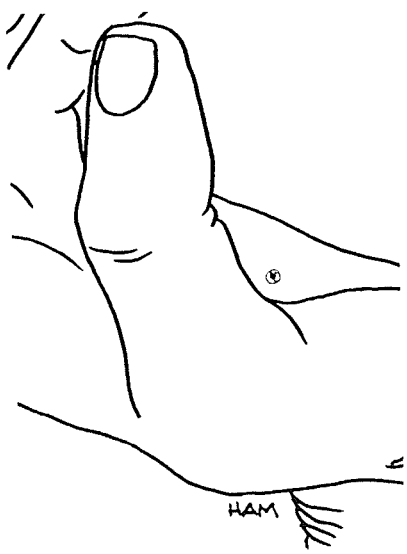
I. *Basics*

1. *Pertinent Embryology*

THERE are many missing links, and much is still unknown about the embryology of the human face and head. This deficiency is not surprising with so much happening in such a short period of time. Anatomist Robert Bean calculated:

> If the rate of growth of the first month of embryonic life were to be maintained until adulthood, the resultant individual would be 128,350 to the 1,100 power light years in length.



The Dicksons clarified the perspective of this figure when they determined that such a rate of growth, if continued, would produce a person who at 4 years would span the galaxy, by 6 years would span the universe and as an adult could hold the universe in his hand like a grain of sand.

VEAU

In 1938 Veau proposed—and he was seconded by Streeter in 1951—that masses of mesoderm migrate between two continuous sheets of ectoderm covering the face and roof of the primitive oral cavity. Stark added in 1954 that unless this ectoderm is supported by an intervening layer of mesoderm it will eventually break down and give rise to various degrees of clefting.

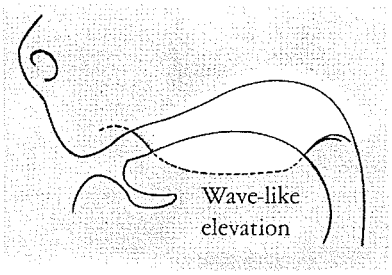
The secondary palate posterior to the incisive foramen is formed by fusion of the two palatal processes which are vertical outgrowths of the maxillae. Lying at first vertically at each side of the tongue, these palatal folds ascend as the neck extends and the tongue descends. Then, between seven and eight weeks, if all goes well they fuse with each other and with the inferior border

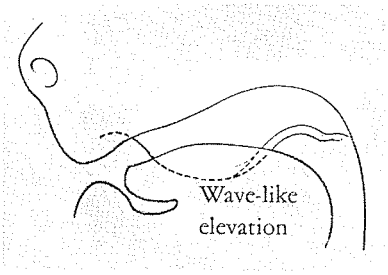
of the septum from before backwards, to form most of the hard and all of the soft palate. Failure of fusion, of course, produces various clefts of the secondary palate.

STARK

In 1971 at the Melbourne Congress Richard Stark reviewed the embryological development of the face, including the palate. He noted:

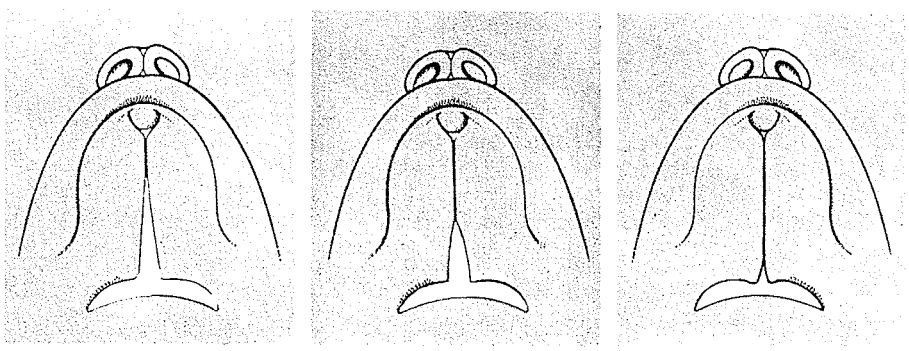
The secondary palate develops as the result of the positional change of palatal processes or shelves, then by their growth and adherence and finally merging of their mesoderm.





At the seventh week the head is acutely flexed and turned to the right. The tongue is thus pushed cephalad between the palatal shelves, which hang downward on either side of the tongue like the ears of a hound dog. Slowly, as the head begins to extend the tongue begins to drop, starting first at the base of the tongue posteriorly. The palatal shelves seize this opportunity to overcome the tongue resistance and start to rise, first posteriorly, then forward as a wave until the anterior portion completes the positioning of shelves above the tongue.

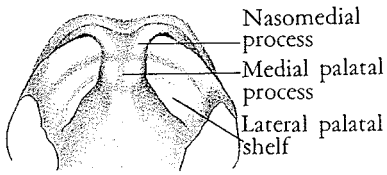
Now the shelves grow, meet and, if they are sufficiently adhesive, fuse, first at the anterior one-third of the hard palate, then forward to the incisive foramen and lastly backward to the uvula.

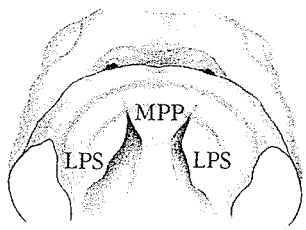


In the *Transactions of the Fifth International Congress of Plastic and Reconstructive Surgery* Stark postulated:

A number of things can occur which can cause this series of events not to take place, with a resultant cleft palate. (1) Increasing upward resistance of

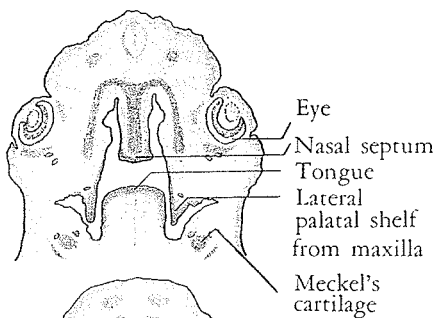
the tongue, such as in Pierre Robin syndrome where the jaw is small and the tongue is pushed upward between the palatal shelves. There is no opportunity then for the shelves to rise over the tongue to meet and fuse. (2) The shelves themselves may be so deficient of mesoderm that they cannot grow and meet each other. (3) The force to lift the shelves up may not be present, as is true in animals treated by excessive doses of cortisone, vitamin A, or X-ray. (4) A broad head as in oxycephaly may prove too wide for normal shelves to meet. (5) There may be postfusion rupture, as suggested by the presence of epithelial pearls found along the cleft margin by Kraus. (6) The head may not extend or stay flexed, in which case the tongue is pushed upward and the palatal shelves are unable to get into proper position for fusion. This would be true in Klippel-Feil syndrome. (7) An encephalocele may hang between the shelves, proving an insurmountable obstacle.

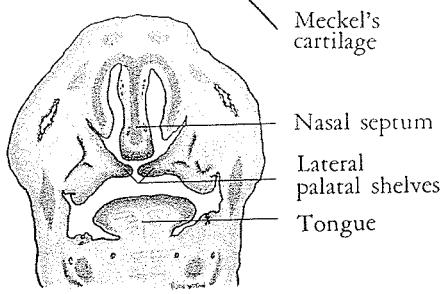


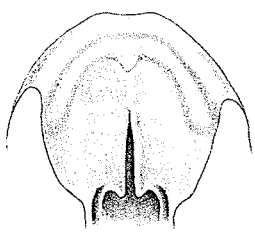


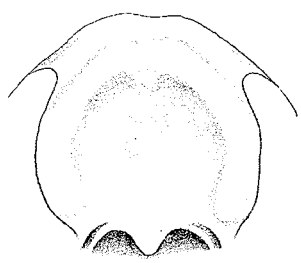
PATTEN

Bradley M. Patten of the University of Michigan noted in *Cleft Lip and Palate* (edited by Grabb, Rosenstein and Bzoch in 1971):



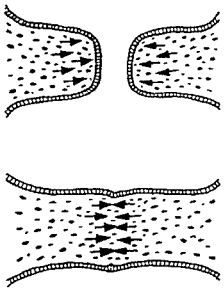




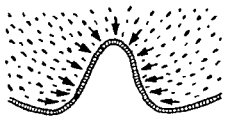


The palate is contributed to by the nasomedial processes. From their deeper portions, the small, triangular, median part of the palate is formed. It is to this portion of the palate that I would restrict the use of the term *primary palate.* The main part of the palate is derived from that portion of the upper jaw which arises from the maxillary processes. Shelflike outgrowths of these processes arise on either side during the seventh week, and grow toward the midline. These *palatal shelves* form the *secondary palate.* When the palatal shelves first start to develop, the tongue lies between them, and they are directed downward so that their margins lie along the floor of the mouth on either side of the root of the tongue. As development progresses, the position of the tongue is shifted downward and the margins of the palatal shelves are free to swing upward and toward the midline. . . . Much more information is needed concerning this process. . . . On the basis of the best available age-length data, this places the withdrawal of the tongue from between the palatal shelves as occurring toward the end of the eighth week, presumptive fertilization age. . . .

When they first move up, the shelves are not sufficiently developed to meet each other. Their growth is vigorous, however, and by the eighth week, they have made contact. Thereafter fusion progresses from the rostral part toward the uvula. Burdi is convinced that the typical fusion of the palatal shelves with the characteristic incarnation of epithelial remnants does not extend to the uvula end of the soft palate. He regards the absence of epithelial remnants in this territory as indicating that the lengthening of the



A Fusion

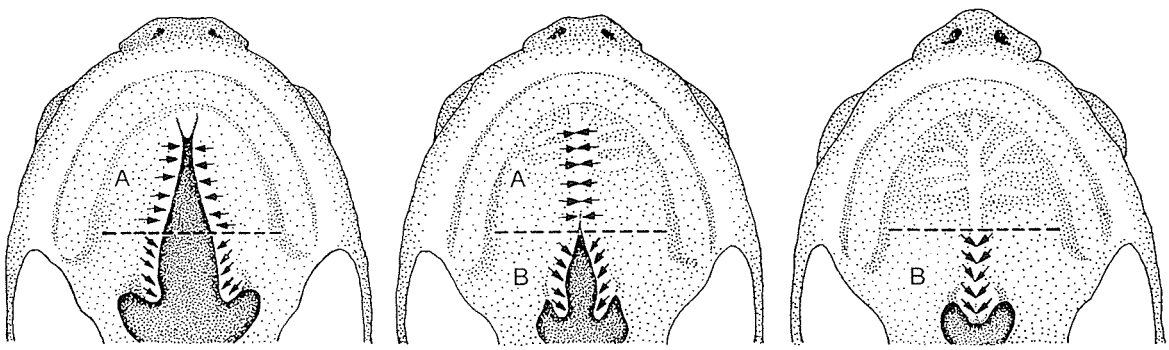


B Merging

soft palate and the formation of the uvula is brought about by merging rather than fusion. . . . At the same time that the palate is thus being formed, the nasal septum grows downward toward it and soon becomes fused to its upper face.

Patten championed the theory that growth of mesenchymal masses beneath the surface brings originally separate structures together in the lip by pushing the epithelium out from between the elevations in the process of *merging*. Yet in the palate he accepted the *fusion* theory, except in the uvula.

One of these is familiar in the formation of the palate. For this process the usual term *fusion* is entirely appropriate. As the two processes come together, the covering epithelial layers are brought into contact. Shortly thereafter, the epithelium that no longer has an external exposure begins to regress. . . . The epithelial changes in this process have been well described by Barry.



David Poswillo

POSWILLO

David E. Poswillo has long been interested in the pathogenesis of cleft lip and palate. Upon completion of his oral surgery training in England, he returned to New Zealand in 1953 as senior oral surgeon at the Plastic Surgical Unit, Christchurch, and co-director of the cleft palate clinic. He explained how he got started:

I got into palatal study in New Zealand because I was attempting to find an animal model in which I could do control experiments on the surgical repair of the palate. Ironically, some years after I had been struggling to find a reasonable model of cleft lip and/or palate, my work became well known. As

a result of a newspaper article, a lady who lived only a few hundred yards from my hospital rang me up. All the time I had been working to produce an animal model of cleft lip and palate, she had been trying to breed the same malformation out of her pedigree colony of dachshund dogs. Luckily she had not succeeded and then for a year or two my plastic surgical colleague, John Roy, and I carried out further experiments on the dog model at home at our expense.

Poswillo's work was recognized by Sir Harold Himsworth, Secretary of the Medical Research Council of Great Britain, during a search visit to New Zealand. His report to the British government stated that the most exciting research he had seen on his one-month visit was being carried out at the bottom of a garden in Christchurch by a young man called David Poswillo.

In 1968 Poswillo devoted his first Hunterian Lecture to the isolated cleft palate and particularly the form that is associated with postural molding, entitling the lecture "The Aetiology and Surgery of Cleft Palate with Micrognathia." Poswillo eventually became professor of teratology in the Royal College of Surgeons of England and consultant oral surgeon at Queen Victoria Hospital, East Grinstead.

In the May 1974 *Proceedings of the Royal Society of Medicine* he wrote:

For thousands of years mankind has been intrigued by disturbances in the physical development of the human body. Even before descriptions of such deformities were recorded on the clay tablets of Babylon, in 3000 B.C., they were illustrated in the rock drawings of primitive cave dwellers. But it was not until the time of Harvey, in the seventeenth century, that the scientific study of malformation began. After the development of the cell theory the significance of the foldings and invaginations of the three germ layers came to be understood, and it was possible to comprehend many anomalies of development in terms of mechanical difficulties. For example, cleft lip and palate became recognized as a failure of fusion of the maxillary processes. . . .

Clefts of the posterior palate may be classified into two principal groups. In one there are those clefts, both unilateral and bilateral, which accompany cleft lip. In the other are the solitary clefts of the secondary palate. Clinically these two groups may easily be distinguished. Most authors agree that these two groups are distinct entities. The difference in incidence, sex predisposi-

tion and prevalence of associated anomalies all support this division into cleft lip and isolated cleft palate.

The frequent association of cleft palate with the cleft lip anomaly has been investigated by many workers. As has already been described, animal embryos susceptible to cleft lip have a large median nasal process. Trasler & Fraser (1963) have shown that in such circumstances, at the commencement of palatal shelf closure, the tongue does not move forward between the lips as is usually the case. Instead the tip of the tongue remains pressed against the median process and arches up into the nasal cavity between the palatal shelves. Thus movement of the shelf or shelves towards the midline is impeded. Therefore in an embryo with cleft lip it is likely that cleft palate results because movement of the shelves from vertical to horizontal is delayed by the intervening tongue. If eventually the shelves do become horizontal it is unlikely that they will meet each other or the nasal septum; thus fusion fails to take place.

The prevalence figures for isolated cleft palate are lower than those for cleft lip and palate, but the ratio of racial incidence is much the same. In Caucasians it occurs once in 3000 live births. An excess of females over males in the ratio of 60:40 exists in isolated cleft palate. Associated congenital anomalies occur twice as often with isolated cleft palate as with combined lip and palate clefts. Micrognathia has a very high association with isolated cleft palate due in part to the simultaneous occurrence of the two anomalies in the Pierre Robin syndrome.

Normal palate fusion involves synchronized interaction between growth and convergence of the palatal processes, tongue withdrawal and muscular activity, mandibular growth, changes in cranial base and cranial flexure, and steady increases in the width of the developing head. It can be postulated that any significant interference with these time-specific interactions could lead to incomplete fusion of the palatal shelves, both with each other and with the nasal septum. In addition, changes affecting the fusion and subsequent breakdown of the epithelial seam could induce malformation. Shelves which merge and fuse could be later disrupted, either by abnormal mechanical pressures or by growth traction if mesodermal bridging is incomplete. Such phenomena could lead to palatal fistula, submucous clefts or even complete rupture of the palate. One can hypothesize, therefore, that cleft palate may arise from one or more of the following causes: interference with the intrinsic shelf force; excessive head width, or diminutive palatal shelves; excessive resistance from the tongue; non-fusion of the palatal shelves; and fusion of the palate with subsequent breakdown.

Walker and Fraser (1956) were the first to propose the existence of an intrinsic shelf force which they ascribed to the presence of elastic fibres

within the shelf mesoderm. Poswillo and Roy (1965) believed that the intrinsic shelf force arose from a combination of the expanding fibrillar mesoderm and increased mitotic activity along the lower margin of the shelf. This latter hypothesis was reinforced by the work of Andersen and Matthiessen (1967) who showed that increasing mitotic activity was an important factor contributing to the overall rise in tension of the shelf tissues. Verrusio (1970) proposed that a gradual decrease in the angulation of the cranial base could provide the "internal shelf force." It is likely in a multifactorial system such as palate closure that interference with the cranial base, be it mechanical or biochemical, will contribute to failure of palate closure.

Small palatal shelves may also contribute to palatal clefting; X-irradiation produces reduced mitotic activity and small palatal shelves in both rodents and primates. Other teratogens, including glucocorticoids, have been shown to do likewise. Mesenchymal deficiency, however it may arise, will obviously affect the developing palatal shelf mechanism with consequences leading towards malformation.

The role of the tongue in palate closure is still a matter for debate. Complete tongue obstruction over a time-specific period can produce 100% cleft palate in rodents, accompanied by a high proportion of moulding defects of the Pierre Robin type when induced by amniocentesis (Poswillo & Roy 1965).

Harris (1967) has shown that glucocorticoids produce oligohydramnios in mice, with postural-type defects of the palate caused by interference with angulation of the cranial base and subsequent tongue withdrawal. The role of corticosteroids in the induction of cleft palate is still not clear. . . . It has often been demonstrated that pregnant mice exposed to starvation, noise, cold or transportation near the critical time for palate closure will have a high incidence of cleft palate in their offspring.

Disturbances of fusion are believed by Smiley (1972) to be responsible for cleft palate. . . .

Submucous cleft palate, in association with bifid uvula, is likely to be a microform of posterior cleft palate. Submucous cleft palate can be induced in the mouse by the administration of phenobarbitone on Day 12 of development. It results in a delay in the centripetal flow of palatal shelf ossification of increasing magnitude from before backwards, which leaves an unreinforced palatal vault prone to rupture under growth traction or tongue pressures. The absence of bone reinforcement across the midline of the vault, combined with a deficient osseous inductive force in the midline of the palate, contributes to the failure of the velar mesenchyme to merge and elongate. Thus bifid uvula, either alone or combined with submucous cleft

palate, may result from disturbances in the processes of ossification and merging which take place between the seventh and tenth weeks of human development.

SMILEY

Gary Smiley

Gary R. Smiley, research orthodontist at the University of North Carolina at Chapel Hill, who raises ringneck doves as a hobby, worked as a laboratory technician with an embryologist during the summer of his freshman year in dental school. After graduate training in orthodontics he was invited by D. W. Warren to join the University of North Carolina Oral, Facial and Communicative Disorders Program and was thus provided research time for study of the secondary palate. He began work with anatomist A. D. Dixon and from him learned electron microscopy, which aided his investigation of palate fusion. He noted that, as the palate halves come together, the epithelial edges at their union must break down as nasal and oral accumulation of epithelial cells with lysosome bodies gives way by lytic activity to allow mesenchymal union across the midline. The epithelial plate, which is four to six cells thick at time of contact, separates the approaching mesoderm and, by degeneration and desquamation, goes to one-cell thickness at the presumptive area of fusion.

It does not take contact to cause this epithelial breakdown. Smiley notes that epithelial death is programmed before contact, so if timing is off for any reason, the keratinized edges of the cleft will not join each other. If, for instance, the palatal plates are late getting up to their horizontal position, programmed epithelial death along the cleft edges may proceed according to its own schedule, but it will be too late for union to be achieved by the time the palatal halves actually touch each other.

In 1968 M. Pourtois ascertained that

> Fusion of palatal processes is time-critical. That is, if the palatal shelves meet after the critical period for fusion, fusion will not take place.

In 1972 Smiley noted:

Studies which indicate that the soft palate forms by a process of merging could easily explain the occurrence of a bifid uvula, but cannot explain the typical submucous cleft (which has an intact oral and nasal epithelium covering, muscle failing to reach the midline of the velum and usually a deficiency of bone at the posterior border of the hard palate). . . . *There is no satisfactory single explanation for the etiology of the submucous cleft, or even for all clefts of the secondary palate.* Nevertheless, an abnormal epithelial seam either in its formation or breakdown seems to be a most likely explanation for submucous cleft palate.

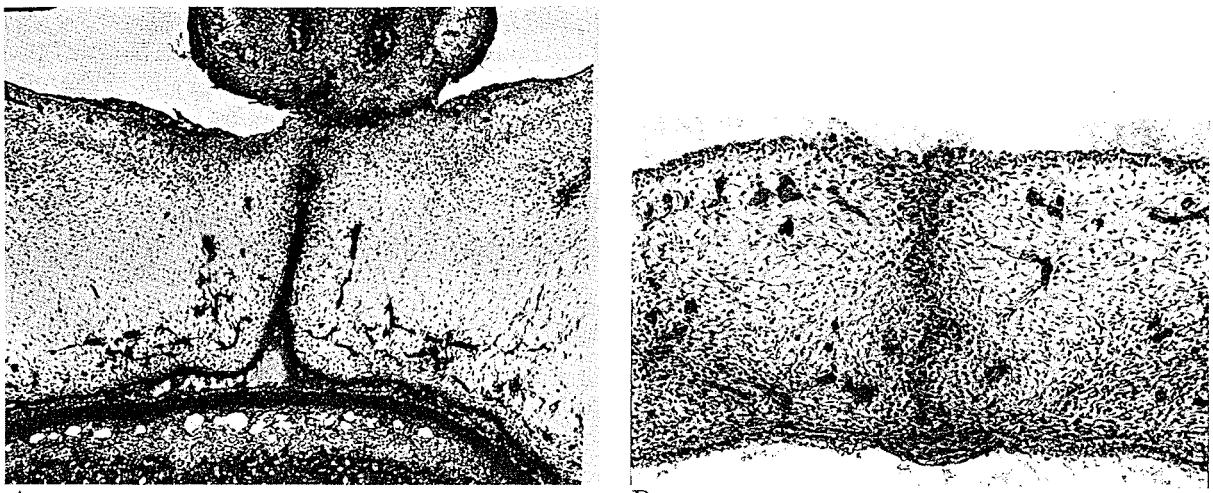
In the *Archives of Oral Biology* Smiley noted in 1975:

There are many studies on the midline epithelial seam during palatogenesis but few have distinguished between the presumptive hard and soft palates. Burdi and Faist (1967) and Burdi (1968) in man, and Bollert and Hendrickx (1971) studying baboons, described the development of both the hard and soft palate suggesting that the soft palate develops by mesenchymal merging rather than fusion because epithelial remnants are not found in the soft palate. However, Shah and Chaudhry (1974) indicated that the soft palate in hamsters formed by the process of fusion of the opposing epithelia. This inconsistency and lack of studies on soft palate formation in mice prompted this investigation on normal palatogenesis to determine whether the soft palate forms primarily by epithelial adherence and mesenchymal fusion or by merging.

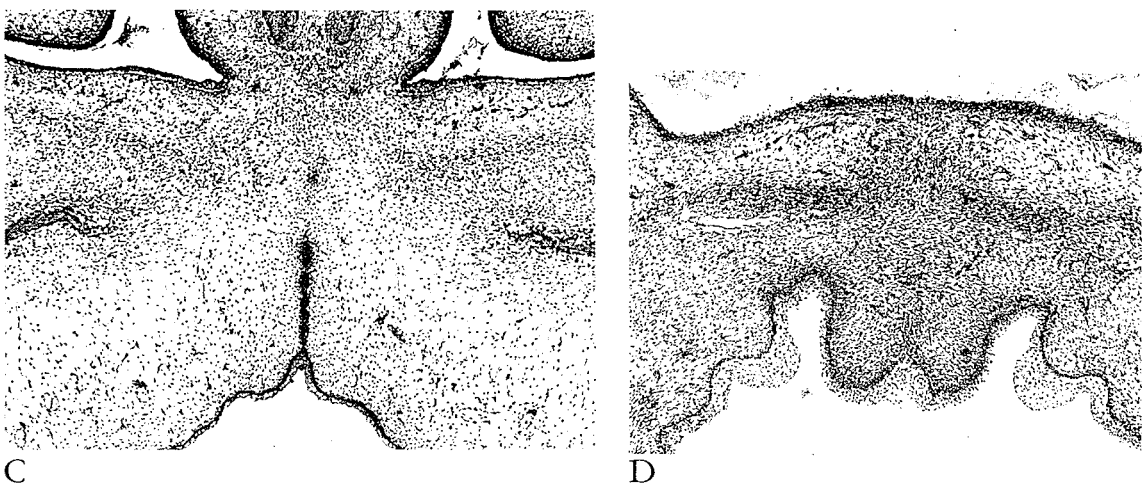
He concluded:

A midline seam of epithelium was observed in the region of the future soft palate [in rodents and man for a relatively short period of time] indicating that epithelial adherence and mesenchymal fusion was occurring, and not merging. Epithelial breakdown was more rapid and complete in the presumptive soft palate and along the junction of the nasal septum and palate than in the midline of the future hard palate.

In his 1975 histological study in *Archives of Oral Biology* Smiley presented some convincing microscopic sections of human fetuses with and without the midline epithelial seam:



"Human 10-week foetus. (A) Future hard palate—midline epithelium is intact except for early breakdown nasally and epithelium is present between the nasal septum and palate. Note glossopalatine epithelium adherence and partial separation of the nasal septum from the palate. (B) Future soft palate—midline epithelium is present and appears to be in clumps in some areas."



"Human 12-week foetus. (C) Potential hard palate—midline epithelium is intact near the oral groove and has broken down nasally. Epithelium between the nasal septum and palate is absent. (D) Potential soft palate—midline epithelium is absent and the uvula has a furrow."

Based upon these observations . . . the hypothesis is proposed that the medial palatal epithelium is different and/or is acted upon differently in the anterior and posterior regions of the developing secondary palate. . . . Besides the palatal epithelium covering the oral and nasal surfaces, the hard and soft palate oral epithelium itself is different. . . . Differential development also occurs in the underlying palatal mesenchyme, e.g., bone forms in

the hard palate and muscle in the soft palate. The palatal mesenchyme that develops into these different tissues could significantly influence the midline epithelium of the respective regions, suggesting that the difference in epithelial breakdown may not reside in the epithelium per se.

IN VITRO STUDIES OF PALATAL DEVELOPMENT IN MICE

Information on the embryological development of the palate is being gleaned from laboratory studies, and, of course, even greater knowledge will eventually be gained from such investigations.

Comparison of secondary palate development with different in vitro techniques, reported by Gary R. Smiley and William E. Koch in 1975, suggest:

> The mesenchyme may play an important role in epithelial degeneration along the medial edge of palatal processes, since epithelial disruption did not occur in the absence of a viable underlying subjacent palatal mesenchyme.

Mary S. Tyler and William E. Koch of the University of North Carolina School of Medicine found that palatal processes removed from 12-day mouse embryos under particular culture conditions were able to continue their differentiation. The discovery enabled these researchers to make certain interesting deductions.

1. They confirmed the assumption that the epithelium at the tip of the vertically oriented palatal process was indeed the future medial epithelium of the horizontally positioned process because "it was always this epithelium at the tip of the vertical process which underwent regression."
2. Their results also confirmed for 12-day palatal processes the 1972 report by Smiley and Koch for 14-day mouse palates that "cellular contact between palatal processes is not a prerequisite for midline epithelial disruption."
3. They clarified the probability that "from the time it becomes identifiable as two ridges projecting from the maxillary arch, the mouse palate is capable of in vitro development and eventual fusion."

4. Finally, as suitable in vitro environmental conditions may be provided which are fully adequate for supporting morphogenesis and histogenesis of early palatal tissues, "it seems appropriate to suggest, therefore, that the concept of the 'acquisition' of a 'potential for fusion' does not identify a specific in vivo period of differentiation in the ontogeny of the mammalian secondary palate."

The administration of excess vitamin A to pregnant laboratory animals has been used extensively to produce a high incidence of cleft palate in offspring (A. Giroud and M. Martinet; H. Kalter; D. H. M. Woollam and J. W. Millen). Explanations differ, however, as to how maternal vitaminosis A leads to fetal cleft palate. Ravindra Nanda, formerly of the University of Nymegen, the Netherlands, and now at the University of Connecticut, Hartford, reported in the 1974 *Cleft Palate Journal* that his recent studies suggest:

> Vitamin A retards the growth of the palatal process in vivo and subsequently the processes do not come in contact with each other at the morphogenetically determined time. The growth of the head subsequently moves the processes apart and fusion does not take place. However, the palatal processes retain their potential to fuse in vitro in the absence of cranio-facial structures and maternal metabolism and environment. This further suggests that vitamin A probably does not irreversibly disturb normal in vivo events of fusion mechanism.

Of course in vitro studies in the human are more enlightening since there are variations from development of the rodent primarily related to differences in behavior of the epithelium and the area of fusion.

Alastair N. Goss of Adelaide, South Australia, noted in the *Cleft Palate Journal* in 1975:

> Only foetuses obtained by open surgical methods are suitable for palatal culture.

His five successful human cultures indicated that it is possible to stimulate in vivo fusion and in vitro epithelial pure formation and to investigate aspects of postfusion rupture. His case I demonstrated that in vitro fusion of human palates does occur,

the fused area showing rapid mesenchymal penetration. Cases III and IV demonstrated that if the intact palate is ruptured, normal healing by epithelial covering of the exposed mesenchyme occurs. As rupture of the previously fused palate was postulated as a mechanism of cleft palate in humans by H. Kitamura in 1966, Goss is in the process of showing that cleft palate can be induced in vivo in the rat by rupture of the intact palate. He reported:

With some types of palatal rupture continued growth of the face distracts the ruptured palate, thus increasing the width of the cleft. Other sites and sizes of palatal rupture heal with time so that the palate has reformed by birth.

Mark Ferguson

Mark W. J. Ferguson of Queen's University of Belfast (center of the troubled zone), who is interested in philately and paleopathology, has studied normal Wistar rat fetuses and those with cleft palate induced by 5-fluoro-2-desoxyuridine to elucidate the mechanisms of palatal shelf elevation and the pathogenesis of cleft palate. In 1977 he wrote:

The following theory is advanced to account for shelf elevation. The gradual build up of mucopolysaccharides, predominantly hyaluronic acid in the palatal shelves from day 14 to day 16.3 produces an increasingly powerful elevating force because of the turgor associated with the strong water binding tendencies of these substances. At 16.3 days this turgor reaches a threshold level and the elevating force becomes sufficient to overcome the resistance offered by the tongue, so enabling flip up to occur. The tongue is passively depressed, flattened, and its tip protruded out of the oral cavity, so making room for the common nasal passage. Other factors aid the transposition of the palatal shelves. Firstly, the undercutting of the underside of the shelf base by epithelium provides a fulcrum for shelf elevation. Secondly, maxillary and palatine osteogenic blastemata are present just exterior to the shelves and afford a firm base for flip up. The subsequent rapid invasion of the elevated shelves by these blastemata, and the ensuing ossification, soon consolidate the elevated palate. . . .

The present theory of shelf elevation postulates a confrontation between shelf elevating force and tongue resistance, and so it is not surprising that depression of the tongue should lead to premature shelf elevation (even at 14 days). It follows that cleft palate is theoretically producible in at least two ways: (1) by decrease in shelf force (as in F.U.D.R. fetuses); (2) by increase in tongue resistance (as seems probable in Pierre Robin–like anomalies

produced by amniocentesis and contraction of the fetal membranes—Poswillo, 1968). . . .

The avoidance, at least during the first twelve weeks of pregnancy, of drugs known to depress mucopolysaccharide synthesis is recommended.

and the persistence of violence in Northern Ireland is now not so much the battle of Protestants vs Catholics as it is a reflection of economic, political and even communistic undertones....

In 1978, as the Winston Churchill Fellow lecturing at the University of Miami School of Medicine, Ferguson added:

The posterior one-fifth of the palatal shelves (i.e., the future soft palate) are horizontal from their first appearance at day 15 and so do not have to elevate. Furthermore these "soft palate shelves" do not approximate each other till day 17.5, whereas the future hard palate shelves have fused within five hours of flip up (which occurs at day 16.4). . . .

All the F.U.D.R. induced abnormalities are readily explicable by depressed mucopolysaccharide synthesis and it is interesting to note that cleft palate in man is frequently associated with such anomalies. . . .

OSSIFICATION CENTERS OF THE MAXILLOFACIAL REGION

According to Patten,

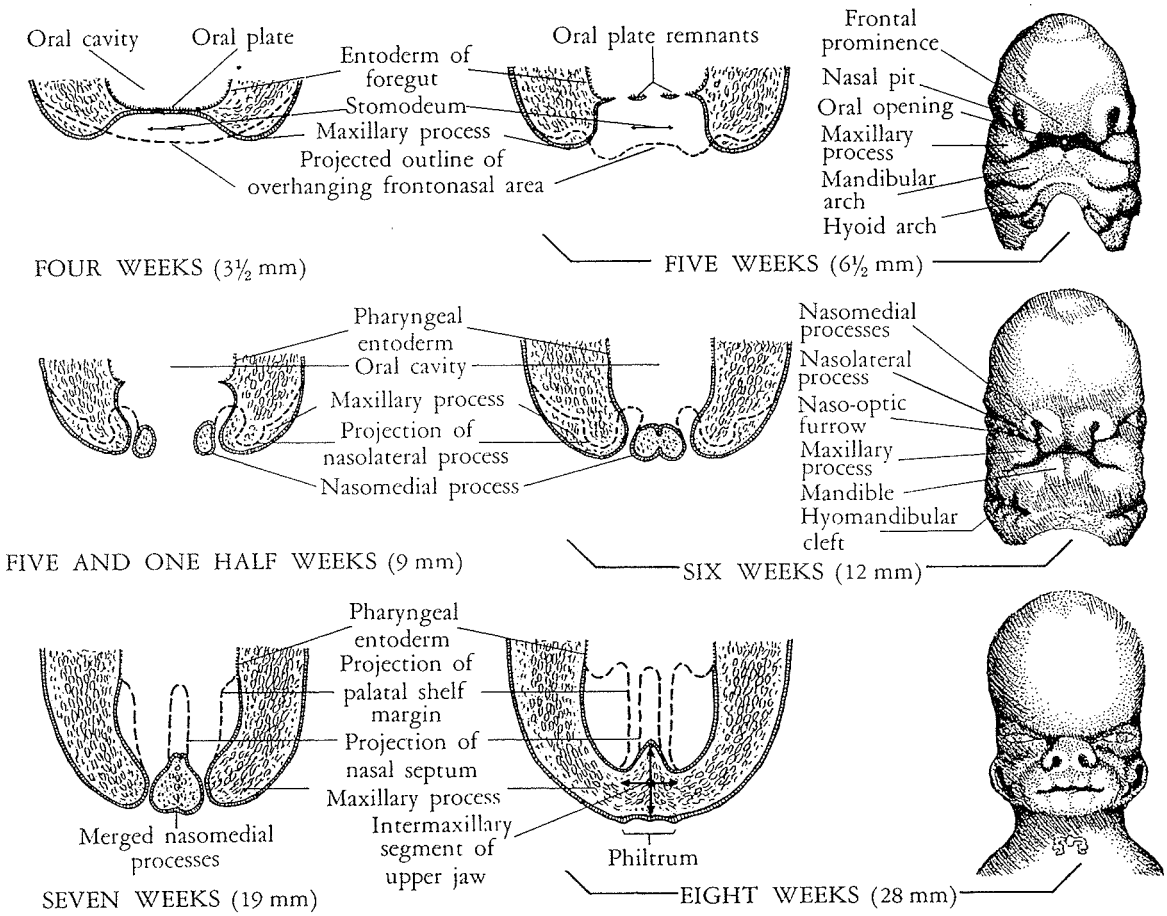
The primary support of the mandibular arch is Meckel's cartilage, which appears late in the seventh week. By the early part of the eighth week the mandibular bone starts to be intramembranously formed as a number of trabeculae lateral to Meckel's cartilage. As ossification spreads, the newly formed mandibular bone tends to enclose Meckel's cartilage.

The maxilla also appears early in the eighth week as intramembranously formed trabeculae in the mesenchyme of the maxillary process. It expands rapidly, but its extensions into the palatal shelves do not ordinarily appear until toward the end of the eighth week when the palatal shelves have moved up from their initial position on either side of the tongue. During the ninth week ossification progresses rapidly, and by the end of the tenth or beginning of the eleventh week, trabeculae extending from the primary ossification areas of the maxillae have laid the foundation for the bony support of the hard palate.

The more medial portion of the maxillary arch which carries the incisor teeth arises, during the late eighth or ninth week, from separate ossification centers formed in the part of the upper jaw which is of nasomedial origin. This independent origin of the incisive portion of the human maxilla emphasizes its homology with what, in lower forms, is a separate bone known as the premaxilla. . . .

The cartilage primordia of the nasal septum and the nasal capsule are clearly differentiated by the end of the seventh week (embryos of 18 to 20 mm. C-R). The paired ossification centers for the vomer appear on either side of the lower part of the cartilaginous septum toward the close of the eighth or the beginning of the ninth week (embryos of 28 to 32 mm. C-R). By the eleventh week the two ossification centers are united below the septal cartilage. A week later the progress of ossification extends so that the periosteum of the vomer merges with that of the palatal bones just above their meeting with each other in the midline.

Here are schematic diagrams showing in the horizontal plane the changing relations at lip level in the developing upper jaw. (From Patten, Normal Development of the Facial Region, in Pruzansky's *Congenital Anomalies of the Face and Associated Structures.*)



As noted by Patten:

The youngest stage represents relations at the level of the originally shallow stomodeal depression before the rupture of the oral plate. The extent to

which the stomodeum is overhung by the frontal area is indicated by a broken line. . . . The downward component of the growth, which is particularly active in the nasomedial processes, soon brings them into the plane of section. Their union is normally a matter of merging rather than of fusing. . . .

Of basic importance in understanding the development of the maxillofacial region are the relationships of the nasomedial processes. Their merging in the midline is readily seen in face views. . . . Their deep relations to the nasal septum are best seen when the developing upper jaw is looked at from below. In such views the deep continuity of nasomedial processes with the primordial nasal septum is clearly evident. Because these primordia lie at slightly different levels, this important relationship can only be suggested in diagrams of horizontal sections at the level of the upper lip by dotting in the position of the nasal septum, as has been done in [the accompanying diagrams].