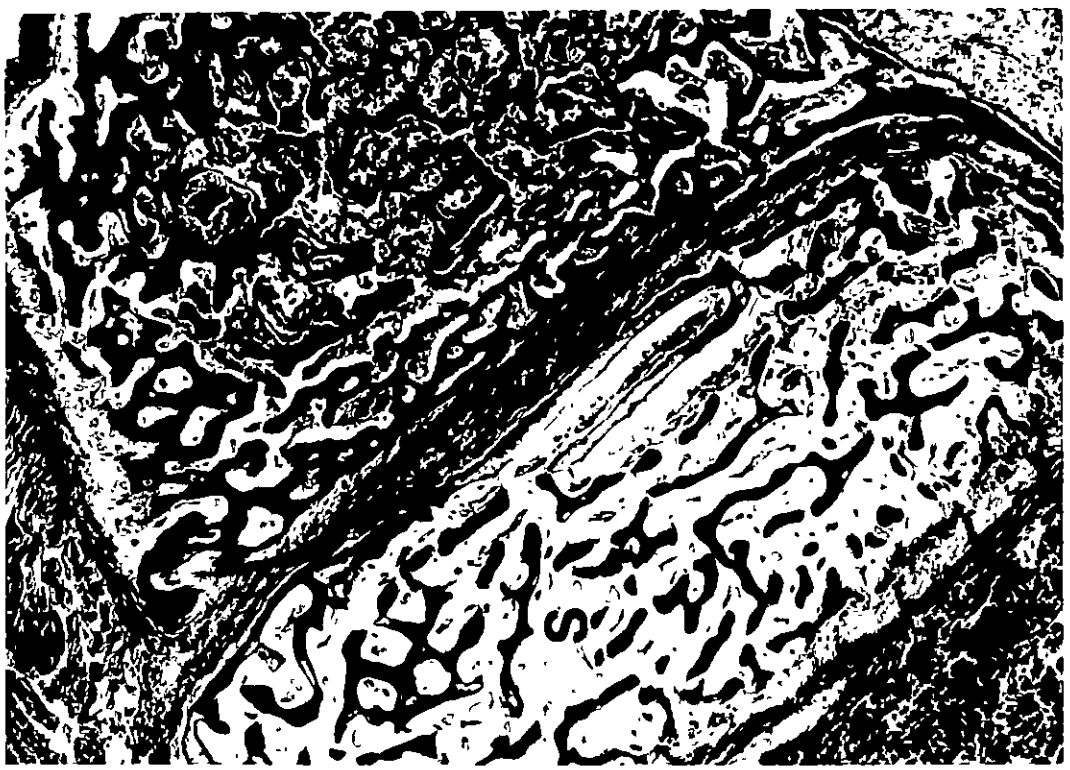


PLATE XV

Coronal section through the temporal-sphenoidal suture of fetus No. 2. Left-low power (20X), right-high power (200X). Note sutural resportion. Hematoxylin and eosin.





nerve VIII is present and well developed (Plates XVI and XVII). The zygomatic process of the temporal bone is resorptive medially and depository on all other external surfaces. The glenoid fossa anteriorly is not covered by cartilage, as it would be in normal fetuses. The ectocranial (inferior) surface of the temporal bone is depository.

The squama of the occipital bone is not well developed, leading to a lack of formation of the posterior rim of the foramen magnum. The foramen magnum itself is also not present. The basilar part of the occipital bone is depository both endocranially and ectocranially. The lateral part of the occipital bone is largely resorptive with a small amount of deposition occurring on the lateral one-quarter on the endocranial surface. The ectocranial surface is resorptive only in the lateral one-quarter, and the remainder of the ectocranial surface is depository. The occipital condyle is mostly cartilaginous with beginnings of endochondral ossification. The spinal column appears normal and the atlas articulates with occipital condyles of the anencephalic as seen in normal fetuses.

Mandible

The morphology of the mandible appears normal, but both anencephalic fetuses exhibited prognathism (Figure 3).

On the condylar neck, both buccal and lingual external surfaces are resorptive (Figures 6, 7, 8 and 9). Along the posterior margin of the ramus, deposition occurs along the entire posterior facing margin, both bucally and lingually. Along the lingual

PLATE XVI

Sagittal section of temporal bone of fetus No. 2 showing Cranial Nerve VIII foramen drift, low power (20X). Hematoxylin and eosin.

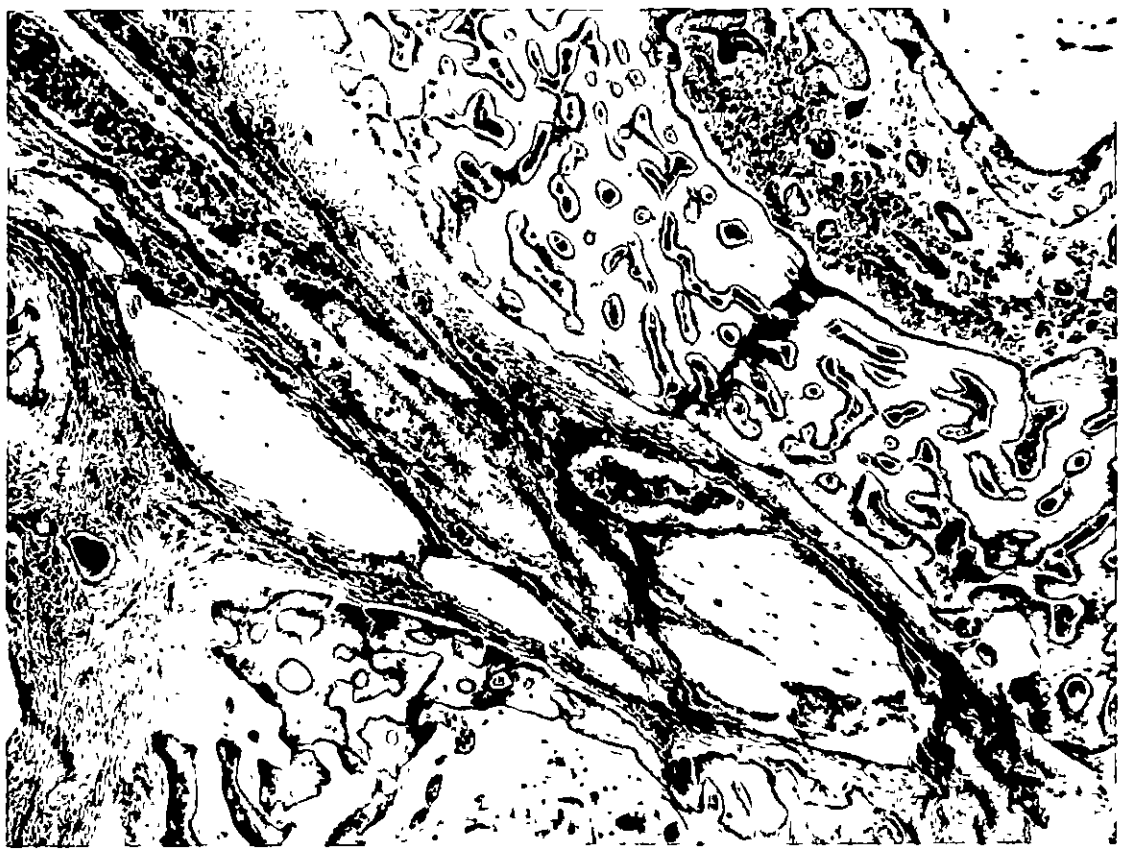
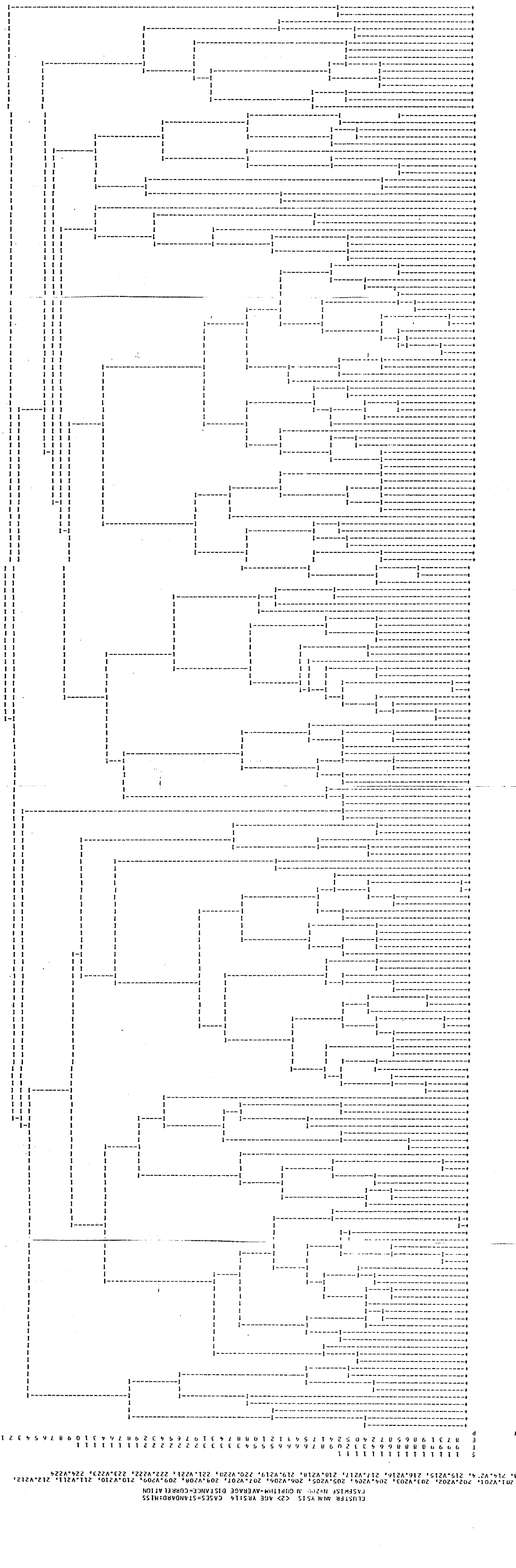


PLATE XVII

Same view as in Plate XVI, high power (200X), left-surface resorption, right-surface deposition.


SJNVISIO
CASE#
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CASEWISE N=200 AI COPELIM=AVERAGE DISTANCE=CORRELATION
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CLUSTER ANALYSIS <1> AGE YRS:10 CASES=STANDARD:MISS
CASEWISE N=201 ALGORITHM=AVERAGE DISTANCE=CORRELATION

USING: 201.V201, 202.V202, 203.V203, 204.V204, 205.V205, 206.V206, 207.V207, 208.V208, 209.V209, 210.V210, 211.V211, 212.V212, 213.V213, 214.V214, 215.V215, 216.V216, 217.V217, 218.V218, 219.V219, 220.V220, 221.V221, 222.V222, 223.V223, 224.V224





Figure 6. Buccal view of mandible, anencephalic top (enlarged 3X); normal prenatal in the last trimester, lower left; normal postnatal, lower right.

Figure 7. Anterior view of the labial and buccal surface of the mandible, anencephalic top; normal prenatal, lower left; normal postnatal, lower right.

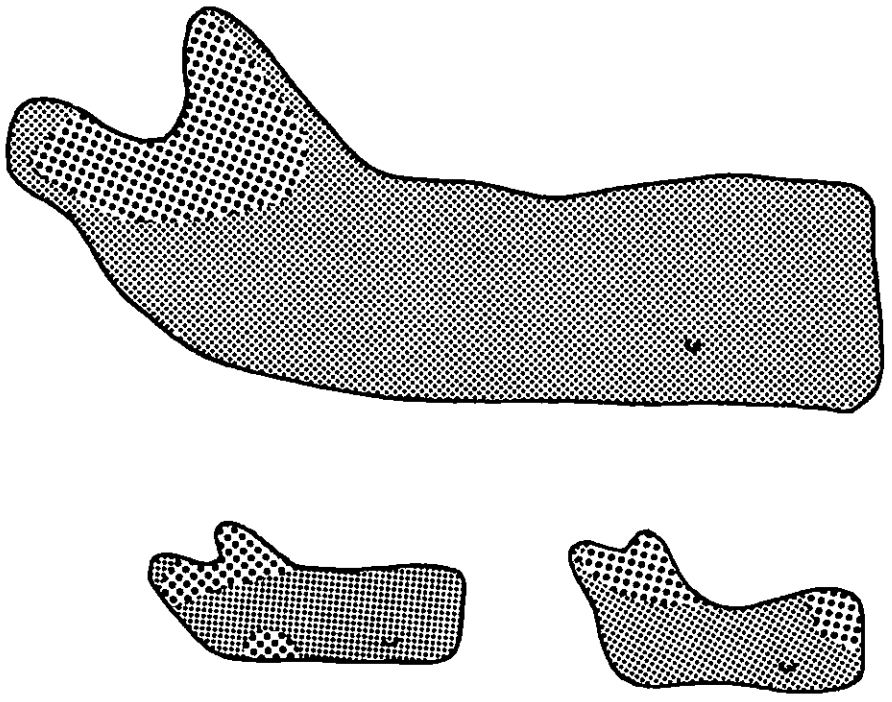
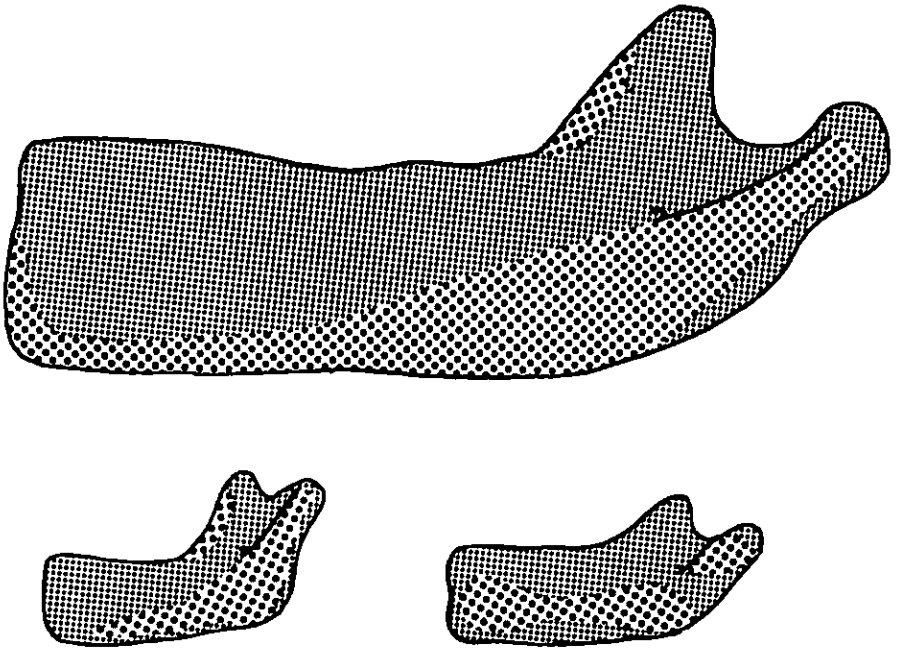


Figure 8. Lingual view of the mandible, anencephalic top (enlarged 3X); normal postnatal, lower left; normal prenatal in the last trimester, lower right.

Figure 9. Posterior view of the lingual surface of the mandible, anencephalic top; normal postnatal, lower left; normal prenatal, lower right.



surface of the mandibular (sigmoid) notch, deposition continues down from the condylar head and then extend up to the apex of the coronoid process. The crest of the lingual side of the sigmoid notch is also depository. The entire buccal surface of the sigmoid notch of the ramus, however, is resorptive.

The greater portion of the lingual surface of the coronoid process is depository except along the anterior border where it is resorptive. The entire buccal surface of the coronoid process is resorptive except on the anterior border where it is depository. On the buccal side of the ramus, below the ridge that projects downward from the neck across the upper portion of the ramus where a prominent change in contour occurs, the ramus is depository. On the lingual side of the ramus, that part located anteriorly and superiorly to the oblique ridge extending down from the neck onto the ramus is depository. This depository field continues obliquely across the ramus to the lingual tuberosity of the mandibular body superior to the mylohyoid line. Below the ridge of the mandibular neck and the mylohyoid line, where a prominent change in contour occurs, the periosteal surface on the lingual side of the ramus is resorptive. This resorptive zone on the lingual side of the condylar neck descends in an obliquely forward direction and extends across the entire breadth of the ramus into the resorptive submandibular fossa of the corpus (Figures 8 and 9). On the lingual side of the mandibular body, the broad resorptive band extending from the condylar neck obliquely down and across the lingual side of the ramus continues directly into the deep sublingual fossa inferior to

the lingual tuberosity and the mylohyoid line directly to the inferior border of the mandible, and continues anteriorly to the genial tubercles (Plate XVIII). On the buccal side of the mandibular body, the entire periosteal surface is depository (Figures 6 and 7).

PLATE XVIII

Sagittal section through symphysis region of mandible, fetus No. 1. Left-low power (20X), right-high power (200X). Note resorption on inferior border of mandible.





DISCUSSION

Comparison with the Normal Prenatal and Postnatal Skull

Nasomaxillary Complex

Premaxilla. The palatal part of the premaxilla in the anencephalic skull, as in the normal prenatal and postnatal skulls is depository on the oral side and resorptive nasally. This remodeling pattern produces a downward movement providing for the vertical enlargement of the overlying nasal region. The external labial surface of the entire premaxillary region is depository in both anencephalic and prenatal skulls, but becomes resorptive at birth or during the first year in the normal face. This depository labial surface during the fetal period provides for increasing arch length to accomodate the developing tooth buds. The bony surfaces lining the tooth crypts are uniformly resorptive. By the first postnatal year, all the deciduous teeth have attained approximately maximum crown size, and the anterior expansion of the premaxilla is no longer needed. These external surfaces now begin to become resorptive in order to produce the continuing downward movement of the premaxilla.

Maxilla and Palatine Bones. The external surface of the maxilla in the region below the orbit and also the posterior surface of the maxillary tuberosity are depository in the anencephalic and the normal prenatal and postnatal skulls. Infraorbital deposition is

required to maintain a constant positional relationship with the enlargement of the bulbus oculi. The bulbus oculi expand in volume by over 100% during the fourth to fifth prenatal months, 50% during the sixth and seventh months and by 23 to 30% during the eighth and ninth months (Scammon and Armstrong, 1925). Remodeling of the orbital floor is necessary because the entire maxilla is displaced in a progressively inferior direction in association with fronto-maxillary sutural growth. Deposition on the orbital floor serves to carry it superiorly to maintain constant position relative to the bulbus oculi. Deposition on posterior surfaces serves to increase the maxilla in horizontal length as the whole maxillary complex becomes simultaneously carried anteriorly. The infra-orbital canal drifts superiorly and laterally during growth of the anencephalic as well as the normal face by the combination of superolateral resorption and inferomedial deposition on its lining surface. This drifting movement of the canal maintains a constant relationship between the nerve and the orbit, vertically, and the nasal cavity laterally as the nasal region continues lateral expansion. The entire anterior surface of the maxilla is depository in both anencephalic and normal prenatal skulls. This provides for increasing arch length and width in conjunction with tooth buds development and their continuing enlargement. The lining of the tooth crypts are correspondingly resorptive. Postnatally, the anterior surface of the maxilla becomes resorptive. This change in remodeling pattern occurs after the deciduous teeth have attained maximum arch length and produces the downward movement of the

maxilla associated with vertical nasomaxillary lengthening.

The external surface of the frontal process of the maxilla is depository in the anencephalic, normal prenatal, and postnatal skulls. The mucosal surface lining the nasal chamber in the normal fetus is mostly depository during early development but shows an increasing distribution of resorptive field at advanced fetal ages. In the anencephalic skulls examined as well as the normal postnatal skull, this surface is entirely resorptive. The latter part of fetal life is a transition period when the lateral nasal surfaces are just beginning their expansive lateral movements. The nasal side of the entire palate is resorptive and the oral palatal side is entirely depository in the anencephalic, normal prenatal and postnatal skulls. This provides for the inferior movement of the palate and occurs in conjunction with the enlargement of the nasal chambers. The nasal mucosal surface on the vertical plate of the palatine bone is resorptive, and all other surfaces are depository in both the anencephalic, normal prenatal, and postnatal skulls. This permits the expansion in width of the nasal chamber in this area.

Nasal and Lacrimal Bones. The anencephalic, as well as the normal prenatal and postnatal remodeling pattern of the nasal bone is resorptive on the nasal mucosal surface and depository on all other surfaces. This provides for the anterior movement of the bony ridge and the roof of the external nasal protuberance and permits enlargement of the upper part of the nasal chamber.

The lacrimal bone in the anencephalic and normal prenatal skulls is resorptive only on the surface adjacent to the nasolacrimal canal. Postnatally it becomes resorptive on its superolateral and infromedial surfaces but remains depository on all other surfaces. This prenatal to postnatal change in remodeling pattern relates to the growth function of the lacrimal bone. The sutures surrounding it function to adjust this part of the skull to the changing relative positions of the complex of other bones with which it articulates as they grow at different rates. The facial and cranial changes in both the normal fetal and anencephalic skulls are not nearly as pronounced, and the remodeling patterns characterizing the postnatal lacrimal bone have not yet developed.

Zygomatic Bone. The zygomatic bone in both the normal prenatal and anencephalic skulls are mostly depository but with resorption occurring along the infraorbital margin where the zygoma overlaps the maxilla. This provides for the lateral expansion of the zygomatic bone. In the postnatal skull, both the anterior and orbital surfaces begin to become resorptive. Transition from the fetal to the postnatal pattern occurs during the first year when the premaxillary region ceases to grow in a direct anterior direction. The entire medial side of the zygomatic arch in the anencephalic, the prenatal, and postnatal skulls, including both its temporal and zygomatic components, within the temporal fossa is resorptive. This provides the lateral drift of the whole zygomatic arch. The posterosuperior inclination of the zygomatic bone in the anen-

cephalic relates to its articulation with the severely malformed frontal bone caused by lack of frontal lobe development.

The entire anencephalic nasomaxillary complex is in a retrusive position. In the normal prenatal and postnatal skulls, the growth and development of the anterior cranial fossa produces a secondary displacement of the entire nasomaxillary complex in a forward direction. In the anencephalic skull, however, lack of frontal lobe development precludes much of the growth of the anterior cranial fossa, with a corresponding, marked reduction in the extent of forward maxillary displacement. The whole nasomaxillary complex thus becomes placed in a retrusive position in conjunction with the foreshortened anterior cranial floor.

Calvaria and Cranial Base

Frontal Bone. The squamae of the frontal bone in the anencephalic skull, as in both the normal prenatal and postnatal skulls, is characterized by endocranial resorption and ectocranial deposition. In the anencephalic, however, the squamae appear collapsed and diverge laterally and extend posterolaterally. The supraorbital margins have a backward alignment. The squamae and supraorbital margins have remained essentially horizontal in the absence of frontal lobe expansion rather than undergoing forward displacement into the protrusive, upright position characterizing the normal forehead. The backward alignment of the supraorbital margin is a composite result of the forward displacement of the medial portion, in conjunction with the development of the nasal cavities, and a

lack of forward displacement of the lateral portion in conjunction with deficient cerebral growth. The medial half of the posterior wall of the orbit is resorptive on the anterior side and depository on the dural side; the opposite is true for the lateral one-half of the posterior wall. The late normal prenatal and postnatal wall is depository on the anterior orbital side and resorptive on the dural side. The difference between the anencephalic and the late normal prenatal and postnatal remodeling patterns is based on the differential growth rates of the bulbus oculi and the frontal lobe of the cerebrum. The bulbus oculi growth rate decreases after 24 weeks gestation (Scammon and Armstrong, 1925). The frontal lobes of the brain until 26 weeks gestation show little growth (Graber, 1968). In the anencephalic the paired bulbus oculi have not yet passed their stage of maximum expansion and the secondary displacement due to frontal lobe development never occurs and the reversal to the late prenatal or postnatal remodeling pattern of endocranial resorption to create space for frontal lobe expansion does not occur. The reversal usually occurs when the growth of the eyeball is just slowing and the frontal lobe growth spurt is just beginning. The squamae exhibit endocranial resorption and ectocranial deposition effecting a movement anteriorly and laterally to allow for frontal lobe development which never occurs. The parietal bone is lacking or rudimentary in size if present, due to destruction of the brain, after which any further stimulus for its ossification appears to be lost. The anterior cranial base is laterally and anteriorly constricted in the anencephalic due to lack of frontal and temporal

lobe development.

The anencephalic as well as the normal prenatal and postnatal remodeling pattern of the greater wing of the sphenoid bone is characteristically resorptive endocranially and depository ectocranially. In the normal skull, this provides for the expansion of the temporal lobes of the cerebrum along with cranial base sutural and synchondrosis growth. In the anencephalic, this basic remodeling pattern is retained, although at a presumably lesser rate, even though the temporal lobe itself is lacking at the ages examined.

The late normal fetal and postnatal pterygoid plates are mostly depository but with resorption fields on the anteroinferior and posterior surfaces. The anencephalic pterygoid plates, however, are entirely depository. The normal fetal and postnatal remodeling pattern functions to channel, deepen, and relocate the pterygoid fossa, a change which does not occur in the anencephalic skull.

The anencephalic and normal prenatal lesser wing of the sphenoid is depository superiorly and resorptive inferiorly. This remodeling pattern coincides with the bulbus oculi expanding differentially more rapidly than the frontal lobes. The postnatal pattern of endocranial resorption relates to the much more massive differential growth of the frontal lobes, thereby accomodating its expansion. The petrous part of the temporal bone in the anencephalic, normal prenatal, and postnatal skulls all follow the same pattern of remodeling. This involves deposition on the medial

portion of the petrous ridge with resorption on the distant lateral portion. The petrous bone is characteristically depository ectocranially, and the middle and posterior cranial fossae are divided by this petrous elevation. The medial ridge elevation is depository so that as the floor of the fossae expand outward by resorption, the partitions between them enlarge inward, in proportion, by deposition. It is noted that the petrous part of the anencephalic temporal bone remodels in this manner even though it lacks the induction stimulus of normal temporal lobe development, but that the extent of the remodeling movements is severely constrained. Brain destruction, however, does not interfere with the normal development of the inner ear, and mandibular development also proceeds relatively normally. Otic and mandibular development provide stimulus for lateral and anterior expansion of the middle cranial fossa by the combination of endocranial resorption, ectocranial deposition and synchondrosis growth. The squama of the temporal bone in the anencephalic is resorptive ectocranially and depository endocranially, which is the reverse of the normal prenatal and postnatal remodeling pattern due to the lack of influence of the normally expanding temporal lobes. The causation of the resorptive ectocranial surface appears to be associated with a compressive effect on the surface. The developing brain is replaced by a mass of undifferentiated fibrovascular tissue which balloons over the walls of the vault aperature creating pressure on the ectocranial surfaces. The squamae thereby remodel in an inward direction rather than in an ectocranial direction.

The basilar part of the occipital bone is depository both ectocranially and endocranially in the anencephalic. The normal prenatal and postnatal remodeling pattern in contrast, is resorptive endocranially and depository ectocranially. This difference in remodelling pattern also relates to the lack of stimulus by the developing base of the brain. In the anencephalic, the lateral part of the occipital bone is largely resorptive on the endocranial side as in normal prenatal and postnatal skulls. This relates to the influence of the more or less normally developing spinal column in holoacrania anencephalics. The ectocranial surface is mostly depository, as in the normal prenatal and postnatal remodeling patterns, but with the exception of the approximate lateral one-quarter which is resorptive. This resorptive surface appears due to the compressive effect of the prominent fibrovascular mass found on this external surface area in the holoacrania anencephalic fetuses.

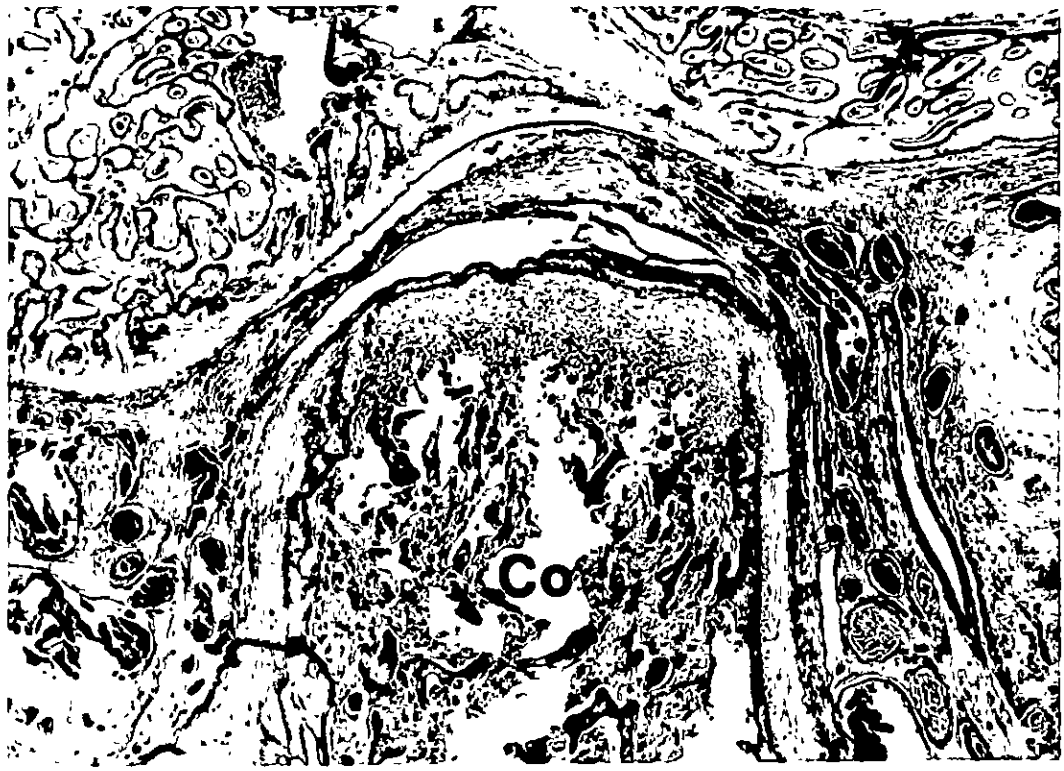
Mandible

The external buccal and lingual surfaces of the condylar neck of the anencephalic, normal prenatal, and postnatal mandible are resorptive. This permits the broad condylar head to be remodeled into the narrow neck as the neck becomes progressively relocated into areas previously held by the wider superoposterior growing condylar head. As in the normal condyle, the anencephalic condylar cartilage is also characterized by a cellular arrangement in which the growth zone does not have linear columns of daughter

cells (Plates XIX and XX). The posterior margin of the ramus in anencephaly, as in the normal prenatal and postnatal mandible, is depository. This keeps pace with posteriorly-moving condylar growth. The anencephalic, normal prenatal, and postnatal lingual surface of the sigmoid notch is depository and the buccal surface is resorptive, a combination producing the superior and posterior growth of the ramus in this region. The buccal surface of the coronoid process of the anencephalic is resorptive and the lingual side is depository, as in normal prenatal and postnatal mandibles, but the buccal forward-facing anterior margin is depository, unlike the normal pattern. In the anencephalic as well as the normal skull, the lingual surface of the coronoid process faces three directions all at once, posteriorly, superiorly, and medially, which represent its direction of growth movement. When bone is deposited on the lingual surface, growth proceeds superiorly, and an increase in vertical dimension results because the lingual surface faces superiorly. This is an example of Enlow's enlarging "V" principle, with the "V" oriented vertically. These same lingual deposits of bone produce a posterior direction of growth movement of the two coronoid processes. This is also an example of the expanding "V" principle, with the "V" oriented horizontally and its apex pointing anteriorly. These same lingual deposits carry the base of the coronoid process medially. This serves to lengthen the corpus, which lies on an axis well medial to the coronoid process. The area occupied by the anterior part of the ramus thereby becomes relocated and remodeled into the posterior part of

PLATE XIX

Sagittal section through condyle of mandible of fetus No. 1. Top-more anterior, bottom-more posterior. Low power (20X). Hematoxylin and eosin.


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Co

PLATE XX

Same view as in Plate XIX top, high power (200X) showing condylar cartilage.



the lengthening corpus. The forward-facing region of the lingual surface anterior to the temporal crest of the coronoid in the anencephalic and postnatal mandible faces away from the direction of movement and is resorptive. The buccal surface of the coronoid process faces away from the combined superior and posterior course of ramus growth and is resorptive. The buccal surface of the coronoid process moves in a posterior and cephalic direction by progressive reduction in transverse dimension resulting from addition of bone on the endosteal surface of the cortex and periosteal resorption. The anterior margin of the buccal surface of the coronoid process of the anencephalic is depository suggesting a rotation to a more upright position. Also the malpositioned zygomatic bone possibly affects the temporalis muscle's direction of insertion onto the anterior margin of the buccal surface of the coronoid process thereby redirecting its direction of growth in the anterior direction and causing this surface to be depository. The anencephalic, normal prenatal and postnatal ramus, the buccal surface below the lateral mandibular reversal line (Enlow, 1968) faces the posterior direction of ramus growth and is depository. The lateral mandibular reversal line is marked by the prominent change in contour along with the ridge that projects downward from the condylar neck across the upper portion of the ramus. The lingual side of the ramus of the anencephalic, normal prenatal and postnatal mandibles anterior and superior to this oblique ridge is characteristically depository, grading into the lingual tuberosity of the mandibular body superior to the mylohyoid line. This area

likewise conforms to the "V" principle with the "V" oriented in a horizontal direction with the apex pointed anteriorly. Periosteal deposits of bone on the lingual side moves the area formerly located as the anterior basal part of the ramus into line with the more lingually situated axis of the body and dental arch. The surface on the lingual side of the ramus below the ridge of the mandibular neck, the mylohyoid line, and the mandibular reversal line following this ridge is predominantly resorptive. A prominent change in topographic contour occurs inferior to the ridge. The buccal surface is depository. The remodeling pattern brings about a progressive, continuous drift of the entire buccal and lingual cortical plates in a lateral direction. The lateral node of remodeling also widens and separates the lower portions of the two rami from each other.

In the anencephalic, normal prenatal and postnatal mandibles, the lingual side of the mandibular body is resorptive and is involved in moving this part of the mandible in a buccal direction, opposite to that of the prominent overhanging tuberosity above it. This relocates the basal part of the posterior part of the corpus laterally to keep pace with the rest of the mandibular body as it moves in a buccal direction and increases in vertical dimension while undercutting the superior-growing lingual tuberosity. The lingual side of both the normal prenatal and anencephalic corpus in the incisor region is resorptive so as to contribute to a forward growth movement of the entire incisor region of the corpus. The remainder of the lingual side of the mandibular

body is depository in order to increase the medial as well as posterior dimension in conjunction with primary and secondary dentition development. The entire buccal surface of the anencephalic, normal prenatal and postnatal mandible is depository in order to provide for the posterior and lateral direction of growth of the mandible in concert with tooth bud development and the lateral expansion of the basicranium.

From the study of the anencephalic growth and remodeling process it is apparent that craniofacial growth and development involves more factors than just ectocranial accretion, endocranial resorption, and endochondral replacement without need for brain development and its expansive influence, as earlier theorized by Brash (1934). Weidenreich (1941) was the first to consider the brain as a major determinant of the form of the mammalian skull. It was Sicher (1947) who first realized the importance of the links among neural growth, sutural growth, and synchondrosal growth. The present study harmonizes with Sicher's theory, however, that both the chondrocranium and the desmocranium are under strong genetic control with only minor remodeling of surface configuration subject to local epigenetic factors. It appears from this comparative study between normal and abnormal skull growth that only minor intrinsic genetic control is involved in craniofacial development, and without the epigenetic influence of other adjacent head structures, normal craniofacial shape, size, and position cannot be achieved. Scott (1953) modified Sicher's earlier hypothesis (that the primary controlling factors are only in the cartilage and the

periosteum) by adding that sutural growth is passive and can be altered by local and environmental factors. He considered the growth of the skull to be coordinated with the growth of adjacent head structures. Ford (1956) considered that cranial growth conforms to the neural pattern of growth, but that facial growth is independent of brain growth. The present study, in contrast, reveals anomalous shapes and positions of the anencephalic facial bones, and this appears to be due primarily to the abnormal development of the cranial base and calvaria. While the concept of the functional matrix (Moss, 1959) can explain the anomalous shapes, size, and positions of the anencephalic facial skeleton and cranial base, this theory cannot entirely explain the continuing presence of endocranial resorption and ectocranial deposition in the bones of the anencephalic calvaria and cranial base. The membranes of these bones appear to have some degree of intrinsic control to be able to produce remodeling in this manner in the absence of normal soft tissue pressure. Moss (1959) denies any intrinsic genetic control within the bones or cartilage. Moss (1971a) suggests that neurotrophic processes are at least in part involved in the growth and maintenance of the functional matrices and for the regulation of the craniofacial skeleton. The presence of normal-appearing cranial nerves and ganglion cells in the anencephalic cranial base and peripheral extensions in the facial skeleton may support the possible role of neurotrophic influence of nerves and ganglion cells on the cranial base and facial skeleton morphology and remodeling patterns. Enlow (1968) believes that the cranial base

has become epigenetically established to accomodate an interdependent association with the developing brain but can develop at least partially without the brain. According to Enlow, the face develops in conjunction with the cranial floor and the brain as well as its own soft tissues. In general, the remodeling patterns, sizes, shape, and position of the various bones in the anencephalic fetus can be explained by the concepts brought forward by Enlow in his theory of control of craniofacial morphogenesis. The cranial base and calvarial bones appear to have some intrinsic control (whether "genetic" or otherwise) to remodel by the process of deposition in order to produce skull growth in the absence of brain development. The anomalous shapes, size, and positions of the facial bones appear to be due to their articulation with the severely malformed cranial base for as the dentitions, muscles, glands, and sensory organ development all appear essentially normal.

SUMMARY AND CONCLUSIONS

The main objectives of this study were to investigate the remodeling patterns of the human anencephalic fetal craniofacial skeleton and to compare these patterns with those characterizing the normal prenatal and postnatal skulls. Serial sections of two anencephalic skulls of six and seven months menstrual age were analyzed for resorptive and depository surfaces. The remodeling patterns were then mapped for the entire face, calvaria, and cranial base. The anencephalic patterns were compared with normal prenatal and postnatal remodeling patterns and the similarities and differences were evaluated.

It was determined that the remodeling patterns of the anencephalic fetal skull were much the same as in the normal prenatal skull with certain areas resembling the postnatal patterns. The notable exceptions were:

1. the endocranial surface of the basioccipital part of the occipital bone, which was depository;
2. the squamous portion of the temporal bone, which displayed resorption ectocranially and deposition endocranially;
3. the medial half of the posterior wall of the orbit, which resembled the early normal prenatal pattern with resorption orbitally and deposition on the dural side;
4. the pterygoid plates, which were entirely depository;
5. the forward facing anterior margin of the buccal surface of the coronoid process, which was depository; and

6. lack of formation of the posterior margin of the foramen magnum.

There was an observed anterior and lateral constriction to the anencephalic anterior, middle, and posterior cranial fossae, increasing in severity in the order listed. The bones of the calvaria were lacking or rudimentary in size. Some of the facial bones were severely affected in morphology, size, and spatial relationships. The zygomatic bone had a superior and posterior inclination. The squamae of the frontal bone were collapsed horizontally and diverged posteriorly and laterally. This study implicates a relationship between soft tissue development and the process of remodeling and craniofacial form, with bone remodeling and craniofacial form appearing to represent a response to soft tissue development. Bone-soft tissue relationships were seen in the movement of foramina and their nerves in directions that maintain constant positional relationships. Lack of or minimum development of the neural mass resulted in minimum anterior and lateral displacement of the anterior and middle cranial fossae. The anteriorly constricted anterior cranial fossae resulted in a retruded positioning of the nasomaxillary complex. In the medial half of the posterior wall of the orbit, the abnormal posterior direction of growth appears to be in direct response to the rapid growth of the bulbus oculi into a region either lacking or having a minimum extent of frontal lobe development in the anencephalic fetus.

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