Oral Tissue Changes in Infants with Cleft Palate

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The condition of the maxillary soft tissues following orthopedic treatment in neonates with cleft palate has been of considerable interest. Since the orthopedic appliance is now being used more frequently, it is the opinion of the authors that fundamental knowledge relative to the changes in these tissues is of importance.

It is a well-known fact that soft tissue changes occur in individuals wearing ill-fitting complete dentures, sometimes with very serious complications (*12*). From clinical experience, changes have been observed in specific maxillary soft tissue sites of cleft palate patients. In addition there are references in the literature to such change.

In a previous publication by Shiere and Fisher (*11*), it was stated that certain benefits were derived from delayed closure of the lip of those patients who had undergone this treatment. In general, it was noted that more tissue was available for repair and that an increased blood supply assured better healing. Similarly, it was the subjective impression of the surgeon (JF) that, at the time of palatal closure, gross changes had occurred in the soft tissues which should be evaluated.

In a recent publication, Maisels (*8*) asserted that 'the mucoperiosteum of the palate seems to hypertrophy and thicken.'

It has also been reported by Jacobsen and Rosenstein (*6*) that the hard palate is stimulated by the orthopedic appliance when used in either an active or passive manner. They continued by stating that 'some of the appliances have remained inserted without removal for as long as three weeks, demonstrating little or no clinical evidence of tissue irritation or accumulation of debris.'

Brauer and associates (*2*) observed that the neonates quickly be-

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came accustomed to the prosthesis and tolerated it well. We interpret the word *tolerate* to mean comfort, non-irritating, lack of feeding problems, and acceptance to change during maxillary alignment.

Burston (*3*) states that 'following lip closure a plate is inserted to maintain arch alignment and to stimulate growth of the palatal processes.' 'The rationale of this procedure is such that, if the blood supply to growing tissue can be increased, hypertrophy is likely to occur.' Burston maintains that, in his experience, the size of the cleft is reduced prior to palatal closure, in which case the closer apposition of the palatal folds permits the surgeon to concentrate on lengthening the soft palate rather than closing a wide lateral defect.

McNeil (*9*) concludes that a 'narrowing of the cleft is due to growth of the underlying bone.' By histological examination, he has shown that 'instead of proliferation of soft tissue there is, in fact, thinning of the marginal tissues.'

Grob (*5*) noticed that the anterior segments of the cleft area had become smaller because of an overlapping of palatal mucosa over the edge of the bony cleft. 'This mucous membrane showed a granular surface and was friable.' 'Histological examination revealed inflammatory infiltration probably resulting from the pressure of the orthopedic appliance.'

Fogh-Anderson and Dahl (*4*) remarked that the oral mucous membrane was somewhat irritated and edematous when a prosthesis had been worn by the cleft palate babies. Neither Grob nor Fough-Anderson and Dahl believed that this changed condition of the soft tissues enhanced their surgical procedures.

It is the purpose of this investigation to determine, by histologic section, differences in the soft tissues of the maxilla obtained from neonates with cleft palate, beginning shortly after birth to approximately one year of age. Infants without a cleft palate deformity were included in the sample for control purposes.

Materials and Method

During the past three years a total of sixty newborn children with cleft lips and palates has been seen at the Boston Floating Hospital. Of these children, 48 have undergone pre-lip repair orthopedic treatment for periods of time extending from five weeks to about twelve months. It was expected that those babies wearing the appliance would show an improvement in maxillary arch alignment, approach a more normal posterior muscular development, and achieve proper tongue placement.

The twelve babies who were not participating in the orthopedic rehabilitation had only small posterior palatal clefts and were feeding well. A few, also included in this number, had severe congenital anom-

TABLE 1. Composition of the three subject groups.

	group 1	*group 2*	*group 3*
	noncleft subjects	*cleft palate without prosthesis*	*cleft palate with prosthesis*
male	4	3	6
female	7	2	3
total	11	5	9

alies in addition to the cleft palate, such a hydrocephaly. The investigators did not think that an orthopedic prosthesis was either necessary or desirable in these cases.

In order to evaluate any changes occurring in the soft tissues of the palate under this appliance, three groups were devised for comparative purposes (Table 1). Patient selection was made arbitrarily in all groups for biopsy sections. The first group included infants who were hospitalized for surgical problems, such as a hernia, but had no oral anomalies. The number in this group was 11 (4 males and 7 females), ranging in age from two to 348 days.

The second group encompassed five cleft palate patients, three males and two females, who did not wear prostheses. The earliest biopsy was taken at three days of age, while the latest was secured at the time of surgical palate closure at 417 days.

The third group consisted of nine babies, six males and three females, who had a cleft palate and wore the prosthesis. The earliest biopsy was taken at 58 days and the latest in this group at 345 days of age. Although the appliance was inserted as soon after birth as possible, it was necessary to permit the infant to wear it for a period of time before the biopsy specimen was secured. With one exception, all biopsy specimens were from different individuals.

Two cases of premature infants were included in the normal group, while autopsy material was secured from six infants in Group I and one infant in Group II. Since one of the reasons for the use of the appliance is to improve the maxillary arch form, it is necessary to alter the construction model and to remake the appliance at frequent intervals. When the appliance is inserted, it naturally does not conform accurately to the subject's maxillary arch configuration. Therefore, the selection of the biopsy sites have to be determined on the basis of choosing areas exposed to increased pressures from the appliance. It was obvious that these susceptible areas were the maxillary alveolar ridge and the hard and soft palate in the area of the cleft. These, then, were the sites selected for biopsies.

Each individual specimen was placed in a small, coded bottle containing formalin and sent to the Oral Pathology Laboratory. The

specimens were embedded in paraffin, sectioned at six microns, and stained with hematoxylin and eosin. The sections were read and interpreted by one of the authors (EC) on a blind basis and afterwards decoded and compared with each other.

Results

Clinical Observations. From the point of view of the surgeon (JF), the neonatal orthopedic treatment was successful. Not only were the gross bony deformities improved, but also a remarkable thickening of the soft tissues of the maxilla was observed (Figure 1).

During the surgical repair of the cleft palate, a number of observations were made. In those cases where the prosthesis was not worn beforehand, the mucoperiosteum appeared to be approximately 1 mm thick and the soft tissues were friable, showing a rather tenuous blood supply after the flaps were developed. For those who had worn the orthopedic prosthesis over a period of several months, the mucoperiosteum appeared to be three to four times thicker, and the fibrous layer was firmer, capable of holding sutures easily. The area was well supplied with large blood vessels. It was felt that a successful palate closure at six to eight months of age could be readily achieved.

The occasional breakdown of the suture line with either a complete separation or a residual fistula found in from 10% to 20% of typical

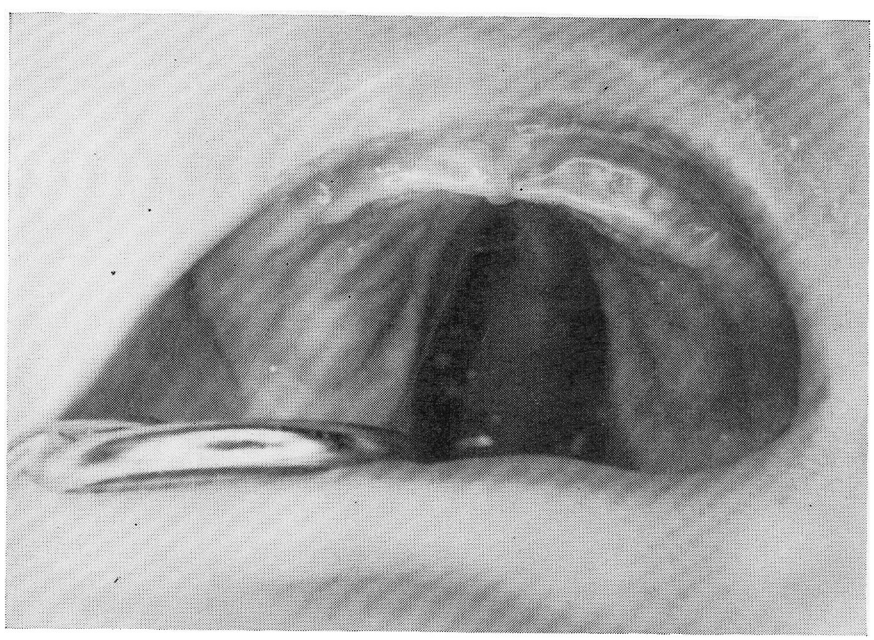

FIGURE 1. Clinical photograph of a patient who has worn a prothesis.

cases did not occur in those patients who had orthopedic treatment prior to surgery.

Microscopic Observations

Group I: Noncleft Subjects. The epithelium of the sections of alveolar ridge revealed formation of a stratum corneum and occasional accentuation of the stratum granulosum. The epithelium varied in thickness but consisted of approximately fifteen cell layers. The rete pegs were arranged in the usual configuration. The submucosa was composed of dense collagenous connective tissue with prominent vascular channels (Figure 2). Three specimens from the alveolar ridge contained a light chronic inflammatory infiltrate consisting of plasma cells and lymphocytes.

Sections of the hard palate presented essentially the same epithelial and submucosal characteristics as the alveolar mucosa (Figure 3).

The soft palate epithelium was usually composed of fewer cell layers than the hard palate epithelium and revealed slight keratosis and fewer rete pegs. The submucosa consisted of a loose, vascular connective tissue (Figure 4).

In six of the eleven biopsies of the alveolar ridge, epidermoid cysts were noted. These microcysts were usually multiple and varied in

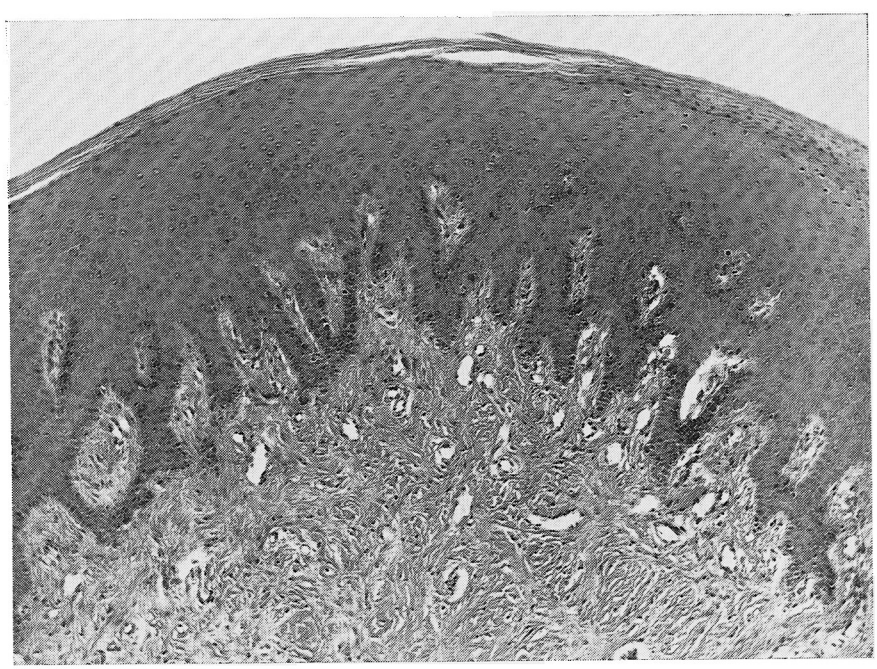

FIGURE 2. Alveolar mucosa of noncleft infant. Note moderate keratin formation. Hematoxylin and eosin. Magnification × 160.

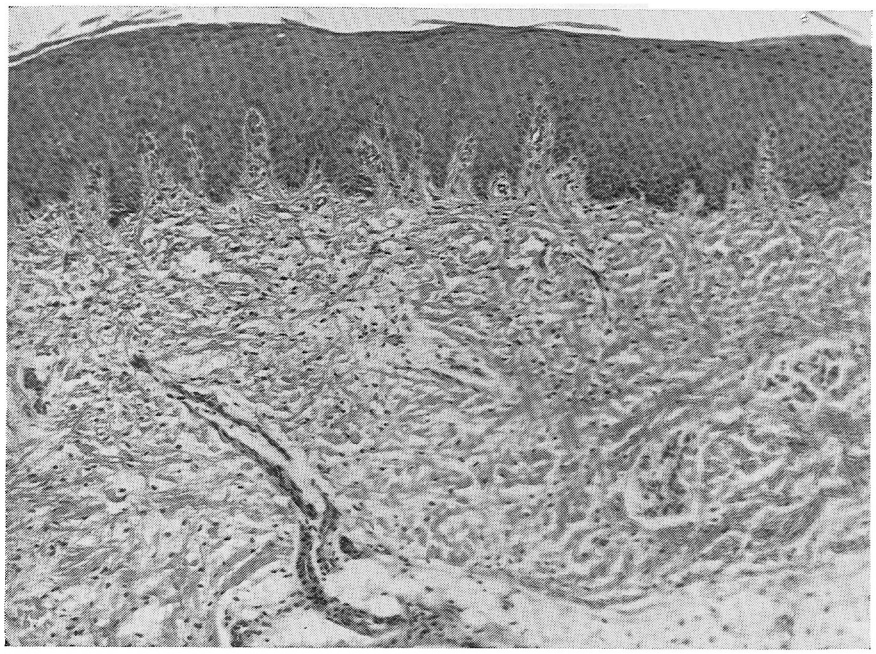

FIGURE 3. Mucosa of hard palate of noncleft infant. Hemotoxylin and eosin. Magnification × 160.

size, but were not observed clinically. The cyst walls were composed of stratified squamous epithelium and the lumina of some of the cysts were filled with keratin. Small epithelial islands, which resembled the rests of Malassez, were often seen in association with the cysts. The epithelial islands, consisting of cubiodal cells, underwent metaplastic alteration to epithelium of the stratified squamous type with subsequent formation of keratin and early cyst formation. Desquamated epithelium and basophilic calcified material were occasionally seen in the lumina of cysts (Figure 5).

Group II: Clefts without Prosthesis. The oral epithelium from the alveolar ridge and hard palate was very similar to the mucosa of the noncleft patients. Two of the five specimens revealed epidermoid cysts in the alveolar ridge tissue.

In the tissue specimens taken from the cleft area, stratified squamous epithelium, transitional epithelium, and ciliated columnar epithelium were seen. The transitional and respiratory epithelium was thinner and composed of fewer cell layers than the epithelium of the soft palate. Rete pegs were not seen in the transitional epithelium. In three of the five specimens taken from the cleft, a light-to-moderate chronic inflammatory infiltrate was noted in the submucosa. The inflammatory infiltrate consisted of lymphocytes, plasma cells, and scattered poly-

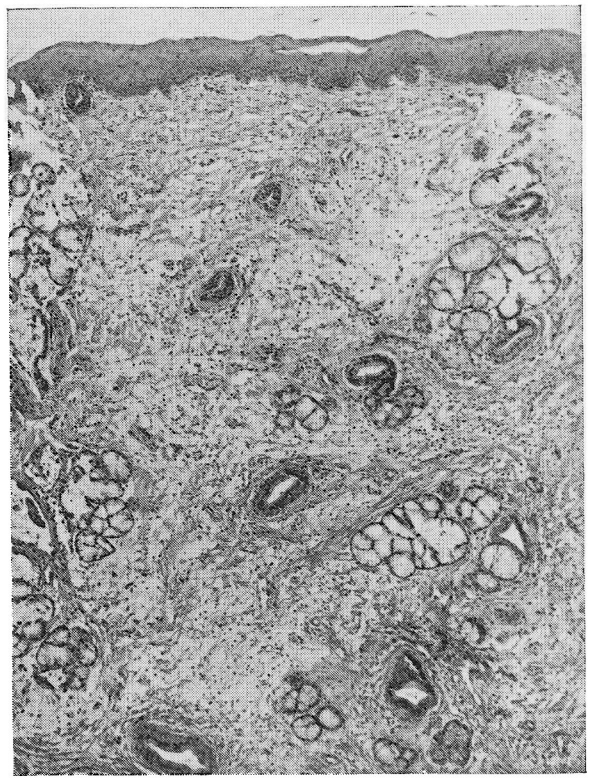

FIGURE 4. Soft palate mucosa of noncleft infant. Numerous mucous glands are seen in the connective tissue. Hematoxylin and eosin. Magnification × 90.

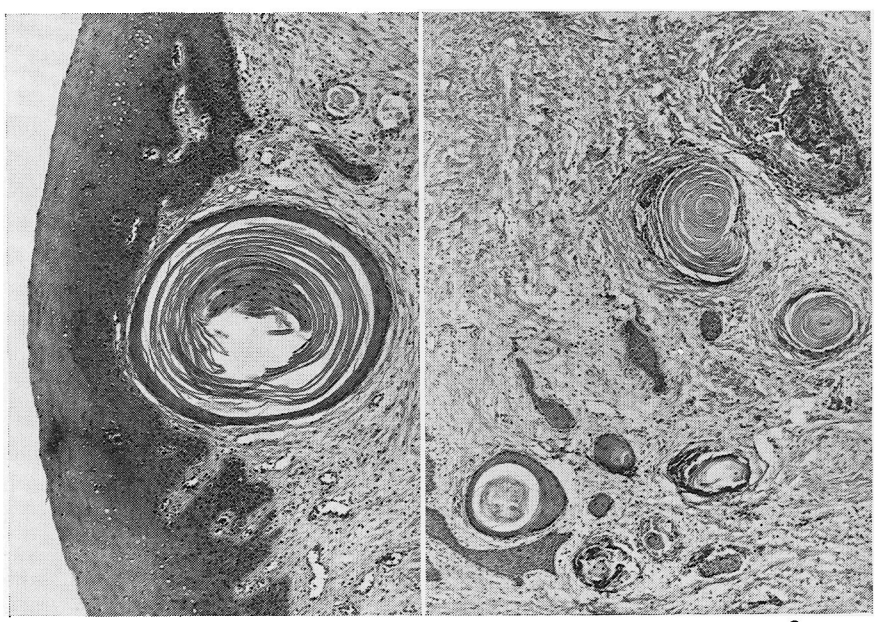

FIGURE 5. Left, alveolar mucosa of noncleft infant revealing a keratin filled cyst. Hematoxylin and eosin. Magnification × 160. Right, alveolar ridge tissue of noncleft infant containing several epidermoid cysts. Rete pegs of oral epithelium can be seen in the upper left corner of photomicrograph. Hematoxylin and eosin. Magnification × 160.

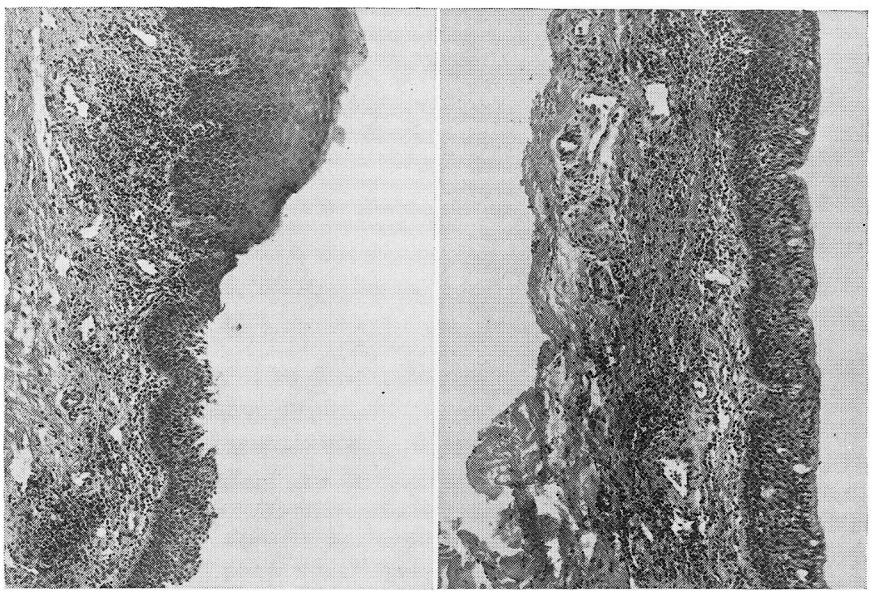

FIGURE 6. Left, tissue from the cleft of a patient without a prosthesis. Oral epithelium and transitional epithelium is seen. The connective tissue is infiltrated with plasma cells and lymphocytes. Hematoxylin and eosin. Magnification × 160. Right, section of respiratory epithelium from the cleft of a patient without a prosthesis. A chronic inflammatory infiltrate is seen in the connective tissue. Hematoxylin and eosin. Magnification × 160.

morphonuclear leukocytes, and was observed in the connective tissue beneath the respiratory and transitional epithelium as well as the oral epithelium. The sections which contained accessory mucous glands presented ductal and acinar distention with mucous and a mild inflammatory infiltrate. The submucosa was highly vascular and appeared to be edematous and less dense than the soft palate tissue of noncleft patients (Figure 6).

Group III: Clefts with Prosthesis. The mucosa of the alveolar ridge and hard palate did not show any remarkable changes from the corresponding areas in the other groups. Two specimens from the alveolar ridge contained epidermoid cysts.

All specimens taken from the cleft areas contained a chronic inflammatory infiltrate consisting of plasma cells, lymphocytes, and polymorphonuclear leukocytes. In some instances, the inflammatory infiltrate appeared more dense than the inflammatory reaction seen in the cleft patients without an appliance. The cellular infiltrate was noted beneath the oral as well as the transitional and respiratory epithelium. In some sections, the inflammatory reaction was very dense beneath the respiratory epithelium (Figure 7).

Moderate keratinization was seen in some areas of the oral epithelium. Some of the specimens containing mucous glands presented ductal

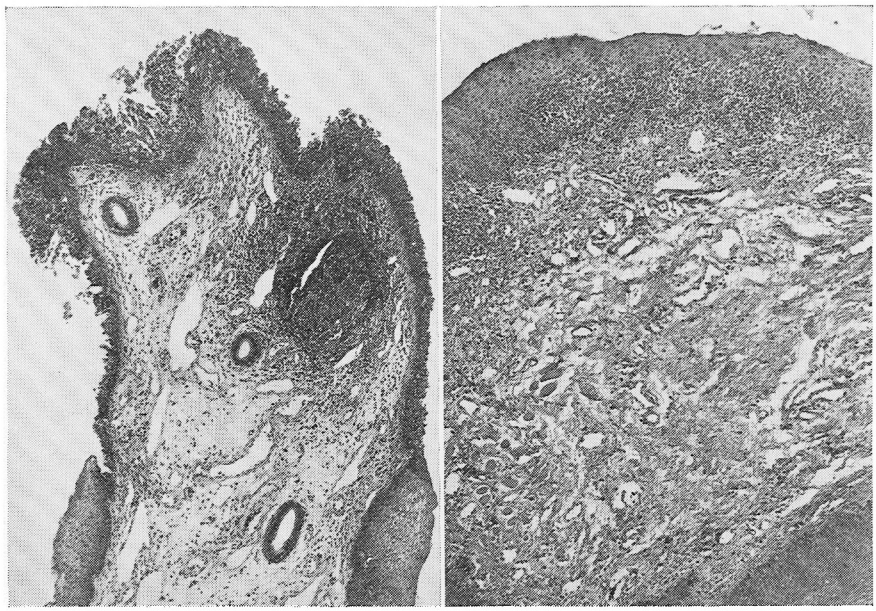

FIGURE 7. Left, tissue from the cleft of a patient wearing a prosthesis. Both respiratory and oral epithelium are seen. A chronic inflammatory infiltrate is evident in the connective tissue. Note the vascularity of the submucosa. Three mucous ducts are also seen in the connective tissue. Hematoxylin and eosin. Magnification × 100. Right, tissue from a cleft of a patient without a prosthesis. A dense inflammatory infiltrate is seen in the connective tissue. Hematoxylin and eosin. Magnification × 100.

and acinar distention with mucus, areas of mucous pooling, and a periductal inflammatory infiltrate. The appearance of the connective tissue was similar to that in cleft patients without a prosthesis.

Discussion

The neonatal orthopedic prosthesis has been proposed as a means to correct the severe bony deformities present in some patients born with cleft lip and palate. Although all but the widest clefts can be closed surgically, the persistent and progressive bony deformities mar the cosmetic and functional results. The preoperative orthopedic treatment is undertaken in the hope of improving these bony deformities before soft tissue closure.

In the findings reported here, no great differences in histological findings were observed among the various groups. To some degree, inflammation was observed in the sections of all three groups. However, it was found most commonly among the cleft palate patients. This inflammation was more dense in the cleft areas in those subjects who wore the prosthesis and was seen in all subjects in this group. A moderate amount of keratinization was observed in the cleft palate

group with the appliance, but it was seen too infrequently to draw any conclusions.

In general, it can be stated that the epithelium of the alveolar ridge was similar in all subjects and corresponded somewhat to that of healthy edentulous adult patients.

Although the prediction could be made from clinical observations that a possible proliferation of connective tissues would be seen in the microscopic sections, this was not found to be true. On the contrary, a slight thinning of the epithelium at the margins of the cleft was found in some sections, a finding which was also observed by McNeil (*9*).

However, the clinical observations of a definite narrowing of the clefts, the conclusions of the surgeon at the time of operation, and finally, the results of the operation itself, strongly suggests that there must be an increased activity in the mucoperiosteum and even in the bone. McNeil (*9*) has previously expressed similar thoughts.

The knowledge gained by the surgeon during the time of the operation concerning the increased thickness of the mucoperiosteum, the firmness of the fibrous layer, and the increased size of the blood vessels seemed to indicate that the sections obtained in this study were not of a sufficient depth and were definitely not adequate in size. It is obvious that, for future evaluations, biopsy material covering a cross-section of the entire maxilla would be invaluable to substantiate the suspected changes that are perhaps occurring in the periosteum and bone.

It is also interesting to note that residual fistulas following surgery did not occur in those cases in which the orthopedic appliance had been utilized.

It is our opinion that these findings indicate that there are benefits derived from neonatal treatment for surgery. Therefore, we cannot concur with Grob and Fogh-Anderson.

The inflammatory infiltrate of the respiratory epithelium was consistent for all cleft palate subjects. It was suggested by Routledge (*10*) that this inflammation might be responsible for middle ear infections common in children with cleft palates, resulting from a chronic upper respiratory tract infection, thought to be caused by stagnated food in the nasal pharynx. Since the appliance does not cover the entire cleft area, it can be expected that the respiratory epithelium would be inflamed.

One of the most interesting findings was the presence of a large number of epidermoid cysts in all groups. Such cysts were found only in the areas of the alveolar ridge. These cysts seem to be a consistent finding in the infant oral mucosa and merit closer investigation. The presence of cysts in the maxilla, mandible, and oral mucous membrane

of fetuses and of infants has been previously reported by Kreshover (*7*) and Bhaskar (*1*).

Summary

An investigation has been made of the palatal soft tissues of a group of normal and cleft palate infants. The following conditions were noted. a) The clinical evaluation showed thicker tissues in the cleft area in the orthopedic patients. b) Surgical results were enhanced in those patients wearing the prosthesis. c) Inflammation was noted in the cleft areas of both groups of cleft palate patients. d) Epidermoid cysts were seen in some alveolar ridge tissue of all groups. e) Further histological examinations are indicated.

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