# THE MORPHOGENESIS OF THE PALATE AND ASSOCIATED STRUCTURES IN THE BABOON (*PAPIO CYNOCEPHALUS*)

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ABSTRACT

THE MORPHOGENESIS OF THE PALATE AND ASSOCIATED STRUCTURES IN THE BABOON (PAPIO CYNOCEPHALUS)

By

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This study was undertaken as the preliminary step in a series of studies dealing with the experimental production of orofacial anomalies in the baboon. A controlled breeding program was used to collect baboon embryos of known insemination ages. Serial sections of these embryos, ranging from 30 to 64 days, were studied microscopically and by graphic or wax reconstruction.

The olfactory system appears at 30 days, represented by the nasal placodes. By 33 days the nasal placodes have become nasal pits. This is followed by primary palate development at 36 days. At 40 days the palatine process of the maxillary process appears on either side of the tongue. Subsequent development produces antero-posterior and vertical lengthening of the palatine processes. Anteriorly the processes slant inferomedially toward the base of the tongue. Posteriorly they remain vertically orientated lateral to the tongue. At 46 days the middle section of the palatine process begins to rotate to a horizontal position superior to the tongue. By 47 days this rotation has brought the anterior two-thirds of the palatine processes into position superior to the tongue. Fusion of the processes

to each other and to the nasal septum is taking place. The posterior one-third of the palatine process is assuming a horizontal position by a transformational process of medial bulging and ventral regression. This area of palatine process transformation constitutes both the area of the presumptive hard palate in which the palatine bone is forming and the area of the soft palate. At 53 days the hard and soft palates are formed except for the uvula which remains divided until sometime after 64 days. Union of the palatine process mesenchyme in the presumptive hard palate is brought about by a fusion followed by the breakdown and dissolution of the epithelial layers which separate them. The areas of the palatine processes destined to become the soft palate are united by a merging process whereby the uniting mesenchymal areas push their epithelia posteriorly and no epithelial fusion takes place. Thus the soft palate is devoid of any epithelial remnants of fusion as are found in the hard palate.

Dental lamina development commences at 36 days and is evidenced by an epithelial thickening and slight indentation into the mesenchyme of the presumptive upper and lower jaws. The antero-posterior lengthening and enlargement of the indentation increases and at 40 days the anterior end of the maxillary dental lamina curves medially on the oral surface of the primary palate. By 43 days medial curving of the mandibular dental lamina is noted. At 46 days both maxillary and mandibular dental laminae have met at the midline. In addition, deciduous tooth buds representing the central and lateral incisors, canine and first molar teeth are present in both jaws. Continued tooth differentiation results in early cap stage lateral incisor and canine teeth and cap stage molar teeth in both jaws at 47 days. The central incisor remains in bud form. By 50 days the second molar tooth is present in the mandible in the early cap stage of development. By 53 days all teeth have reached the bell stage in both jaws except for the second molars which have reached the cap stage.

Meckel's cartilage anlage is present at 36 days and is characterized by chondroblasts at 39 days and chondrocytes at 40 days. At this time maxillary and mandibular osteoblasts differentiate. Ossification of these and the premaxillary bone commences at 45 days. Palatine bone ossification begins at 47 days and nasal and vomer bone ossification begins by 53 days.

The nasal septum anlage appears at 36 days while the paraseptal cartilage anlage is noted at 37 days. The lateral nasal capsule and anterior transverse lamina anlagen differentiate by 40 days. The nasal septum and lateral nasal capsule become partially cartilaginous at 45 days while paraseptal cartilage differentiation occurs by 46 days. The anterior transverse lamina becomes cartilaginous by 47 days.

The inferior nasal concha appears at 36 days and the middle nasal concha at 40 days. The superior nasal concha is present at 43 days. Cartilage extending from the lateral nasal capsule is found in the inferior nasal concha by 47 days and in the middle by 53 days.

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By

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# INTRODUCTION

In the past several years there has been an increasing interest on the part of the scientific community in the cause and prevention of congenital anomalies. One of the areas which has received a considerable measure of attention is cleft palate and cleft lip. Presently in the United States one child in every 750 is born with one or both of these defects (Morris and Greulich, 1968). In order to understand the etiology and mechanisms involved in the production of these defects, either singularly or in combination, much research has concentrated on their experimental production in mice, rats and rabbits. While such work has contributed much to the understanding of palate closure mechanisms, additional studies in other species, particularly nonhuman primates, might provide assistance in relating these findings to man.

A prerequisite to any study of abnormal development is a knowledge of the normal development. The purpose of this study is to describe the normal morphogenesis of the primary and secondary palates and associated structures in a nonhuman primate, the baboon. This project was undertaken as the initial step in a study of the production of orofacial anomalies, specifically cleft palate, in this laboratory primate. It is hoped that the information presented here will provide some basis for future interpretation of both normal and abnormal palates, experimental or natural, in laboratory animals and that this work on a nonhuman primate will further aid in the interpretation of palate development in man.

## REVIEW OF THE LITERATURE

Normal palate development has been studied in several species including man. The closure of the palate was reported in three strains of mice by Walker and Fraser (1956) and this work involved gross as well as microscopic observations. Histochemical, electron microscopic and radioautographic studies were carried out by Walker (1961) in the same species. Further histochemical and radioautographic work in the mouse was performed by Larsson (1962). Additional studies on the movement of palatine processes in the mouse were reported by Ross and Walker (1967).

Rat palate closure was studied by Asling *et al.* (1960). In 1963 Moriarty *et al.* published on *in vivo* and *in vitro* fusion of rat palatine processes and Zeiler *et al.* (1964) worked on the morphology and time of closure in this species. Coleman (1965) and Poswillo and Roy (1965) also published accounts of palatine closure in the rat.

The morphogenesis and closure of the palate in man has been the subject of several investigations. Bergengrün (1909) described the development of the palatine raphe. Peter (1924) as cited by Walker and Fraser (1956), reviewed the subject of secondary palate closure in mammals. Polzl (1904) and Pons-Tortella

(1937) also reported on the development of the human palate. Fischel (1929) described the fusion of the palatine processes as did Hochstetter (1936). Early work in the area of human palate development was also furnished by His (1901), Retzius (1906), Sicher (1915) and Frazer (1911, 1931). More recent studies include those by Streeter (1951), Fulton (1957), Wood and Kraus (1962), Scott (1966), Yokoh (1967), Burdi and Faist (1967) and Burdi (1968b).

One study on the development of the palate in nonhuman primates has been reported. Asling and van Wagenen (1967) published a brief account of gross observations of the palate in three rhesus monkey embryos during palate formation.

Embryonic bone development in the palate region of human embryos has been widely studied. Reports on premaxillary and maxillary ossification have been made by Fawcett (1911), Chase (1942), Wood Jones (1947), Woo (1949), Dixon (1953), Shepherd and McCarthy (1955), Kraus (1960), Kraus and Decker (1960), Burdi (1965) and Wood *et al.* (1967). Palatine bone ossification was described by Fawcett (1906) and Kraus (1960) and mandibular ossification by Gardner (1956).

Dental arch development has been reported by several investigators in man. More recently Burdi and Lillie (1966) published an account of maxillary dental arch formation and Burdi (1968a) gave a similar report on the mandibular dental arch.

The development of the nasal cavity was studied by Schaeffer (1910), Wen (1930), Scott (1953, 1959), Stark and Ehrmann (1958) and

Warbrick (1960, 1963). Pearson (1941) described the development of the olfactory nerve.

The morphogenesis of the vomeronasal organ and the naso-palatine ducts was described by Noyes (1935), and Negus (1956).

# MATERIALS AND METHODS

## SPECIES, HOUSING AND FEEDING

The baboons (*Papio cynocephalus*) used in this study were trapped in Kenya, East Africa and shipped to San Antonio, Texas. Complete quarantine procedures were carried out in Kenya and San Antonio before the baboons were used in the embryology studies (Hummer, 1967). The animals were housed in individual cages which were grouped so that 11 females and one male were in visual contact with each other (Hendrickx and Kriewaldt, 1967). Each male was used for matings only in the group of females which had been in visual contact with him. The cages were cleaned twice daily with water and twice weekly by a portable pressurized steam cleaner. The animals were fed a special formula baboon ration (Ralston Purina Company, St. Louis, Missouri) four times per day such that each animal received approximately 20 gm ration/kg body weight/day which contained isoniazid (5 mg/kg/day). Water was available *ad libitum* via a displacement valve which was activated by the animal.

## MENSTRUAL CYCLE AND BREEDING

The menstrual cycle of *Papio cynocephalus* has been reported by Hendrickx (1967) and Hendrickx and Kraemer (1968). The length of the cycle is subject to individual variation with an average of 33 days as measured from the onset of menstrual bleeding until the onset of the next menstrual bleeding. The range of the cycle lengths was 18-52 days. Menses are not extensive and occur sometimes without external signs of blood. They last approximately three days.

The changes in size and color of the perineal area (sex skin) provide the most practical evaluation of the stage of the menstrual cycle and its corresponding hormonal activity. As the cycle progresses from menstruation to ovulation the sex skin swells with subcutaneous fluid and becomes shiny and smooth as the skin is stretched. These changes reach a peak at ovulation after which the process is reversed and the amount of fluid is reduced. Subsequently the size of swelling decreases and the skin becomes dull and wrinkled again. Observations of the degree of perineal swelling and color were made daily and recorded on the basis of a 0 to 4 arbitrary rating with 0 indicating perineal rest and 4, maximum turgescence with 2 and 3 as intermediary levels. Because of individual variation it was necessary to be familiar with each animal and its past record when applying this grading scale to determine the optimal day of mating. The changes in the sex skin were divided into four stages: 1) perineal turgescence; 2) maximum turgescence; 3) perineal deturgescence;

and 4) perineal rest.

1. Perineal turgescence (Figure 1). This stage or progression of changes lasts four days and is usually accompanied by menstruation at its initiation. It is characterized by a progressive swelling of the labia majora and clitoris as well as adjacent perineal skin. During the process of swelling the skin wrinkles are lost and a shiny appearance as well as color change from pink to red is noted.

2. Maximum turgescence (Figure 2). During this stage the sex skin is fully distended and colored a bright pink or red. The skin is sometimes stretched to the point of cracking and some bleeding from these cracks may be noted. The clitoris is enlarged so as to extend between the legs. Based on controlled single matings and other information, ovulation has been determined to occur most frequently on the third day prior to the beginning deturgescence. Optimal conditions for a successful pregnancy occur when mating takes place on this day, although successful matings were recorded as early as the seventh day predeturgescence. The stage of maximum turgescence lasts between five and 20 days.

3. Perineal deturgescence (Figure 3). Approximately three days after ovulation the perineal color begins to change to a dull pink and the size of the clitoris begins to decrease. This is rapidly followed by a decrease in size of the rest of the sex skin and is accompanied by the reappearance of wrinkles in the skin of this area. Deturgescence occurs as fast or faster than the preceding turgescence

and lasts approximately four days.

4. Perineal rest (Figure 4). During this stage the sex skin consists of many wrinkles and a dull pink to gray-white color. The labia majora and clitoris are small and inconspicuous. Perineal rest may vary from five to 15 days, and is followed by menstruation and a new cycle if pregnancy has not been initiated.

As mentioned above optimal conditions for a successful pregnancy occur when mating takes place on the third day before deturgescence. By inspection of the animal's previous menstrual cycle mating is carried out on the expected third day prior to deturgescence by placing a male in the cage with the female for 12 hours or less if mating is observed sooner. A vaginal smear is taken at the end of the mating period to confirm the presence of sperm. By this process embryos can be obtained whose insemination ages are known within a 12 hour period. Normal deturgescence and perineal rest follow the period of maximum turgescence. If the animal continues in a state of perineal rest beyond the time of expected recycling, pregnancy may be suspected. Palpation of the uterus via the rectum after day twenty of pregnancy usually will confirm the pregnancy. In addition, the perineal area of a pregnant baboon becomes pink-red but usually remains relatively unswollen.

Using the information given above pregnancies were initiated and embryos of known insemination ages were collected at various stages of development.

## COLLECTION OF EMBRYOS AND PREPARATION OF SERIAL SECTIONS

Table 1 summarizes the data on the materials used in this study. The insemination ages of the embryos were based on single matings of up to 12 hours as described above and the day of mating was considered day zero. At the desired insemination age the embryos were delivered by Cesarean section by the surgical team at the Southwest Foundation for Research and Education according to the method of Clayborn *et al.* (1967).

The embryos were fixed in 10% buffered formalin, Bouin's fluid or FAA (5 parts formalin, 5 parts glacial acetic acid, and 90 parts 80% ethyl alcohol). Following paraffin embedding the embryos were sectioned frontally or transversely at 6 to 10 microns. Complete serial sections of the embryo or in some cases the head alone were mounted and stained with hematoxylin and eosin. Preparation of the embryos was done by technicians at the Southwest Foundation for Research and Education.

## RECONSTRUCTION OF EMBRYOS AND PHOTOGRAPHY

The head and neck regions of the embryos studied were reconstructed graphically or with wax. The nasal and oral cavities were also modeled in the wax reconstructions. The graphic reconstructions were prepared by the method of Gasser (1967) and the wax

TABLE 1

EMBRYOS USED IN STUDY

| CASE NO. | INSEMINATION AGE IN DAYS | CROWN-RUMP LENGTH IN MM |
|---|---|---|
| A64-102 | 30 | 4.3 |
| A65-196 | 30 | 5.8 |
| A64-83* | 30 | 6.0 |
| A65-160 | 30 | 6.0 |
| A64-72 | 32 | 7.2 |
| A65-116 | 33 | 6.9 |
| A64-101* | 33 | 9.0 |
| A65-336** | 36 | 11.6 |
| A65-197** | 37 | 14.8 |
| A64-96** | 39 | 16.5 |
| A64-91** | 40 | 16.3 |
| A68-93 | 41 | 17.8 |
| A67-271** | 43 | 18.1 |
| A65-103** | 45 | 18.3 |
| A65-97** | 45 | 19.4 |
| A68-53** | 46 | 24.0 |
| A65-127** | 47 | 27.6 |
| A64-94** | 50 | 28.0 |
| A67-41** | 53 | 39.6 |
| A68-55** | 53 | 48.0 |
| A66-80** | 54 | 36.0 |
| A65-126 | 54 | 39.4 |
| A68-54 | 60 | 56.0 |
| A66-78 | 64 | 63.0 |

* graphically reconstructed
** reconstructed with wax

reconstructions after the method of Born (1883, 1888). From both types of reconstructions a drawing of the right side of the embryo's head was made with the section levels indicated. Drawings were also made of the palate region of the wax reconstructions. Following microscopic examination of the serial sections, the location, arrangement and extent of the structures studied were plotted on the drawings.

Photographs of selected sections were taken on a camera microscope ULTRAPHOT II (Carl Zeiss, Inc., New York) using a 4" x 5" photo head.

# RESULTS

The development of the palate and its associated structures is a continuum of activities and like all embryological processes is not a static, stage by stage development of precise levels. However, for the purposes of description and discussion it is easier to consider it as such, bearing in mind that this classification is arbitrarily imposed for the sake of clarity and organization. Basically the development of the palate can be divided into two major divisions; the development of the primary palate and the development of the secondary palate. In general, observations on the baboon have been consistent with previously studied animals.

The primary palate develops as a horizontal bar of mesoderm which penetrates the nasal fin, an epithelial lamina formed at the inferior border of the deepening nasal pit. When the communication of the blind end of the nasal pit is established with the primitive oral cavity by the rupture of the bucconasal membrane, the primary nasal cavity is created superior to the primary palate. The aperture where the bucconasal membrane ruptured becomes the primary choana. The two primary nasal cavities and their choanae are separated by the nasal septum. The primary palate contributes to the formation of the central portion of the lip and the premaxilla. The alveolar ridge of the premaxilla bears the incisor teeth. In the adult baboon the premaxilla remains a separate and grossly definable bone.

The secondary palate develops posterior to the primary palate from mesodermal proliferations of the maxillary processes known as palatine processes. These palatine processes develop as vertical projections from the maxillary processes on both sides of the tongue. Further developmental changes cause them to move to a horizontal position above the tongue where they meet in the midline. With the midline fusion of the palatine processes on the same plane as the primary palate the primary nasal cavities are extended posteriorly as the secondary nasal cavities above the secondary palate. The maxillary and palatine portions of the hard palate, the soft palate, and the uvula compose the secondary palate. The posterior and inferior proliferation of the nasal septum coupled with an elevation and arching of the roof of the bucconasal cavity provide the partitioning and space superior to the tongue to allow the separation of the oral cavity from the nasal passages.

The report which follows will describe in detail the development of the above mentioned structures.

## 30 DAY EMBRYO

Reconstruction drawing in Figure 5 indicates the level of sections shown in Figures 6 and 7.

### Nasal Placode

The nasal placodes first appear on the anterolateral region (frontal aspect) of the head as bilaterally thickened, circumscribed areas of a multilayered ectoderm (Figure 6). The undifferentiated mesenchyme between the brain and the olfactory ectoderm has become slightly condensed immediately deep to the nasal placode.

### Mandibular Process

The paired mandibular processes are not united anteriorly at this stage (Figure 6). The maxillary processes are forming from the mandibular processes as swellings of condensed mesenchyme (Figure 7). The tuberculum impar is noted developing posterior to the hyoid arch.

## 33 DAY EMBRYO

Reconstruction drawing in Figure 8 indicates the level of sections shown in Figures 9 and 10.

### Nasal Pit

The mesenchyme which surrounds the nasal placode has proliferated resulting in an elevation of its margins. These elevations become quite prominent and are known as the medial and lateral nasal processes (Figure 9). The depressions thus formed are rectangular and are located on the frontal surface of the head.

These depressions, the nasal pits, extend in a anteroposterior direction. At the posterior end of the pit opening, the tip of the maxillary process contributes to the inferolateral margin of the nasal pit (Figure 9). The epithelium which separates the mesenchymes of the maxillary process and medial nasal process is the nasal fin (Streeter, 1951) which will later be penetrated by the mesenchymes of these processes forming a bridge of mesenchyme which is the primary palate. The nasal pits are rather widely separated by the mesenchyme of the medialnasal processes. This separation will later attenuate until only a narrow tissue partition, the nasal septum, divides the nasal cavities.

### Mandibular and Maxillary Processes

The mandibular processes have met in the midline and the maxillary processes are well developed (Figure 10). The anlage of Meckel's cartilage is first noted at this age as a condensation of mesenchyme immediately medial to the mandibular division of the trigeminal nerve (Figure 10). The lateral lingual swellings are also noted at this level.

## 36 DAY EMBRYO

Reconstruction drawing in Figure 11 indicates level of sections shown in Figures 12 through 16.

### Primary Palate

There has been an anterior development of the upper facial region (Figure 11). The opening of the nasal pit anterior to the primary palate corresponds to the external naris and opens toward the heart (Figure 12). The laterial nasal processes are prominent. The primary palate has formed as a continuous bar of mesenchyme extending from the midline area inferior to the nasal septum anlage, laterally to the maxillary process mesenchyme (Figure 13). This bar of mesenchyme extends through the nasal fin epithelium which is still present at the posterior edge of the primary palate as the bucconasal membrane which was not penetrated by the mesenchyme (Figure 14). This membrane now separates the blind end of the primary nasal cavity from the bucconasal cavity. The bucconasal cavity is bounded superiorly by the nasal septum anlage, laterally by the maxillary processes and inferiorly by the lower jaw. The nasal chambers located superior to the primary palate are the primary nasal cavities. A midline condensation of mesenchyme, which separates the primary nasal cavities, has occurred in the medial nasal process area. This condensation, representing the anlage of the nasal septum cartilage (Figure 14), extends from a point located immediately posterior to the external naris to the end of the nasal cavity posterior to the premaxilla.

## Nasolacrimal Duct

The epithelial mass which will give rise to the nasolacrimal duct is evident at this age. It originates from the laterial surface of the head between the superior aspect of the maxillary process and the lateral nasal process. It extends inferomedially (Figure 14) and anteriorly to end as a solid core of epithelial cells approximately midway between the floor of the primary nasal cavity and the lateral surface of the head (Figure 13). The anterior end of the nasolacrimal duct anlage is located at approximately the middle of the anteroposterior dimension of the primary palate.

## Olfactory Nerve and Olfactory Bulb

Fibrous projections of cells from the epithelium of the superior and medial aspect of the primary nasal cavity represent the development of the olfactory nerve (Figure 13). These fibers pass anterosuperiorly and are continuous with the area of the brain from which the olfactory bulb will develop.

## Nasal Conchae

The first indication of the nasal conchae is found as a medial projection of the lateral wall of the primary nasal cavity (Figure 13). This projection, the maxillary fold, will become the inferior nasal concha and extends anteriorly from a point anterior to the bucconasal membrane. The anterior end is located posterior to the anterior end of the nasal septum anlage. The epithelium lining the primary nasal cavity beginning at the posterior extent of the olfactory nerve is thickened and projects into the primary nasal cavity from its superior aspect. This constitutes the ethmoid fold which will differentiate into the middle and superior nasal conchae. The ethmoid fold extends posteriorly beyond the primary palate (Figure 14).

## Tongue and Bucconasal Cavity

The anterior aspect of the tongue is now located immediately posterior to the developing primary nasal cavities (Figure 15) where the bucconasal cavity is beginning to develop an elevated appearance. The areas from which the palatine processes will develop form a rounded right angle on both sides of the developing tongue. Further posteriorly, the elevation of the bucconasal cavity is more marked and the tongue incompletely fills this area, (Figure 16). The palatine processes are slightly more angular in appearance.

## Dental Lamina

The maxillary dental lamina (Figure 14) is first observed as a short, shallow epithelial thickening and mesenchyme indentation on the oral surface of the maxillary process. It extends from a point immediately anterior to the bucconasal membrane to a position posterior and lateral to this membrane. The maxillary dental lamina becomes thinner and is not evident posterior to the primary nasal cavities.

The mandibular dental lamina is similar to the maxillary dental lamina. It extends from a position immediately anterior to the tongue to a point lateral to the anterior portion of the tongue.

## Meckel's Cartilage

The anlage of Meckel's cartilage has lengthened. Anteriorly it consists of a bilateral aggregation of mesenchyme located inferior and slightly lateral to the anterior portion of the tongue (Figure 15). Posteriorly the anlage enlarges, is situated more laterally, and is found between the inferior dental and lingual nerves (Figure 16).

## 39 DAY EMBRYO

Reconstruction drawing in Figure 17 indicates the level of sections shown in Figures 18 through 22.

### Primary Palate

The external naris continues to open toward the heart, however, a slight lateral angulation is now evident (Figure 18). The configuration of the posterior end of the primary palate is still noted to be a lateral extension of the premaxillary mesenchyme at the inferior border of the nasal septum (Figure 20). The epithelial abuttment which forms the nasal fin thins to become the bucconasal membrane (Figure 20). The anlage of the nasal septum cartilage has extended anteriorly and is now located between the posterior ends of the external nares (Figure 18). The anlagen of the paraseptal cartilages are evident as bilateral mesenchymal condensations inferior and lateral to the nasal septum anlage (Figure 19). They extend along the posterior half of the nasal septum which now protrudes slightly posterior to the primary palate.

### Nasolacrimal Duct

No distinct advances have occurred in the development of this duct from those described in the 36 day embryo. Its origin is noted in the nasolacrimal groove (Figure 20) which separates the maxillary process from the lateral nasal process on the surface of the head, and it ends anteriorly and medially as a clump of epithelial cells (Figure 19).

## Olfactory Nerve and Olfactory Bulb

The olfactory nerve fibers arise from the medial and superior epithelium of the primary nasal cavity (Figure 20) and pass antero-superiorly to meet the olfactory bulb (Figure 19). The olfactory bulb has extended posteriorly and inferiorly below the telencephalon to a point immediately anterior to the primary choanae. No vomero-nasal organ is noted on the medial wall of the primary nasal cavity, however, a distinct bundle of nerve fibers is observed anterior to the olfactory nerve which supplies the epithelium in the area which will become the vomeronasal organ (Figure 19).

## Nasal Conchae

The maxillary fold (Figure 19) has lengthened and now extends posteriorly beyond the anterior aspect of the bucconasal membrane. The ethmoid fold (Figure 20) has not undergone any additional development and is still represented by a thickened epithelium and mesenchymal projection at the superior aspect of the primary nasal cavity.

## Tongue and Bucconasal Cavity

The anterior aspect of the tongue still lies posterior to the primary palate while the bucconasal cavity has become markedly elevated (Figure 21). The palatine processes have not developed as distinct projections in this area and retain a right angle configuration on either side of the tongue. Further posteriorly (Figure 22) the body of the tongue almost completely fills the elevated bucconasal cavity and the palatine processes are evident as slight projections from the maxillary tissue toward the base of the tongue.

## Dental Lamina

The portion of the maxillary dental lamina located anterior to the bucconasal membrane is composed of an epithelial thickening (Figure 20). Posteriorly this epithelial thickening forms a slight indentation into the underlying mesenchyme immediately anterior and lateral to the bucconasal membrane. This indentation decreases posteriorly along the oral surface of the upper jaw and is not apparent posterior to the primary nasal cavity.

The mandibular dental lamina is evident as an epithelial thickening and slight indentation lateral to the anterior portion of the tongue (Figure 21).

## Meckel's Cartilage

The anlage of Meckel's cartilage is closer to the midline anteriorly. It extends posterolaterally from a point anterior to the tongue to a position medial to the inferior dental nerve (Figure 21). At the level of the origin of the lingual nerve chondroblasts are located inferior to the inferior dental nerve (Figure 22).

## 40 DAY EMBRYO

Reconstruction drawing in Figure 23 indicates the level of sections shown in Figures 24 through 31.

### Primary Palate and Palatine Process

The upper jaw now projects anteriorly beyond the plane of the forehead (Figure 23). The bucconasal membrane is no longer observed (Figure 26) and in its absence the primary choana is established as the communication between the primary nasal cavity and the bucconasal cavity, and the first stage of the oral bypass is completed. The configuration of the posterior edge of the primary palate has changed from that found in younger embryos. The lateral extension of the primary palate from the mesenchyme inferior to the nasal septum into the maxillary mesenchyme is no longer evident. This union is now brought about by a medial projection of maxillary mesenchyme representing the anterior portion of the developing palatine process (Figure 26) and constitutes the anterior boundary of what will become the nasopalatine duct. Posteriorly, at the tip of the tongue, the palatine processes appear as rounded blunt projections of maxillary mesenchyme whose inferior borders contain a thin layer of condensed mesenchyme (Figure 27). Along the body of the tongue and posterior to the developing nasal septum, the palatine processes become elongated and project toward the base of the tongue (Figure 31). The condensation of mesenchyme within the process is very evident. The external naris now opens laterally instead of toward the heart due to the anterior development of the primary palate (Figure 24). Posterior to the external naris, the lumen of the primary nasal cavity is reduced by an epithelial proliferation. This results in the formation of an epithelial plug which incompletely fills the primary nasal cavity for a short distance.

Nasal Septum and Capsule

Anteriorly the condensation of mesenchyme forming the nasal septum anlage is very evident (Figure 25) and the thickness of the tissue separating the primary nasal cavities has attenuated. The nasal septum condensation appears to join inferiorly with the premaxillary mesenchymal condensation which is continuous laterally with maxillary mesenchyme. In addition, bilateral mesenchymal condensations are now evident lateral to the primary nasal cavities. They represent the anlagen of the lateral nasal capsule. The medially concave areas of condensation are continuous for a short distance posteriorly with the nasal septum anlage at its superior aspect. At the level of the middle nasal concha the inferior aspect of the lateral nasal capsule anlage becomes spherical and is located lateral to the inferior nasal concha (Figure 27). In the middle of the posterior half of the primary palate the inferior end of the lateral nasal capsule anlage extends inferomedially and is in close approximation and will later join and become continuous with the inferior end of the nasal septum for a short distance. This proliferative extension constitutes the anterior transverse lamina anlage which is continuous with the paraseptal cartilage anlage posteriorly

(Figure 26). The paraseptal cartilage anlage projects inferolaterally from the nasal septum along most of its length at this age. The nasal septum now projects posteriorly beyond the primary palate (Figure 27). The inferior border of the nasal septum recedes into the roof of the bucconasal cavity near its termination (Figure 30). The paraseptal cartilage anlage is only slightly evident and the lateral nasal capusle anlage is present as a spherical condensation whose center is located laterally and slightly inferior to the nasal septum anlage.

Nasolacrimal Duct

The central area of the strand of epithelial cells which comprises the nasolacrimal duct is noticeably less cellular and filled with fibrous processes. In addition, there has been some lengthening of the duct due to the anterior development of the facial region so that the solid termination of the duct is now located anterior to the anterior transverse lamina anlage and inferior to the lateral nasal capsule anlage (Figure 25).

Olfactory Nerve, Olfactory Bulb and Vomeronasal Organ

The olfactory nerve fibers arise from the epithelium lining the superior and medial aspect of the nasal cavities from an area anterior to the developing middle nasal concha (Figure 26) to the posterior end of the superior nasal concha (Figure 29). These fibers join the olfactory bulb (Figure 28) which extends from the telencephalon superior to the middle and superior nasal conchae. In addition, fibers from the olfactory nerve proceed anteriorly in the nasal septum tissue to the vomeronasal organ which has developed on the lower half of the medial wall of the primary nasal cavity across from the inferior nasal concha (Figure 26). The vomeronasal organ consists of a shallow indentation of epithelial cells which have elongated and whose nuclei have become basally located. The anterior end of the organ is located anterior to the primary choana and it extends posteriorly beyond the area of palatine process fusion to the lateral aspect of the primary palate.

Nasal Conchae

The inferior nasal concha has lengthened and extends from a point anterior to the primary choana (Figure 26) to a position over the body of the tongue (Figure 28). The ethmoid fold has differentiated into two separate structures, the middle and superior nasal conchae. The middle nasal concha develops superior to the middle third of the inferior nasal concha. Anteriorly it is preceded by a lateral indentation of epithelium into the mesenchyme forming the lateral wall of the primary nasal cavity. This constitutes the middle nasal meatus. The middle nasal concha projects medially into this meatus and anteriorly (Figure 27). It is composed of a mesenchymal core and an epithelial covering. Superior and posterior to the middle nasal concha and superior to the posterior end of the inferior nasal concha the superior nasal concha is noted as an epithelial thickening (Figure 29) of the superolateral portion of the nasal cavity.

## Tongue

The tip of the tongue now protrudes anteriorly beyond the point of attachment to the floor of the bucconasal cavity (Figure 27). This short protrusion coupled with the posterior development of the nasal septum and anterior development of the lower jaw brings the tip of the tongue to a position immediately inferior to the nasal septum at the level of the middle nasal concha.

## Dental Lamina

The maxillary dental lamina has lengthened and the area of epithelial thickening begins to curve medially to form the anterior portion of the dental arch (Figure 25). The area of indentation begins anterior to and passes through the level of the anterior transverse lamina anlage. It becomes shallower and wider immediately anterior to the superior nasal concha (Figure 28). The dental lamina continues posteriorly from this point for a short distance as an epithelial thickening.

The mandibular dental lamina has not changed significantly from that described in the 39 day embryo. It remains the same length but due to the posterior development of the nasal septum and fusion of the palatine processes to the lateral aspect of the primary palate, the mandibular dental lamina comes to lie inferior to these structures (Figure 26).

Maxillary Bone

The first indication of maxillary bone formation is found in the 40 day embryo. A cluster of osteoblasts is located superior to the dental lamina and anterior to the primary choana (Figure 26) and extends posteriorly beyond the choana. The intercellular space is filled with fibers and a hyalinized ground substance is absent at this stage.

Meckel's Cartilage and Mandibular Bone

The anterior portion of Meckel's cartilage anlage has approached the midline in the area of the anterior tongue (Figure 27). Posteriorly the structure assumes a more lateral position and chondroblast differentiation is again noted (Figure 28). As the cartilaginous mass approaches the inferior dental nerve a distinction between central and peripheral areas of the mass is noted (Figure 29). The peripheral layer of cells, the chondroblasts, form a ring around the larger central area where the cells entrapped in matrix can now be recognized as chondrocytes and are situated in smooth walled lacunae within the basophilic ground substance. Posteriorly in a more differentiated region near the lingual nerve these lacunae are very obvious (Figure 31).

Anterior to Meckel's cartilage in the midline the first indication of mandibular bone development is noted consisting of a cluster of osteoblasts. Posteriorly the bony tissue is located laterally and becomes localized superior to the inferior dental nerve and more posteriorly the bone partially encircles the nerve (Figure 26). Finally the bone comes to be situated inferior to the nerve (Figure 27) and is not present in the area where Meckel's cartilage is in close approximation to the medial aspect of this nerve.

## 43 DAY EMBRYO

Reconstruction drawing in Figure 32 indicates the level of sections shown in Figures 33 through 40.

### Primary Palate and Palatine Process

Both the upper and lower jaws and the face have continued to develop anteriorly (Figure 32). The lower jaw appears to be lodged in a groove on the oral surface of the primary palate which is created by the maxillary processes lateral to the primary palate (Figure 34). The area of fusion between the primary and secondary palate (i. e. the area of fusion between the palatine process and the lateral aspect of the primary palate) has lengthened (Figure 36). At the anterior aspect of the tongue (Figure 37) the palatine processes are blunted projections whose apexes point toward the base of the tongue. Mesenchymal condensations are evident along their inferior margins. Posterior to the nasal cavities the processes have elongated and become more vertically oriented (Figure 40). The mesenchymal condensations have increased and fill the processes. The anteroposterior length of the palatine processes has increased beyond that found in younger embryos. This is associated with a similar increase in the same dimension of the bucconasal cavity. The posterior portion of the external naris continues to open laterally due to the anterior development of the primary palate in this area. The epithelial plug has lengthened and becomes concentrated along the inferior aspect of the primary nasal cavity and reaches posteriorly to the level of the inferior nasal concha (Figure 33).

## Nasal Septum and Capsule

The development of the nasal septum, lateral nasal capsule and paraseptal anlagen has not changed significantly from that described in the 40 day embryo.

## Nasolacrimal Duct

The nasolacrimal duct has lengthened in conjunction with the anteroposterior development of the face. It passes anteriorly and inferomedially from its origin at the nasolacrimal groove and comes into close approximation to the lateral aspect of the floor of the primary nasal cavity (Figure 35). From this point the duct passes anteriorly and terminates as a clump of epithelial cells inferior and slightly posterior to the anterior aspect of the inferior nasal concha. The developing lumen has become more evident (Figure 35).

## Olfactory Nerve, Olfactory Bulb and Vomeronasal Organ

The olfactory fibers arise from the superior and medial aspect of the primary nasal cavity epithelium along a line which parallels the inferior nasal concha (Figure 34). This line also encompasses the anterior aspect of the middle nasal concha (Figure 37). These fibers join the olfactory bulb which is located superior to the anterior half of the inferior nasal concha (Figure 35). The epithelium of the vomeronasal organ has thickened slightly and its innervation is clearly evident

(Figure 35).

## Nasal Conchae

The inferior nasal concha has lengthened somewhat and increased in height and medial projection (Figure 36). A greater increase in length has occurred in the middle nasal concha which now extends to the posterior limit of the inferior nasal concha. It has also increased in volume (Figure 37). The superior nasal concha has enlarged and is now composed of a mesenchymal core (Figure 38) which projects infero-medially from the superolateral aspect of the nasal cavity. The superior nasal concha now extends posteriorly beyond the inferior and middle nasal conchae. The inferior, as well as the superior, nasal meatuses are now evident (Figure 35, 38).

## Tongue

The unattached tip of the tongue has lengthened anteriorly and now extends to the level of the anterior portion of the middle nasal concha (Figure 37). The body of the tongue continues to fill the bucconasal cavity inferior to the nasal septum (Figure 39).

## Dental Lamina

The anterior portion of the maxillary dental lamina which is composed of an epithelial thickening has lengthened, curved medially, and approaches the midline from both sides on the oral surface of the primary palate (Figure 34). The area of epithelial indentation has lengthened and now extends from a point near the tip of the tongue

(Figure 37) posteriorly beyond the superior nasal concha level (Figure 39) where it becomes wider and shallower. The final posterior section of this dental lamina is represented by an epithelial thickening which extends to the posterior end of the palatine process.

The mandibular dental lamina has lengthened considerably. Anteriorly it curves medially near the tip of the tongue and forms a shallow indentation. Posteriorly it is in a more lateral location (Figure 38). It extends to a position superior to Meckel's cartilage where it is represented as an epithelial thickening with a slight indentation.

## Maxillary Bone

The cluster of maxillary osteoblasts has not lengthened but has increased in diameter slightly and has a more vertical orientation (Figure 37).

## Meckel's Cartilage and the Mandibular Bone

Meckel's cartilage and the mandibular bone are not significantly different from those described at 40 days.

## 45 DAY EMBRYO

Reconstruction drawing in Figure 41 indicates the level of sections shown in Figures 42 through 48.

### Primary Palate and Palatine Process

The anterior development of the premaxilla, maxilla and mandible continues resulting in a lengthening of the groove on the oral surface of the primary palate which contains the anterior projection of the lower jaw (Figure 43). The fusion of the palatine process to the lateral aspect of the primary palate continues in a posterior direction lengthening the presumptive nasopalatine duct area (Figure 44). In the area of the anterior portion of the tongue the palatine processes are thick and medially directed in a horizontal plane toward both sides of the tongue (Figure 45). Immediately anterior to the point where the tongue is attached to the floor of the bucconasal cavity the palatine processes become triangular in shape as the body of the tongue enlarges (Figure 46). The apexes of these processes are obliquely directed toward the undersurface of the unattached tongue. Posteriorly the palatine processes become more slender but maintain an oblique orientation (Figure 47). Posterior to the nasal cavities the palatine processes are vertically disposed on both sides of the tongue reaching almost to the floor of the bucconasal cavity (Figure 48). The lateral halves of these elongated projections are composed of condensed mesenchyme. The anterior development of the primary palate has caused the entire length of the external naris to open laterally. The length of the epithelial plug has increased and the amount of proliferation has increased such that the anterior one-third of the primary nasal cavity is almost completely filled (Figure 42). Posteriorly the size of the epithelial plug decreases and is localized in the inferior portion of the cavity back to the area of the inferior nasal concha.

Nasal Septum and Capsule

The posterior proliferation of the nasal septum continues approaching two-thirds of the anteroposterior length of the palatine processes. The mesenchymal condensation which characterized the nasal septum in younger embryos has differentiated into cartilage in all but the more anterior region of the septum (Figure 43). Cartilage differentiation has also occurred in the superior two-thirds of the lateral nasal capsule (Figure 43), however mesenchymal condensation is still prevalent in the anterior and posterior quarters of the lateral nasal capsule, which has also undergone considerable posterior extension. The length of the area of communication of the superior aspects of the nasal septum and lateral nasal capsule cartilages has increased posteriorly and reached a point near the middle of the middle nasal concha. The anterior transverse lamina anlage is evident as the communication between the inferior aspects of the lateral nasal capsule and nasal septum (Figure 43) and is continuous posteriorly with the paraseptal cartilage anlage (Figure 44). The length of this anlage has not changed and it extends posterior to the primary palate to the level of the unattached tip of the tongue (Figure 45).

## Nasolacrimal Duct

The nasolacrimal duct maintains its origin from the nasolacrimal groove and passes inferomedially to a position superolateral to the lateral aspect of the inferior nasal meatus (Figure 45). From this point the duct passes anteriorly in close proximity to the inferior nasal meatus and ends as a clump of epithelial cells slightly anterior to the inferior nasal concha.

## Olfactory Nerve, Olfactory Bulb and Vomeronasal Organ

The olfactory fibers arise from the superior and medial epithelium of the nasal cavity along a line which parallels the middle nasal concha, which has elongated (Figure 46). The olfactory bulb is located immediately superior to the nerve fibers. The vomeronasal organ is located medial to the anterior one-half of the middle nasal concha (Figure 46).

## Nasal Conchae

All three nasal conchae have lengthened and the middle and superior nasal conchae now extend posterior to the inferior nasal concha. The inferior nasal concha has developed a pendulous appearance at its inferior aspect which enlarges the inferior nasal meatus (Figure 45). As was mentioned above, this structure is associated with the developing nasolacrimal duct. A similar development in the middle nasal concha has enlarged the middle nasal meatus (Figure 46).

## Tongue

The unattached tip of the tongue has undergone a further lengthening and now extends anterior to the middle nasal concha (Figure 45).

## Dental Lamina

The epithelial thickenings which represent the anterior most portion of the maxillary dental laminae have approached the midline on the oral surface of the primary palate advancing the curvature of the anterior dental arch but are not yet continuous (Figure 43). The indented protion of the maxillary dental lamina has lengthened considerably and now extends from a point anterior to the inferior nasal concha (Figure 43) to a point posterior to the nasal septum.

The mandibular dental lamina remains essentially unchanged from that described in the 43 day embryo.

## Maxillary and Premaxillary Bones

The ground substance around the osteoblasts noted in the 43 day embryo as forming the maxillary bone has become calcified and bone spicules are now observed. Immediately anterior to the inferior nasal concha and superior to the dental lamina these spicules have a vertical orientation (Figure 43). This represents the frontal process. At the level of the primary choana the maxillary spicules become more spherical and maintain their position superior to the dental lamina (Figure 44). Maxillary calcification extends posteriorly to the level of the superior nasal concha.

Premaxillary spicule formation has occurred in the form of bilateral, horizontally oriented plates of bone which approach the midline beneath the nasal septum but are not continuous with each other. Anteriorly the premaxillary bone extends beyond the dental lamina and posteriorly it is found superior to this structure as the alveolar process (Figure 43) and is anterior to the area of the nasopalatine ducts.

## Meckel's Cartilage and Mandibular Bone

The bilateral mandibular bone processes approach each other near the midline as mesenchymal condensations with some spicule formation anterior to Meckel's cartilage (Figure 44). Posteriorly near the tip of the tongue these bony spicules separate and move laterally (Figure 45) and surround the inferior dental nerve at the level of the midline union of Meckel's cartilage. Posteriorly the bone persists on the lateral and inferior aspect of the inferior dental nerve and is no longer in contact with Meckel's cartilage (Figure 46) which has assumed a more lateral position. The mandibular bone reaches the level of the lingual nerve and remains lateral to the inferior dental nerve. Cartilage differentiation now extends to all but the anterior tip of the Meckel's cartilage.

## 46 DAY EMBRYO

Reconstruction drawing in Figure 49 indicates the level of sections shown in Figures 50 through 55.

### Primary Palate and Palatine Process

The anterior development of the upper and lower jaws continues (Figure 49). The length of palatine process fusion to the lateral aspect of the primary palate has remained unchanged (Figure 51). Immediately posterior to the nasopalatine duct area the palatine processes project inferomedially as blunt protuberances toward the superolateral portion of the tip of the tongue (Figure 52). At the level of the anterior tongue attachment to the floor of the bucconasal cavity (Figure 53) the palatine processes are triangular in shape and project inferomedially toward the base of the tongue. At the level of the superior nasal concha the palatine processes appear to be rotating to a horizontal orientation and are lifting the tongue in the process (Figure 54). This apparent movement has taken place in the middle of the anteroposterior length of the palatine processes. Posterior to the nasal cavity at the level of the origin of the lingual nerve the palatine processes are again obliquely oriented toward the base of the tongue (Figure 55) while at the posterior extent of the palatine processes a more vertical orientation exists. It is noted that the mesenchyme in the palatine processes which appear to be moving to a horizontal position is not condensed in the process itself but is condensed laterally (Figure 54), whereas in the oblique

(Figure 55) and vertical processes a mesenchymal condensation is present within the actual process. A mesenchymal condensation is apparent in the inferior and medial portions of the anterior region of the processes (Figure 52). Aside from anterior growth, little or no change has occurred in the external naris and the epithelial plug continues to almost completely seal off the primary nasal cavity.

Nasal Septum and Capsule

The posterior proliferation of the nasal septum has continued slightly and cartilaginous tissue is now found throughout the length of the nasal septum except for the anterior most portion. Cartilage differentiation has also continued in the lateral nasal capsule with only the most anterior and posterior portions existing as mesenchymal condensations. The paraseptal cartilage has now undergone cartilage differentiation throughout its length (Figure 51) with the exception of its most posterior section which is still composed of condensed mesenchyme. The anterior transverse lamina and the inferior portion of the lateral nasal capsule remain as a mesenchymal condensation (Figure 50).

Nasolacrimal Duct

The anterior termination of the nasolacrimal duct has now assumed a position immediately inferior to the anterior portion of the inferior nasal meatus (Figure 52) and the presumptive lumen in the vertical portion of the duct has enlarged.

## Olfactory Nerve, Olfactory Bulb and Vomeronasal Organ

No significant changes have occurred from those conditions described in the 45 day embryo (Figure 51).

## Nasal Conchae

All three nasal conchae have lengthened but maintain the same relationships to each other as previously described. The further development by mesenchyme condensation of the inferior portion of the lateral nasal capsule has brought this structure into the mesenchyme of the inferior nasal concha throughout most of its anteroposterior length (Figure 53). Such an occurrence has not yet taken place in the middle and superior nasal conchae.

## Tongue

Further anterior extension of the unattached tip of the tongue has occurred bringing it to a position anterior to the posterior extent of palatine process fusion to the lateral aspect of the primary palate. This forward movement is augmented by the anterior development of the lower jaw (Figure 49) previously noted. In addition to anterior development, the lower jaw appears to be lower than in earlier stages (Figure 54).

## Dental Lamina

The maxillary dental lamina indentations have completed their anterior curvature and meet at the midline. Posteriorly the indentation has also extended slightly beyond that described in the 45 day embryo.

In addition, four separate areas of proliferation of the dental lamina on each side are evident. They represent the deciduous central (Figure 50) and lateral incisors (Figure 51), canine and first molar tooth buds.

The mandibular dental lamina indentations have also completed their anterior curvature and meet in the midline (Figure 51). They also exhibit four sets of tooth buds corresponding to those described in the maxillary dental laminae. The mandibular dental lamina indentation has also undergone considerable posterior development and now extends posterior to the nasal septum, lateral to the tongue (Figure 55).

Maxillary and Premaxillary Bones

The maxillary bone spicules have lengthened and now extend from a point superolateral to the lateral incisor tooth bud (Figure 51) to a position posterior to the superior nasal concha. Anteriorly the frontal process has increased in height and width (Figure 52) and begins to extend inferiorly into close proximity to the dental lamina at the level of the canine tooth bud as a precursor to the outer alveolar process of this bone. The vertical orientation of the bone is noticed throughout its length (Figure 54) and no bony palatine process is yet visible.

The premaxillary bone has lengthened anteroposteriorly. The alveolar portion remains horizontally oriented superior to the dental lamina (Figure 50). The posterior section has a vertical projection representing the frontal process of the premaxillary bone which is located anterior to the nasopalatine duct area.

## Meckel's Cartilage and Mandibular Bone

No significant changes in Meckel's cartilage or the mandibular bone have occurred.

## 47 DAY EMBRYO

Reconstruction drawing in Figure 56 indicates the level of sections shown in Figures 57 through 66.

### Primary and Secondary Palates

The lower jaw has continued to undergo anterior development and now extends to the tip of the nose (Figure 56) while the primary nasal cavity remains filled with an extensive epithelial plug. The length of the nasopalatine duct area has remained unchanged (Figure 58), however, there has been a posterior proliferation of premaxillary tissue inferior to the nasal septum which separates the palatine processes from each other (Figure 59). The anterior two-thirds of the palatine processes are now located in a horizontal position superior to the tongue and are fusing with each other and the inferior border of the nasal septum. The epithelia which separate these three processes are thick and distinct anteriorly (Figure 60) but become irregularly thinner in the region approximating the middle of the anteroposterior length of the palatine processes (Figure 61). This area of fusion with an attenuated epithelium in the process of breakdown indicates the area of oldest fusion and corresponds roughly with that area of the palatine processes which was noted in the 46 day embryo as having begun to move to a horizontal position by rotation. Posterior to this area of epithelial dissolution the epithelia are less attenuated indicating more recent fusion (Figure 62). Near the posterior aspect of the superior nasal concha the palatine processes and nasal septum begin to separate from each other (Figure 64) and in the area medial to the anterior region of the palatine bone (Figure 65) the palatine processes are in the process of transforming by ventral regression and medial protrusion. This condition persists to the posterior portion of the palatine bone (Figure 66). Thus it would appear that the portion of the secondary palate which will become the hard palate first closes by medial rotation at its midpoint (based on 46 day embryo observations) and that fusion profressively takes place anteriorly and posteriorly from that point. In addition, the posterior hard palate area appears to become horizontal by a process of medial protrusion accompanied by ventral regression of the palatine process as opposed to rotation while the area of union of secondary to primary palate also occurs as the result of a medial bulging of the palatine processes.

Nasal Septum and Capsule

The posterior development of the nasal septum has continued along with cartilage differentiation. This has been paralleled by the posterior development of the cartilaginous lateral nasal capsule and a continued posterior development of the union of the lateral nasal capsule to the nasal septum at their superior aspects (Figure 62). The inferior end of the lateral nasal capsule which is located within the inferior nasal concha has become cartilaginous (Figure 61). The anterior transverse lamina has also become cartilaginous (Figure 57) and maintains its previous relationship to the paraseptal cartilage (Figure 58).

Nasolacrimal Duct

The origin of the nasolacrimal duct is more closely associated with the developing eye (Figure 62). No other changes with respect to its terminal relationship with the inferior nasal meatus are noted.

Olfactory Nerve, Olfactory Bulb and Vomeronasal Organ

The olfactory nerve fibers continue to arise from the epithelium lining the superior and medial aspects of the nasal cavities over the superior nasal concha and superior to the posterior half of the middle nasal concha (Figure 62). These fibers pass posteriorly and turn superiorly at the posterior extent of the superior union of the nasal septum and lateral nasal capsule (Figure 63) to join the olfactory bulb (Figure 64). The olfactory bulb extends posteriorly beyond the superior nasal concha and has been penetrated at its posterior end by an extension of the lateral ventricle of the brain (Figure 65). The vomeronasal organ is located immediately posterior to the anterior transverse lamina (Figure 58).

Nasal Conchae

All three nasal conchae have increased in length. The inferior concha now extends from a point near the middle of the nasopalatine duct (Figure 59) to a point slightly posterior to the level of the second molar tooth bud (Figure 63). The middle nasal concha (Figure 62) is found superior to the posterior half and slightly beyond the inferior nasal concha. The superior nasal concha (Figure 63) is located superior to the posterior half and slightly beyond the middle nasal concha. As mentioned above the mesenchymal extension of the lateral nasal capsule into the inferior nasal concha has become cartilaginous (Figure 62) and a similar mesenchymal condensation is found in the middle nasal concha.

## Tongue

The anterior development of the lower jaw and subsequent lengthening of the tongue has brought the tip of the tongue to a position anterior to the maxillary dental arch. The attached portion of the tongue is now located inferior to the nasopalatine duct (Figure 58). In addition, the tongue has now assumed a much flatter appearance and is not in close proximity to the fused palatine processes (Figure 62). The lower jaw is lower than in the previous stage, thus enlarging the oral cavity (Figure 60). The combined actions of depressing the lower jaw and flattening of the tongue appear to have removed the tongue from its previous position where it was lodged between the rotating palatine processes.

## Dental Lamina

Four sets of teeth in various stages of development are found within the maxillary dental lamina. The central incisor tooth is still represented by a tooth bud (Figure 57) while the lateral incisor

(Figure 58) and canine teeth (Figure 59) are in the early cap stage of development. The first molar dental organ has continued to differentiate and is in the cap stage of development (Figure 63) with the development of a dental papilla.

The four sets of developing teeth in the mandible have paralleled their counterparts in the maxillary dental lamina and are at the same level of differentiation (e.g. first molar, Figure 61).

Maxillary and Premaxillary Bones

The maxillary bone has not lengthened anteroposteriorly but has increased in size. At the level of the lateral incisor tooth (Figure 58) the maxillary bone spicules have increased in height while in the area of the canine tooth (Figure 59) the outer alveolar process has lengthened inferiorly to a considerable extent. The palatine process of the maxillary bone has now differentiated (Figure 61) and extends medially into the palatine process from the canine tooth to a point immediately anterior to the developing first molar tooth. The outer alveolar process comprises the posterior extent of this bone (Figure 62).

The alveolar process of the premaxilla (Figure 57) now extends from a point anterior to the dental lamina to the canine tooth and has become thicker. The frontal process shares in this posterior development arising from the posterior half of the alveolar process and reaching superiorly above the inferior portion of the lateral nasal capsule (Figure 58).

## Palatine Bone

The palatine bone has developed as a crescent shaped bar of vertical bone whose concavity faces medially and is located inferior to the lateral nasal capsule. It extends from a point posterior to the first molar tooth (Figure 64) posteriorly beyond the lateral nasal capsule (Figure 66).

## Meckel's Cartilage and Mandibular Bone

The anterior development of the lower jaw has moved the mid-line union of Meckel's cartilages further anteriorly where it exists as a mesenchymal condensation. The laterally positioned mandibular bone has increased in size and the outer alveolar process is evident anteriorly in the area of the canine tooth (Figure 57). In addition bone growth has occurred superior to Meckel's cartilage. Posteriorly the bone maintains its lateral position with respect to Meckel's cartilage in the form of a medially concave bar whose medial end is located inferior to Meckel's cartilage (Figure 61). At the level of the origin of the lingual nerve the concavity is more pronounced (Figure 63).

## 53 DAY EMBRYO

Reconstruction drawing in Figure 67 indicates the level of sections shown in Figures 68 through 77.

### Primary and Secondary Palates

The epithelial plug in the primary nasal cavity remains unchanged and the nasopalatine duct has also undergone no change (Figure 69). The palatine processes have now joined each other at the midline superior to the tongue extending to a point posterior to the palatine bone which includes the soft palate. The uvula remains unjoined at its posterior extent in the pharyngeal region (Figure 77). The epithelium which separated the palatine processes from each other has attenuated and has been reduced to clumps of epithelial cells. The epithelial remnants extend from the region of the nasopalatine ducts to a point near the posterior extent of the vertical portion of the palatine bone (Figure 75). Posterior to this point the soft palate exhibits no epithelial remnants. The absence of epithelial remnants in the soft palate (Figure 76) suggests that this structure is formed by mesenchymal merging and epithelial displacement as opposed to epithelial fusion.

### Nasal Septum and Capsule

The nasal septum has continued its posterior development and now reaches a point posterior to the palatine bone. In the posterior region of the nasal septum (Figure 76) the septal cartilage has receded superiorly and is continuous with the cartilage precursor of the sphenoid bone. Thus the septum is composed of soft tissue only from this point posteriorly. No further posterior development of the lateral nasal capsule has occurred. The posterior extent of the union of the superior aspects of the lateral nasal capsule and nasal septum has also remained unchanged. Anteriorly the lateral nasal capsule has extended into the area of the external naris. The anterior transverse lamina has remained unchanged (Figure 68), however the paraseptal cartilage has developed an anterior projection which is situated inferior to the anterior transverse lamina and premaxillary bone near the anterior end of the nasopalatine duct (Figure 68). Posteriorly this projection joins the inferior aspect of the paraseptal cartilage (Figure 69).

## Nasolacrimal Duct

Dorsal and ventral lacrimal ducts are now present arising from the medial aspect of the eyelids (Figure 71). These two ducts join the lacrimal sac (Figure 71) which is the dilated superior portion of the nasolacrimal duct. The blind end of the duct ends in close approximation to the anterior end of the inferior nasal meatus. The first indication of lacrimal bone ossification is noted as a vertical bar of bone in the area between the nasolacrimal duct and the lateral nasal capsule (Figure 71).

## Olfactory Nerve, Olfactory Bulb and Vomeronasal Organ

The olfactory nerve fibers continue to arise from the epithelium lining the superior and medial aspects of the nasal cavities over the superior and middle nasal conchae (Figure 72). In addition olfactory fibers now arise from the epithelium on the medial and lateral aspects of the middle nasal concha. The olfactory bulb ventricle extends further anteriorly and no change has occurred in the vomeronasal organ (Figure 69).

## Nasal Conchae

All three nasal conchae have increased in length posteriorly but maintain the approximate relationships described at 47 days. The cartilage in the inferior nasal concha extends throughout its length and the mesenchymal condensation noted at 47 days in the middle nasal concha has differentiated into chondroblasts anteriorly and into true cartilage posteriorly (Figure 72). The superior nasal concha has been divided into two conchae by the appearance of a supreme nasal meatus located superior to the superior nasal meatus (Figure 73). The supreme nasal concha thus formed extends along the posterior three-fourths of the superior nasal concha and is located inferior to the olfactory bulb. Anterior to the supreme nasal concha a small projection of cartilage extends from the lateral nasal capsule into the superior nasal concha.

## Tongue

The position of the tip of the tongue and the point of anterior attachment of the tongue to the floor of the oral cavity has remained relatively unchanged, however the height of the tongue is somewhat greater than that described in the 47 day embryo (Figure 72).

Dental Lamina

The maxillary dental lamina now contains five sets of teeth. The central (Figure 68) and lateral incisors (Figure 70), canine (Figure 71) and first molar (Figure 73) teeth are in the bell stage of development and the second molar is now present in the cap stage.

The mandibular teeth are present in the same number and stage of differentiation as their counterparts in the maxillary dental lamina (e. g. canine Figure 71).

Maxillary and Premaxillary Bones

The maxillary bone now extends from a point anterior to the canine tooth posteriorly to the second molar tooth. Anteriorly the frontal process has lengthened superiorly and anteroposteriorly and is found lateral to the frontal process of the premaxillary bone (Figure 70). The nasal bone is also evident at this level forming superior to the cartilage of the lateral nasal capsule and nasal septum. The palatine process of the maxillary bone extends from the canine tooth posteriorly to a point midway between the first and second molar teeth. In the region anterior to the first molar tooth these processes approach the midline within the secondary palate (Figure 72). The outer alveolar process parallels the palatine process of the maxillary bone and the posterior extent of the bone is composed of the inner alveolar process which is oriented medial to the dental lamina from a point anterior to the first molar tooth (Figure 73) posteriorly, almost reaching the second molar tooth (Figure 74).

The alveolar process of the premaxilla has thickened (Figure 68) and remains located superior to the central and lateral incisor teeth. The frontal process of the premaxillary bone has increased in height and thickness (Figure 70). In addition a few spicules of premaxillary bone projects posteriorly from the midline alveolar region into the area between the paraseptal cartilages (Figure 69).

## Palatine and Vomer Bones

The palatine bone has increased in anteroposterior length and now extends from the region of the first molar tooth to the region where epithelial fusion remnants are no longer found between the palatine processes (Figure 75). The anterior one-half of this bone has extended its inferior end into the secondary palate. This extension constitutes the horizontal process of the palatine bone (Figure 74). The posterior half of this bone is represented by a straight bony process which projects obliquely superomedially and is located lateral to the secondary nasal cavity (Figure 75).

Bilateral ossification centers of the vomer bone are now apparent inferior to the nasal septum cartilage. They extend from a point level with the anterior end of the middle nasal concha to a point slightly posterior to that same structure (Figure 74).

## Meckel's Cartilage and Mandibular Bone

The outer alveolar process of the mandible now extends from the medial incisor tooth (Figure 70) posteriorly beyond the second molar tooth. An inner alveolar process is now evident extending from the canine tooth (Figure 71) to the region of the first molar tooth (Figure 73). In addition that portion of the bone located inferior to Meckel's cartilage has thickened (Figure 73) from the area posterior to the canine tooth to the region of the second molar tooth. Posteriorly the development of the ramus of the mandible is noted (Figure 76). No significant changes have occurred in Meckel's cartilage.

## 54-64 DAY EMBRYOS

The posterior tip of the uvula remains divided in all of the embryos studied, which includes specimens up to an age of 64 days. In each case the uvula appears to be forming by a process of merging in its anterior region while the posterior tips remain separated. Dissection of a 100 day fetus revealed a non-split uvula thus final merging of this structure must occur between 64 and 100 days insemination age.

## SUMMARY OF RESULTS

Table 2 gives the chronology of significant changes in the palate and associated structures as noted in baboon embryos of known insemination age. Because of the reproductive procedures followed in the collecting of the baboon embryos used in this study (see Materials and Methods) the exact age of each embryo in days is known. This allows precision in comparing daily developmental stages. The advantage of exactness is somewhat offset by the individual variability of each embryo which becomes evident when one compares chronologically related specimens.

Table 2
Chronology of developmental orofacial characteristics in baboon embryos

| Day | Olfactory system | Palate | Facial skeleton | Dental lamina | Nasal septum and capsule | Nasal conchae |
|---|---|---|---|---|---|---|
| 30 | nasal placode appears | | | | | |
| 33 | nasal pit appears | maxillary process forming | Meckel's cartilage anlage appears | | | |
| 36 | olfactory nerve appears | primary palate appears | | straight maxillary & mandibular dental laminas appear | nasal septum cartilage anlage appears | maxillary fold & ethmoid fold epithelial thickening appear |
| 37 | olfactory bulb appears | | Meckel's cartilage anlage lengthens | | paraseptal cartilage anlage appears | |
| 39 | | external naris opens obliquely | Meckel's cartilage chondroblasts appear | maxillary and mandibular dental laminas lengthen | | maxillary fold lengthens |
| 40 | vomeronasal organ appears | primary and secondary palate unite; external naris opens laterally; epithelial plug appears | maxillary and mandibular osteoblasts & Meckel's cartilage chondrocytes appear | maxillary dental lamina curving medially | lateral nasal capsule & ant. transverse lamina anlagen appear; bucconasal membrane ruptures | middle nasal concha & sup. nasal concha as epithelial thickening appear |
| 43 | | ant. palatine process inferomedial & post., vertical orientation | | maxillary dental lamina approaching midline; mandibular, curves medially | | sup. nasal concha mesenchymal core appears |
| 45 | | epithelial plug lengthens | maxillary, premaxillary & mandibular ossification | | nasal septum & lateral nasal capsule partially cartilaginous | |
| 46 | | palatine process rotation in middle section | ossification in maxilla & premaxilla increases | maxillary and mandibular dental laminas at midline; central & lateral incisors, canine & lst molar tooth buds appear in both jaws | paraseptal cartilage appears; increased cartilage in nasal septum & lateral nasal capsule | cartilage mesenchyme in inf. nasal concha appears |
| 47 | ventricle in olfactory bulb | ant. 2/3 palate fused sup. to tongue; post. l/3 transforming by medial bulging | palatine bone ossification; palatine process of maxillary bone appears | central incisor bud, lateral incisor & canine early cap, lst molar cap stage present in both jaws | ant. transverse lamina cartilage appears | cartilage present in inf. nasal concha; cartilage mesenchyme appears in middle nasal concha |
| 50 | | | | 2nd molar early cap stage present in mandible | ant. mesenchymal projection from paraseptal cartilage appears | |
| 53 | olfactory fibers from middle nasal concha | soft palate formed, uvula still divided | nasal & vomer ossification; horizontal process of palatine bone appears | central & lateral incisors, canine & lst molar bell stage & 2nd molar cap stage present in both jaws | ant. cartilagenous projection from paraseptal cartilage present | cartilage present in middle nasal concha; supreme nasal concha appears |

# DISCUSSION

Several concepts of the mechanism of secondary palate formation involving the change in the orientation of palatine processes from a vertical position lateral to the tongue to a horizontal position superior to the tongue have been proposed. Peter (1924) and later Lazzaro (1940), both cited by Coleman (1965), described this reorientation as the result of a medial rotation of the palatine processes. Polzl (1904) and Pons-Tortella (1937), both cited by Coleman (1965), considered that the palatine processes underwent a transformation from a vertical to a horizontal plane as the result of a regression of their vertical extremities and concomitant protrusion of their medial surfaces at the level of the dorsum of the tongue. This second concept was also described in the mouse by Walker and Fraser (1956). They found that the medial protrusion was first evident at the posterior end of the palatine processes and advanced anteriorly. There was no indication that shelf movement was preceded by a dropping of the tongue. In the rat Asling _et al_. (1960) observed a medial rotation of the palatine process anteriorly but did not describe the posterior regions of the palate. According to their studies the movement of the palatine processes coincided with the descent of the tongue from the area immediately inferior to the nasal septum. Coleman (1965), in a more comprehensive study of the rat palate, found that palate closure was composed of two distinct mechanisms. Anteriorly, the palatine processes rotated medially to assume a horizontal position superior to the tongue. Posteriorly closure resulted from a projection of the medial surface of the palatine process and regression of the free inferior end. Closure first commenced in the anterior third of the palate and proceeded anteriorly and posteriorly. Rotation occurred in the palatal area in which the palatine process of the maxilla developed and medial bulging occurred in the area in which the horizontal portion of the palatine bone developed.

In the current investigation of the baboon palate two distinct mechanisms of secondary palate closure are observed. Anteriorly, in the area which parallels the palatine portion of the maxillary bone, medial rotation is noted. Posteriorly, in the area which parallels the horizontal portion of the palatine bone, medial bulging and inferior regression of the palatine process is noted. Thus it would appear that the baboon palate achieves closure by the same mechanisms that are found in the rat (Coleman, 1965) which combines the theories previously advanced for the human and other mammals (Polzl, 1904, Peter, 1924).

Fischel (1929) indicated that closure of the human palate first occurred at the midpoint of the anteroposterior length of the palatine process. Fulton (1957),after Hochstetter (1936), characterized human palate closure as having an X configuration. Closure was first attained at a point one-fourth of the distance behind the anterior end of the palatine processes and proceeded posteriorly through the middle half, then through the anterior fourth and finally through the posterior fourth.

According to Fulton's study, closure occurred in embryos of 29-33 mm crown-rump length and 47-49 days ovulation age. Similar ages and crown-rump lengths were reported by Wood and Kraus (1962) however they were not able to determine the point of original closure. They described the nine week hard palate (43-46 mm crown-rump) as fused anteriorly and closed posteriorly and the ten week (48-55 mm crown-rump) palate as fusing toward the posterior with the soft palate area horizontal but not closed. In all embryos studied older than eleven weeks complete fusion had occurred throughout the length of the palate.

In the present study closure of the palatine process of the baboon is first noted in an embryo with a 27.6 mm crown-rump measurement which is at 47 days insemination age. Palate fusion has occurred posteriorly to a point near the posterior extent of the palatine process of the maxillary bone. Posteriorly the palatine processes are separated but horizontal and at the level of the palatine bone are transforming from a vertical to a horizontal orientation by medial bulging and ventral regression. In a 53 day embryo (39.6 mm crown-rump) the palatine processes have fused posteriorly through the region of the horizontal process of the palatine bone and a merging process has joined the anterior region of the soft palate while the uvula remains unjoined. The presence of epithelial remnants and their stage of development in the hard palate suggests that fusion first occurs in the region approximating the midpoint of this area and proceeds anteriorly and posteriorly until reaching the soft palate area.

These findings correspond roughly with those presented for the rhesus monkey (Macaca mulatta) by Asling and van Wagenen (1967). They described a 46 day, conception age, embryo with a 25 mm crown-rump length whose palatine processes had undergone translocation to the horizontal position and had fused in their midregion and rostrally.

The localization of remnants of epithelium resulting from the fusion of the palatine processes to each other and to the nasal septum in the hard palate as opposed to the soft palate has been noted by several investigators (Bergengrün, 1909, Schumacher, 1927, Wood and Kraus, 1962). This fact stimulated Burdi and Faist (1967) to compare the mechanism of formation of these two areas of the palate in the human. They found that the hard palate formed as a result of the fusion of the two palatine processes and subsequent breakdown of the epithelium resulted in the persistence of epithelial remnants in that area. In the soft palate, however, their investigation confirmed the earlier reports concerning the absence of epithelial remnants. They suggested that the soft palate developed by a displacement of epithelium as the result of a posterior mesenchymal growth and merging from the hard palate area as opposed to fusion of the lateral palatine processes. The lack of fusion of epithelial layers in the merging process resulted in the absence of epithelial remnants. The obliteration of surface grooves by proliferation of the underlying mesenchymal growth centers had been described by Peter (1913), as cited by Burdi and Faist (1967), and Streeter (1951) and was termed merging mechanism by Patten (1961).

The presence of epithelial remnants in the hard palate along with the lack of epithelial remnants in the soft palate of the baboons observed in this study and the appearance of the furrow on the inferior surface of the soft palate and uvula and its apparent obliteration would indicate that these portions of the palate are formed by the same processes described in man (Burdi and Faist, 1967).

The preclosure palatine processes were described by Wood and Kraus (1962) in 17 to 32 mm crown-rump length human embryos as being thick and blunt anteriorly reaching inferomedially toward the base of the tongue. Posteriorly the shelves appeared to be more vertically oriented as well as longer and thinner. Also apparent was a concentration of cells along the lateral margin of the palatine process especially at the angle between the process and the lateral portion of the oral roof. According to Orban (1957) this area of cell density is the basis of a differential growth theory of palatine process movement which states that the concentration of cells finally forces a sudden elevation of the palatine processes. According to Wood and Kraus (1962), palatal mesenchyme remains relatively undifferentiated during the early part of the active period of secondary palate formation with the exception of the development of osteoblasts at eight through nine weeks and the presence of blood vessels. Fibroblasts appeared in specimens of ten weeks. Similar orientations of palatine processes before closure in the rat have been reported by Moriarty _et al_. (1963) and Coleman (1965). In addition, Moriarty _et al_. (1963) reported mesenchymal condensation areas on the medial aspect of the palatine process and at the base of the process. Whereas the mesenchyme of the rest of the process was composed of loose, undifferentiated stellate cells, the cells in the condensed area were much less stellate as well as closely arranged. Following fusion of the palatine processes the mesenchyme became more loosely arranged and was characterized by an even distribution of mitotic figures throughout the palatine tissue. The condensation which had been present at the medial edge of the process was absent and the condensation at the base of the process was reduced. Poswillo and Roy (1965) also characterized the rat palatine processes by an area of intense cellular activity along its lower border. They postulated that palatine shelf movement was brought about by a combination of differential growth, as indicated by the cellular activity, plus the intrinsic shelf force of Walker and Fraser (1956) which arose from tensions produced within an erectile tissue composed of a highly vascular mesenchyme with an expanding fibrillar reticulum.

In the present study a condensation of mesenchyme is noted in the palatine process. In preclosure embryos through 46 days the condensation fills the whole process posteriorly and is localized more toward the lateral portion of the base of the process anteriorly. In addition vascularity increases in the condensed areas and is extensive in the area of the 46 day embryo where medial rotation of the process is taking place. Following closure in the presumptive hard palate areas the condensed mesenchymal area is thinner, elongated toward the midline and located in the inferior region of the palatal vault. In later stages of palate fusion and merging the vascularity remains noticeable, however, the condensed mesenchyme becomes less evident. The arrangement of mesenchymal cells in the apex of the palatine process before and immediately after closure remains very loose and is characterized by a fibrillar reticulum. The role that this area of differential growth and marked vascularity plays in palate closure in the baboon is unknown at this time but these characteristics do correspond closely with the description given by Poswillo and Roy (1965) in the rat.

The significance of the relationship of the descent of the tongue and lower jaw to the closure of the palatine processes is unsettled and its solution may lie in the recognition of possible species differences in the mechanism of palate closure. In the mouse where palatine process movement is apparently accomplished by a bulging of the medial margin of the palatine process over the dorsum of the tongue, Walker and Fraser (1956) observed that tongue descent and or lower jaw depression was not a prerequisite to palate closure. However, the tongue did change shape slightly in response to the palatine process movement. In the rat where palate closure is apparently effected by medial rotation throughout most of the length of the palatine processes, several investigators (Asling et al., 1960, Coleman, 1965, Poswello and Roy, 1965, and Zeiler et al., 1964) considered that tongue descent either by muscular contraction, descent into the floor of the mouth and/or lower jaw depression and anterior growth were essential processes which freed the tongue from its position immediately inferior to the nasal septum and allowed palatine process movement to proceed. A similar role of the tongue and lower jaw in man has also been suggested by Peter (1924), Lazarro (1940), and Scott (1966). Lower jaw depression can be seen in human embryos depicted by Kraus et al., (1966) by 43 days while palate closure takes place between 45 and 47 days. Humphrey (1968a, b) has reported that human embryos exhibit mouth opening reflexes prior to palate closure and believes that repeated lowering of the mandible pulls the tongue from between the vertical palatine processes as a prerequisite to palate closure. Humphrey (1968c) postulated that the removal of the tongue from this area creates a lower pressure in the primary nasal cavities because the external naris is closed by an epithelial plug and that the lowered pressure results in a rapid upward movement of the palatine processes to the horizontal position.

In the current study depression of the lower jaw in the baboon is first evident at 46 days, at the same time that the initial rotation of palatine processes is noted. Tongue descent is not evident as the palatine processes are cupped under the inferolateral borders of the tongue and the palatine processes appear to be lifting the tongue. It is not inconceivable that a further depression of the lower jaw would pull the tongue from this position and allow the palatine processes to continue their movement to the horizontal position. Such a removal of the tongue from between the palatine processes by lower jaw depression could be facilitated by a contraction of the musculature of the tongue both extrinsic and intrinsic. Indeed at 47 days the shape of the tongue suggests that such a contraction has occurred as the tongue is very much flattened in appearance and the lower jaw is considerably depressed. Gasser (1968) has suggested that the musculature of the tongue at this age may be capable of reflex contraction. Thus it would appear that removal of the tongue from between the palatine processes may also be an integral part of palate closure in the baboon.

The source of the force which brings about the transformation of the palatine processes has been variously described. Walker and Fraser (1956) on the basis of metachromatic staining with toluidine blue and aldehyde fuchsin-positive material in the palatal area suggested that acid mucopolysaccharides in the form of a network of elastic fibers provided this force, which was termed the intrinsic shelf force. Stark and Ehrmann (1958) were unable to confirm the presence of elastic fibers and Walker (1961) reported that electron microscopic examination of the palatine processes failed to reveal any elastic fibers. However, the presence of sulphated acid mucopolysaccharides was confirmed by radioautography by Larsson, Böstrom and Carlsöö (1959) and Walker (1961). In addition, these studies indicated that increasing age of the embryos approaching the time of palate closure was accompanied by an increase in the amount of sulphated mucopolysaccharide in the palate region. In view of the time of appearance, distribution and increasing quantity of this substance in the palatal area and its physical properties which include the transformation from a gel state to a stringy elastic mass when combined in a test tube with certain proteins, Walker (1961) suggested that sulphated mucopolysaccharides may provide the basis for palatine process movement. Such a role was also postulated by Larsson (1962).

The data from the present study do not bear direct relationship to this postulated source of palatine process movement, however that such work might be beneficial when studied in the baboon is clear because of the observed similarities to the other animals studied in the area of palate morphogenesis.

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## LITERATURE CITED


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## EXPLANATION OF FIGURES

| | |
|---|---|
| Figure 1 | Perineal turgescence. |
| Figure 2 | Maximum turgescence. |
| Figure 3 | Perineal deturgescence. |
| Figure 4 | Perineal rest. |
| Figure 5 | Reconstruction drawing of 30 day embryo indicating level of sections shown in Figures 6 and 7. (44 X). |
| Figure 6 | Frontal section from 30 day embryo. (40 X). |

## ABBREVIATIONS

| | |
|---|---|
| NP | nasal placode |
| MP | mandibular process |

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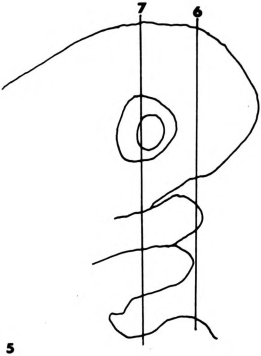


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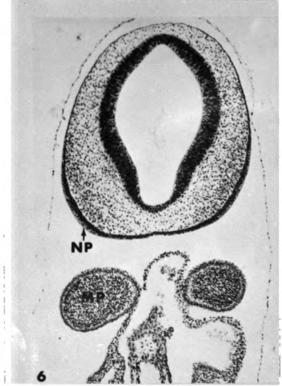


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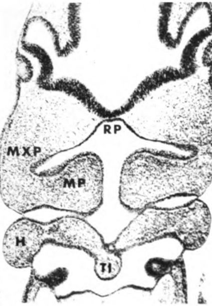
## EXPLANATION OF FIGURES

| | |
|---|---|
| Figure 7 | Frontal section from 30 day embryo. (37 X). |
| Figure 8 | Reconstruction drawing of 33 day embryo indicating level of sections shown in Figures 9 and 10. (19 X). |
| Figure 9 | Frontal section from 33 day embryo. (31 X). |
| Figure 10 | Frontal section from 33 day embryo. (31 X). |
| Figure 11 | Reconstruction drawing of 36 day embryo indicating level of sections shown in Figures 12-16. (12 X). |
| Figure 12 | Frontal section from 36 day embryo. (31 X). |

## ABBREVIATIONS

| | |
|---|---|
| EN | external naris |
| H | hyoid arch |
| LLS | lateral lingual swelling |
| LNP | lateral nasal process |
| MKA | Meckel's cartilage anlage |
| MN | mandibular nerve |
| MNP | medial nasal process |
| MP | mandibular process |
| MXP | maxillary process |
| N | nasal pit |
| RP | Rathke's pouch |
| TI | tuberculum impar |


RP
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TI

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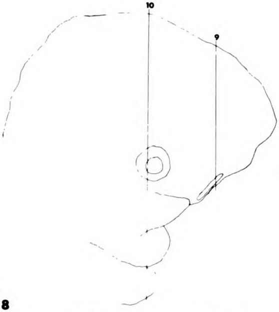
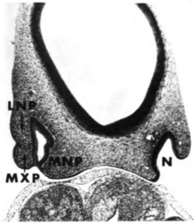

10
9

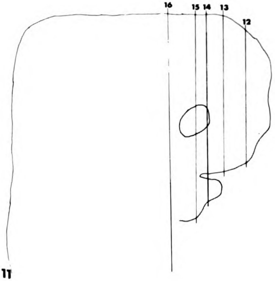
8


LNP
MNP
N
MXP

9


RP
MXP
LLS
MN
MKA

10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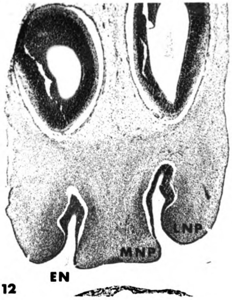
15
14
13
12

11


LNP
MNP
EN

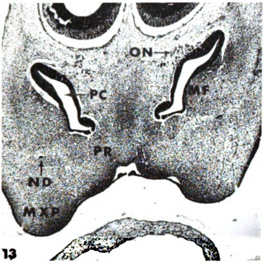
12

## EXPLANATION OF FIGURES

| | |
|---|---|
| Figure 13 | Frontal section from 36 day embryo. (31 X). |
| Figure 14 | Frontal section from 36 day embryo. (31 X). |
| Figure 15 | Frontal section from 36 day embryo. (31 X). |
| Figure 16 | Frontal section from 36 day embryo. (31 X). |
| Figure 17 | Reconstruction drawing of 39 day embryo indicating level of sections shown in Figures 18-22. (13 X). |
| Figure 18 | Frontal section from 39 day embryo. (31 X). |

## ABBREVIATIONS

| | | | |
|---|---|---|---|
| BM | bucconasal membrane | MNP | medial nasal process |
| DL | dental lamina | MXP | maxillary process |
| EF | ethmoid fold | ND | nasolacrimal duct |
| EN | external naris | NSA | nasal septum cartilage anlage |
| IN | inferior dental nerve | ON | olfactory nerve |
| LN | lingual nerve | PC | primary nasal cavity |
| LNP | lateral nasal process | PP | palatine process |
| MF | maxillary fold | PR | primary palate |
| MKA | Meckel's cartilage anlage | T | tongue |



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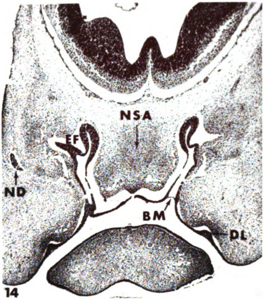

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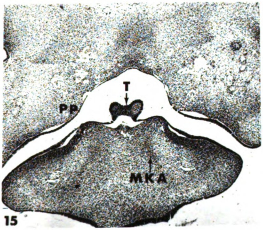
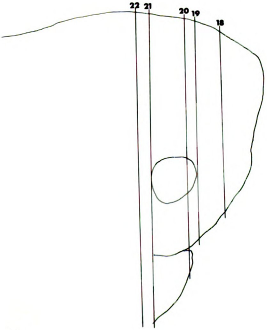


15

16



17

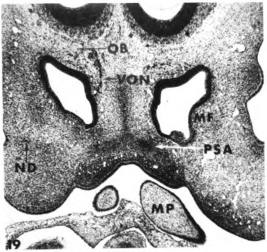
18

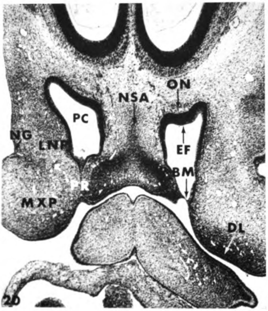
## EXPLANATION OF FIGURES

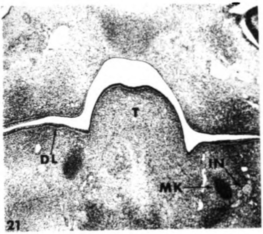
| | |
|---|---|
| Figure 19 | Frontal section from 39 day embryo. (31 X). |
| Figure 20 | Frontal section from 39 day embryo. (31 X). |
| Figure 21 | Frontal section from 39 day embryo. (31 X). |
| Figure 22 | Frontal section from 39 day embryo. (31 X). |
| Figure 23 | Reconstruction drawing of 40 day embryo indicating level of sections shown in Figures 24-31. (10 X). |
| Figure 24 | Frontal section from 40 day embryo. (31 X). |

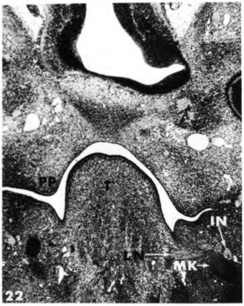
## ABBREVIATIONS

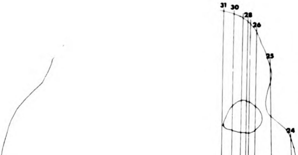
| | | | |
|---|---|---|---|
| BM | bucconasal membrane | ND | nasolacrimal duct |
| DL | dental lamina | NG | nasolacrimal groove |
| EF | ethmoid fold | NSA | nasal septum cartilage anlage |
| EN | external naris | OB | olfactory bulb |
| IN | inferior dental nerve | ON | olfactory nerve |
| LN | lingual nerve | PC | primary nasal cavity |
| LNP | lateral nasal process | PP | palatine process |
| MF | maxillary fold | PR | primary palate |
| MK | Meckel's cartilage | PSA | paraseptal cartilage anlage |
| MP | mandibular process | T | tongue |
| MXP | maxillary process | VON | nerve to vomeronasal organ |


OB
VON
MF
PSA
ND
MP
19

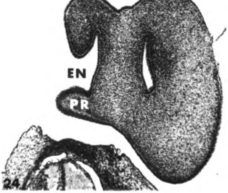

ON
NSA
PC
NG
LNP
EF
BM
PR
MXP
DL
20


T
DL
IN
MK
21


PP
T
IN
LN
MK
22


31
30
28
26
25
24

23


EN
PR
24

## EXPLANATION OF FIGURES

Figure 25 Frontal section from 40 day embryo. (34 X).

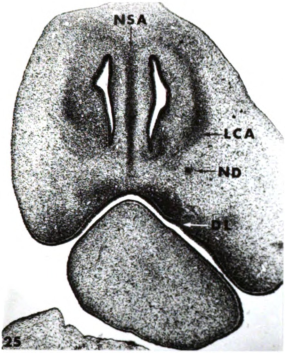
Figure 26 Frontal section from 40 day embryo. (34 X).

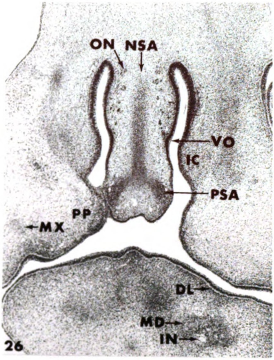
Figure 27 Frontal section from 40 day embryo. (34 X).

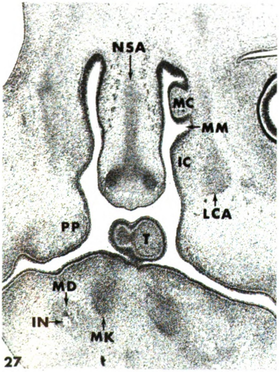
Figure 28 Frontal section from 40 day embryo. (34 X).

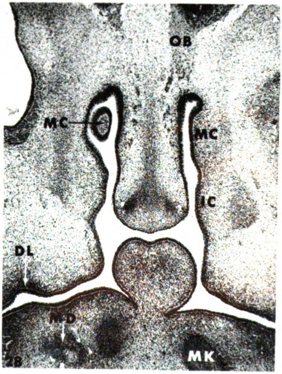
## ABBREVIATIONS

| | | | |
|---|---|---|---|
| DL | dental lamina | ND | nasolacrimal duct |
| IC | inferior nasal concha | NSA | nasal septum cartilage anlage |
| IN | inferior dental nerve | OB | olfactory bulb |
| LCA | lateral nasal capsule anlage | ON | olfactory nerve |
| MC | middle nasal concha | PP | palatine process |
| MD | mandibular bone | PSA | paraseptal cartilage anlage |
| MK | Meckel's cartilage | T | tongue |
| MM | middle nasal meatus | VO | vomeronasal organ |
| MX | maxillary bone | | |


NSA
LCA
ND
DL
25


ON
NSA
VO
IC
PSA
PP
MX
DL
MD
IN
26


NSA
MC
MM
IC
LCA
PP
T
MD
IN
MK
27

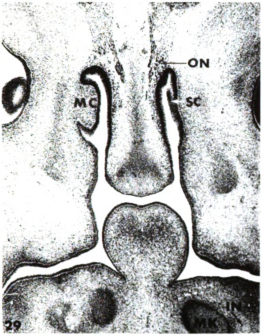

OB
MC
MC
IC
DL
MD
MK
28

# EXPLANATION OF FIGURES

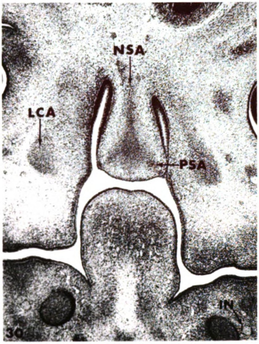
| | |
|---|---|
| Figure 29 | Frontal section from 40 day embryo. (31 X). |
| Figure 30 | Frontal section from 40 day embryo. (31 X). |
| Figure 31 | Frontal section from 40 day embryo. (31 X). |
| Figure 32 | Reconstruction drawing of 43 day embryo indicating level of sections shown in Figures 33-40. (12 X). |
| Figure 33 | Frontal section from 43 day embryo. (31 X). |
| Figure 34 | Frontal section from 43 day embryo. (31 X). |

## ABBREVIATIONS

| | | | |
|---|---|---|---|
| DL | dental lamina | NSA | nasal septum cartilage anlage |
| EN | external naris | ON | olfactory nerve |
| EP | epithelial plug | PP | palatine process |
| IN | inferior dental nerve | PR | primary palate |
| LCA | lateral nasal capsule anlage | PSA | paraseptal cartilage anlage |
| LN | lingual nerve | SC | superior nasal concha |
| MC | middle nasal concha | T | tongue |
| MK | Meckel's cartilage | | |

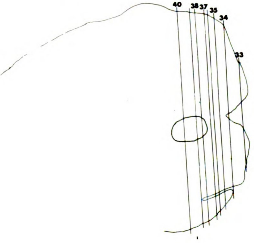


ON
MC
SC
IN
MK
29

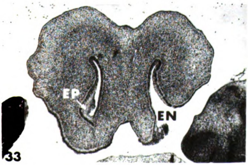
NSA
LCA
PSA
IN
30


T
PP
LN
MK
31

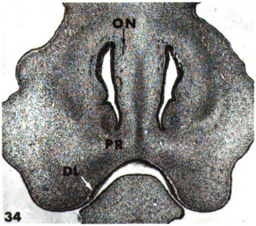



40
38
37
35
34
33


32



EP
EN
33

ON
PR
DL
34

## EXPLANATION OF FIGURES

Figure 35 Frontal section of 43 day embryo. (31 X).

Figure 36 Frontal section of 43 day embryo. (31 X).

Figure 37 Frontal section of 43 day embryo. (31 X).

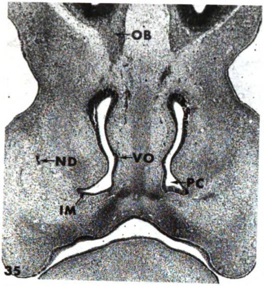
Figure 38 Frontal section of 43 day embryo. (31 X).

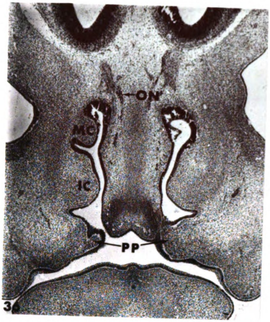
Figure 39 Frontal section of 43 day embryo. (31 X).

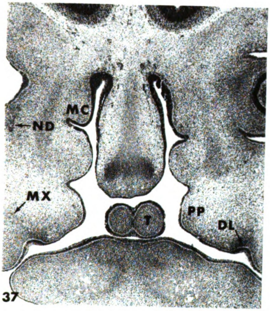
Figure 40 Frontal section of 43 day embryo. (31 X).

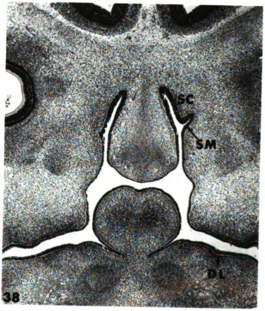
## ABBREVIATIONS

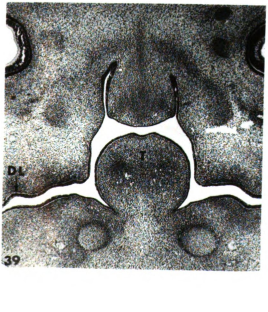
| | | | |
|---|---|---|---|
| DL | dental lamina | ON | olfactory nerve |
| IC | inferior nasal concha | PC | primary nasal cavity |
| IM | inferior nasal meatus | PP | palatine process |
| MC | middle nasal concha | SC | superior nasal concha |
| MK | Meckel's cartilage | SM | superior nasal meatus |
| MX | maxillary bone | T | tongue |
| ND | nasolacrimal duct | VO | vomeronasal organ |
| OB | olfactory bulb | | |

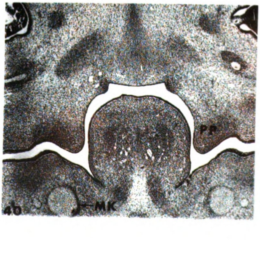

OB
ND
VO
PC
IM
35


ON
MC
IC
PP
36


MC
ND
MX
T
PP
DL
37


SC
SM
DL
38


T
DL
39

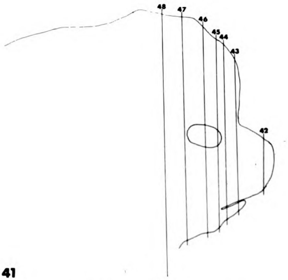

PP
MK
40

## EXPLANATION OF FIGURES

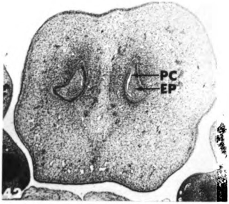
| | |
|---|---|
| Figure 41 | Reconstruction drawing of 45 day embryo indicating level of sections shown in Figures 42-48. (8 X). |
| Figure 42 | Frontal section of 45 day embryo. (30 X). |
| Figure 43 | Frontal section of 45 day embryo. (30 X). |
| Figure 44 | Frontal section of 45 day embryo. (30 X). |
| Figure 45 | Frontal section of 45 day embryo. (30 X). |
| Figure 46 | Frontal section of 45 day embryo. (30 X). |

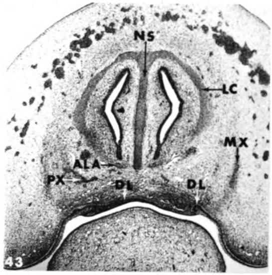
## ABBREVIATIONS

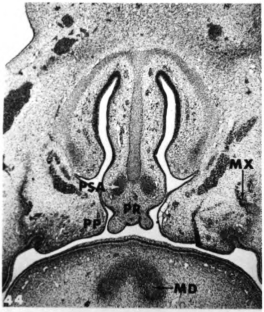
| | | | |
|---|---|---|---|
| ALA | Anterior transverse lamina anlage | MX | maxillary bone |
| DL | dental lamina | ND | nasolacrimal duct |
| EP | epithelial plug | NS | nasal septum cartilage |
| IC | inferior nasal concha | ON | olfactory nerve |
| IM | inferior nasal meatus | PC | primary nasal cavity |
| IN | inferior dental nerve | PP | palatine process |
| LC | lateral nasal capsule | PR | primary palate |
| MC | middle nasal concha | PSA | paraseptal cartilage anlage |
| MD | mandibular bone | PX | premaxillary bone |
| MK | Meckel's cartilage | T | tongue |
| MM | middle nasal meatus | VO | vomeronasal organ |

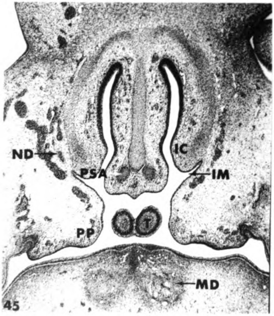

48
47
46
45
44
43
42

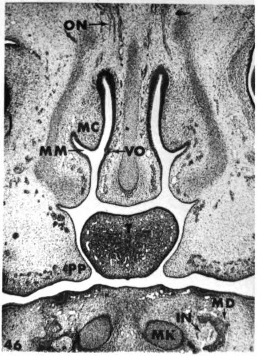
41


PC
EP
42


NS
LC
MX
ALA
PX
DL
DL
43


PSA
PR
PP
MX
MD
44


ND
IC
PSA
IM
PP
T
MD
45

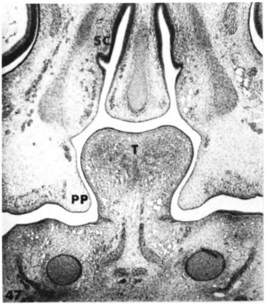

ON
MC
MM
VO
PP
MD
IN
MK
46

## EXPLANATION OF FIGURES

| | |
|---|---|
| Figure 47 | Frontal section of 45 day embryo. (31 X). |
| Figure 48 | Frontal section of 45 day embryo. (31 X). |
| Figure 49 | Reconstruction drawing of 46 day embryo indicating level of sections shown in Figures 50-55. (8 X). |
| Figure 50 | Frontal section of 46 day embryo. (18 X). |
| Figure 51 | Frontal section of 46 day embryo. (18 X). |
| Figure 52 | Frontal section of 46 day embryo. (18 X). |

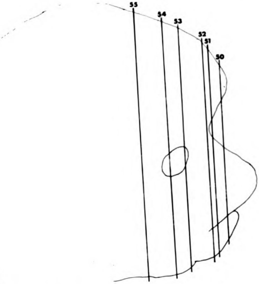
## ABBREVIATIONS

| | |
|---|---|
| ALA | anterior transverse lamina anlage |
| CI | central incisor tooth |
| DL | dental lamina |
| IM | inferior nasal meatus |
| LI | lateral incisor tooth |
| MX | maxillary bone |
| ND | nasolacrimal duct |
| NPD | nasopalatine duct |
| PP | palatine process |
| PS | paraseptal cartilage |
| PX | premaxillary bone |
| SC | superior nasal concha |
| T | tongue |
| VO | vomeronasal organ |



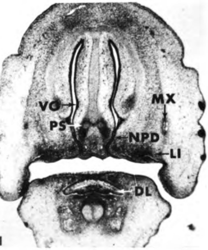
47

48



49

50



51

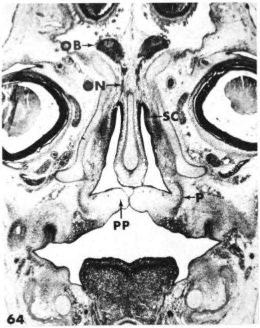
52

## EXPLANATION OF FIGURES

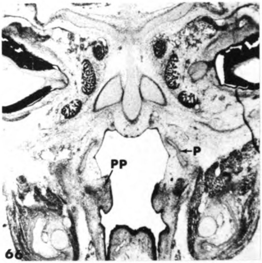
| | |
|---|---|
| Figure 64 | Frontal section of 47 day embryo. (17 X). |
| Figure 65 | Frontal section of 47 day embryo. (17 X). |
| Figure 66 | Frontal section of 47 day embryo. (17 X). |
| Figure 67 | Reconstruction drawing of 53 day embryo indicating level of sections shown in Figures 68-77. (5 X). |
| Figure 68 | Frontal section of 53 day embryo. (12 X). |
| Figure 69 | Frontal section of 53 day embryo. (12 X). |
| Figure 70 | Frontal section of 53 day embryo. (12 X). |

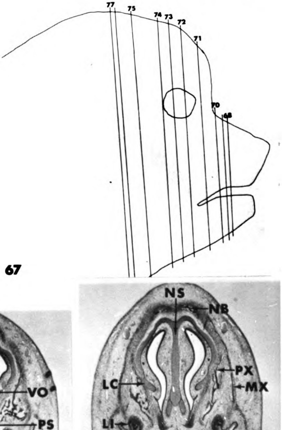
## ABBREVIATIONS

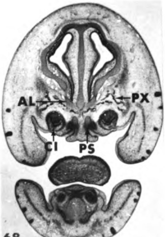
| | | | |
|---|---|---|---|
| AL | anterior transverse lamina | NS | nasal septum cartilage |
| CI | central incisor tooth | OB | olfactory bulb |
| LC | lateral nasal capsule | ON | olfactory nerve |
| LI | lateral incisor tooth | P | palatine bone |
| M1 | first molar tooth | PP | palatine process |
| MD | mandibular bone | PS | paraseptal cartilage |
| MX | maxillary bone | PX | premaxillary bone |
| NB | nasal bone | SC | superior nasal concha |
| NPD | nasopalatine duct | VO | vomeronasal organ |

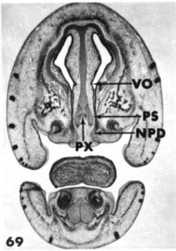

OB
N
SC
P
PP
64


OB
PP
P
65


P
PP
66


77
75
74
73
72
71
70
68
67


AL
PX
CI
PS
68


VO
PS
NPD
PX
69


NS
NB
PX
LC
MX
LI
M1
MD
70

## EXPLANATION OF FIGURES

Figure 60 Frontal section of 47 day embryo. (18 X).

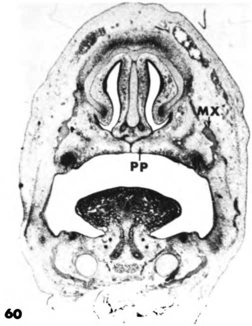
Figure 61 Frontal section of 47 day embryo. (18 X).

Figure 62 Frontal section of 47 day embryo. (18 X).

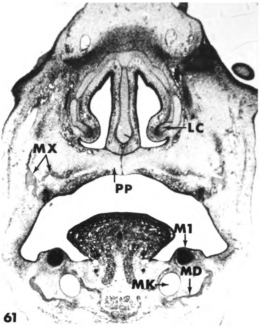
Figure 63 Frontal section of 47 day embryo. (18 X).

## ABBREVIATIONS

| | | | |
|---|---|---|---|
| IC | inferior nasal concha | MX | maxillary bone |
| LC | lateral nasal capsule | ND | nasolacrimal duct |
| LN | lingual nerve | NS | nasal septum cartilage |
| Ml | first molar tooth | ON | olfactory nerve |
| MC | middle nasal concha | PP | palatine process |
| MD | mandibular bone | SC | superior nasal concha |
| MK | Meckel's cartilage | T | tongue |




60

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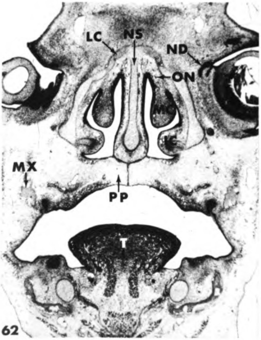
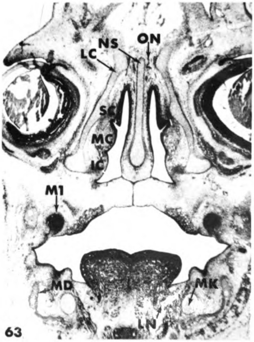



62

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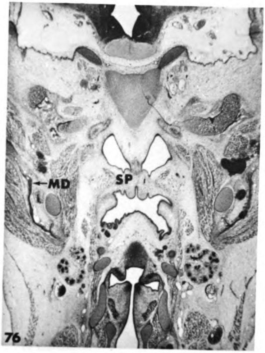
## EXPLANATION OF FIGURES

| | |
|---|---|
| Figure 64 | Frontal section of 47 day embryo. (17 X). |
| Figure 65 | Frontal section of 47 day embryo. (17 X). |
| Figure 66 | Frontal section of 47 day embryo. (17 X). |
| Figure 67 | Reconstruction drawing of 53 day embryo indicating level of sections shown in Figures 68-77. (5 X). |
| Figure 68 | Frontal section of 53 day embryo. (12 X). |
| Figure 69 | Frontal section of 53 day embryo. (12 X). |
| Figure 70 | Frontal section of 53 day embryo. (12 X). |

## ABBREVIATIONS

| | |
|---|---|
| AL | anterior transverse lamina |
| CI | central incisor tooth |
| LC | lateral nasal capsule |
| LI | lateral incisor tooth |
| Ml | first molar tooth |
| MD | mandibular bone |
| MX | maxillary bone |
| NB | nasal bone |
| NPD | nasopalatine duct |
| NS | nasal septum cartilage |
| OB | olfactory bulb |
| ON | olfactory nerve |
| P | palatine bone |
| PP | palatine process |
| PS | paraseptal cartilage |
| PX | premaxillary bone |
| SC | superior nasal concha |
| VO | vomeronasal organ |


75
P
ER


76
MD
SP


77
U

## EXPLANATION OF FIGURES

Figure 71 Frontal section of 53 day embryo. (12 X).

Figure 72 Frontal section of 53 day embryo. (12 X).

Figure 73 Frontal section of 53 day embryo. (12 X).

Figure 74 Frontal section of 53 day embryo. (12 X).

## ABBREVIATIONS

| | | | |
|---|---|---|---|
| C | canine tooth | ND | nasolacrimal duct |
| LB | lacrimal bone | OB | olfactory bulb |
| LD | lacrimal duct | ON | olfactory nerve |
| LS | lacrimal sac | P | palatine bone |
| M1 | first molar tooth | S | supreme nasal concha |
| MC | middle nasal concha | T | tongue |
| MD | mandibular bone | V | vomer |
| MX | maxillary bone | VB | ventricle in olfactory bulb |

## EXPLANATION OF FIGURES

Figure 75 Frontal section of 53 day embryo. (12 X).

Figure 76 Frontal section of 53 day embryo. (12 X).

Figure 77 Frontal section of 53 day embryo. (12 X).

## ABBREVIATIONS

| | |
|---|---|
| ER | epithelial remnants |
| MD | mandibular bone |
| P | palatine bone |
| SP | soft palate |
| U | uvula |

P
ER
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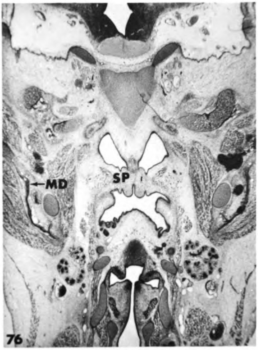

MD
SP
76


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77