Repair of Surgical Clefts of the Hard Palate in Beagles

DAVID P. FORBES, D.D.S. PH.D.
EDWARD J. KAMINSKI, PH.D.
HAROLD T. PERRY D.D.S., PH.D.

The biological response to the repair of palatal clefts has been evaluated principally by monitoring craniofacial growth. Little is known about the regenerative ability of the repaired palate. In the present study, 18 Beagle pups (51 to 58 days old) were assigned to one of three groups: (1) control group, having no surgery; (2) cleft group, having a surgically created cleft of the posterior hard palate (mean bony measurement: 3.1 × 11.7 mm) at 8 weeks of age; and (3) repaired group, same as group 2, and followed by soft-tissue closure at 12 weeks of age. Craniofacial growth was monitored by cephalometric and dental cast measurements. Records were taken at 6-week intervals. Animals were sacrificed either 16 or 28 weeks after time of cleft creation. Routine histologic examination and histochemical detection of alkaline phosphatase activity were performed to examine the quality and extent of soft-tissue repair and bone formation. Analysis of the cleft palate group revealed that the size of the bony cleft increased with time. The histologic examination demonstrated at 24 weeks of age (12 weeks after the repair) active reduction of medial margin of the bony palate as evidenced by osteoclastic activity. At 36 weeks of age, neither osteoblastic nor osteoclastic activity was detected. The mean dimensions of the bony cleft, in the cleft group at 36 weeks, were 7.9 × 18.8 mm. In the repaired group, partial bone repair occurred. However, no consistency was seen in predicting extent or location of repair. Histochemical detection of alkaline phosphatase activity indicated that the repaired group had greater amounts of new bone formation. In some sites, suture regeneration was seen. As with the amount of bone formation, the amount of suture regeneration was variable. This study revealed that the presence of a cleft inhibits osteoblastic activity along the margin of the cleft, and there is limited potential for regeneration of the palate subsequent to the repair.

KEY WORDS: *suture regeneration, cleft palate, alkaline phosphatase, bone repair, maxillary growth.*

Numerous studies (Herfert, 1954, 1958; Kremenak et al 1967, 1970a, 1970b, 1971, 1980; Searles and Biggs, 1974; Jonsson and Stenstrom, 1978) have examined the problem of growth attenuation as a result of surgical repair of the palate. The principal experimental design used to study the postoperative sequelae has involved surgical manipulation to only one-half of the palate, leaving the other one-half to serve as control. As a result of these studies, (Kremenak et al, 1971) have shown that the denudation of the palatal bone and repair by secondary intention adversely altered the growth potential with respect to length and width of the palate. It has been clearly demonstrated that the most negative variable affecting growth of the maxilla is the formation of scar tissue.

Another model of the palatal cleft has been the midline design, in which a defect is created in the midline of the palate. This model more

Dr. Forbes is Associate Professor and Chairman, Department of Orthodontics, Northwestern University Dental School, Chicago, IL. Dr. Kaminski is Professor, Department of Pathology, Northwestern University Dental School, Chicago, IL. Dr. Perry is Professor, Department of Orthodontics, Northwestern University Dental School, Chicago, IL.

Address reprint requests and correspondence to David P. Forbes, D.D.S., Northwestern University Dental School, Department of Orthodontics, Chicago, IL. 60611

closely resembles the cleft palate model. However, very few investigations established total perforation of the palate. Instead, a partial opening was created, in which the palatal bone was excised but the nasal mucosa was left intact. Only studies by Latham et al (1975); Lynch and Peil, (1966); Bardach et al, (1980, 1982); Bardach, (1985, 1987); and Verwoerd et al (1976) used experimental designs involving through and through clefts of the secondary palate. A significant feature of the design of these studies was the creation and repair of the palatal defect performed as a combined surgical procedure. The principal intent of these studies was to evaluate the growth of the maxilla following repair of the palate.

Besides the growth potential, another area of concern is the ability of the osseous tissues to repair and regenerate following surgery. This area has not been as closely investigated. Little is known to what extent the osseous tissue reconstructs a palatal shelf and develops an intervening suture following cleft repair. In studies dealing with the histology of repair of the palate (Freng, 1979; and Barro and Latham, 1981), the palate demonstrated excellent regenerative capacity. In these studies, the nasal mucosa was not altered. As with the studies evaluating the growth potential, no intervening time was used to permit the palatal defect to heal before the surgical repair of the palate took place. Consequently, no distinction could be made between the regeneration of the palatal defect that occurred as a result of the repair procedure or that which occurred spontaneously.

The only histologic study involving a repair of a cleft palate following the formation of a through and through cleft was done by Atherton and White (1970). They partially repaired the palate of a Labrador puppy 6 weeks of age with a congenital cleft and evaluated the tissue after 13 weeks. They reported a limited capacity of the connective to replace the missing bone. Areas of disorganized woven bone were seen adjacent to regions of more mature cancellous bone. The anterior region of the palate tended to have better bone formation than did the posterior regions.

The present study establishes a model in which a surgical cleft of palate was created of a size that did not permit spontaneous closure. After surgically creating the defect, an intervening time of 4 weeks was used to separate the responses of surgical creation and repair. His-

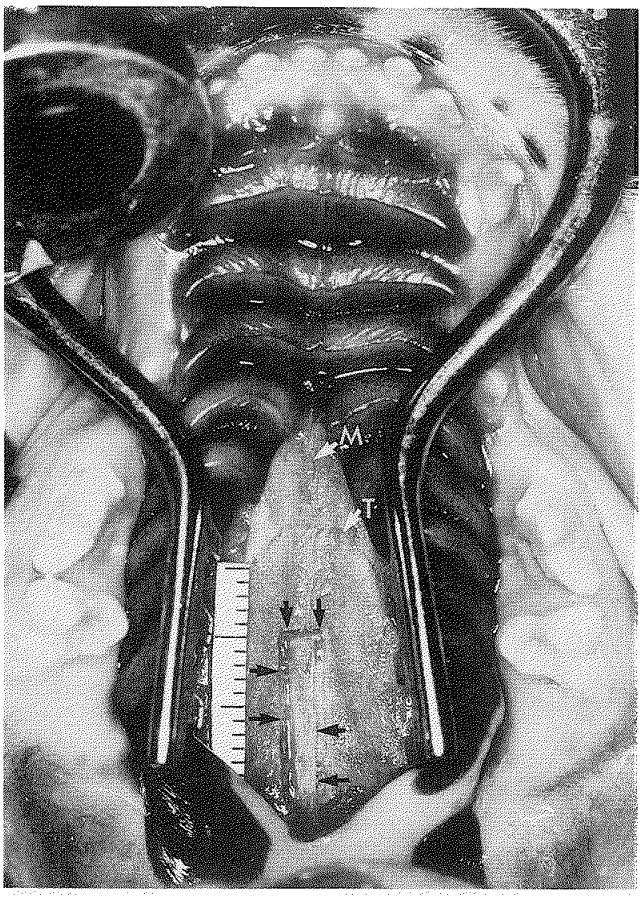

FIGURE 1 Intraoral photograph depicting the surgical procedure to create a cleft of the hard palate in a Beagle pup 8 weeks of age. The outline of the cleft is marked in black arrows. The dimensions of the cleft were confined to the palatine bone. The midpalatal suture is labeled M and the transverse suture is labeled T.

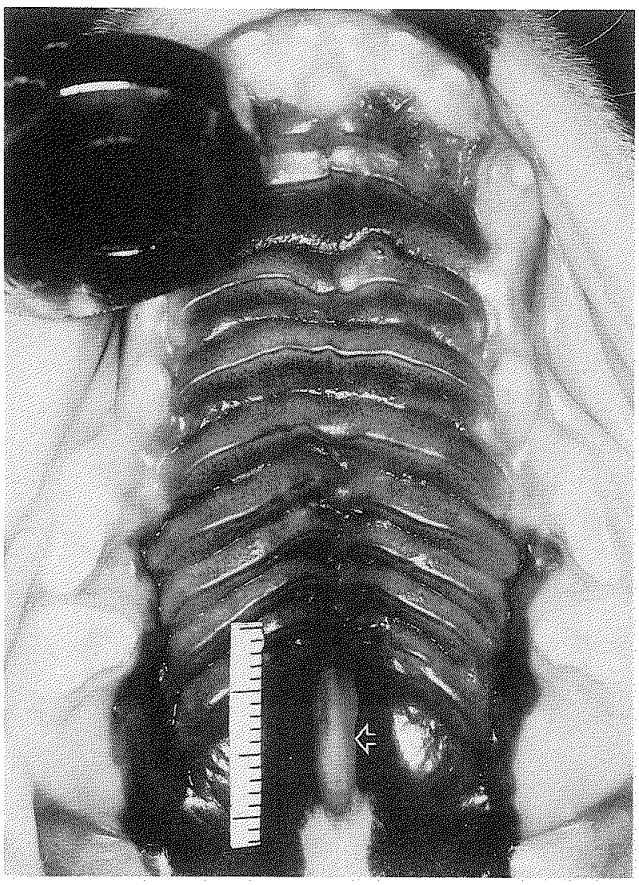

FIGURE 2 The palate photographed at 12 weeks, at the time of repair. The white arrow indicates the soft tissue outline of the cleft. The rule is in millimeters.

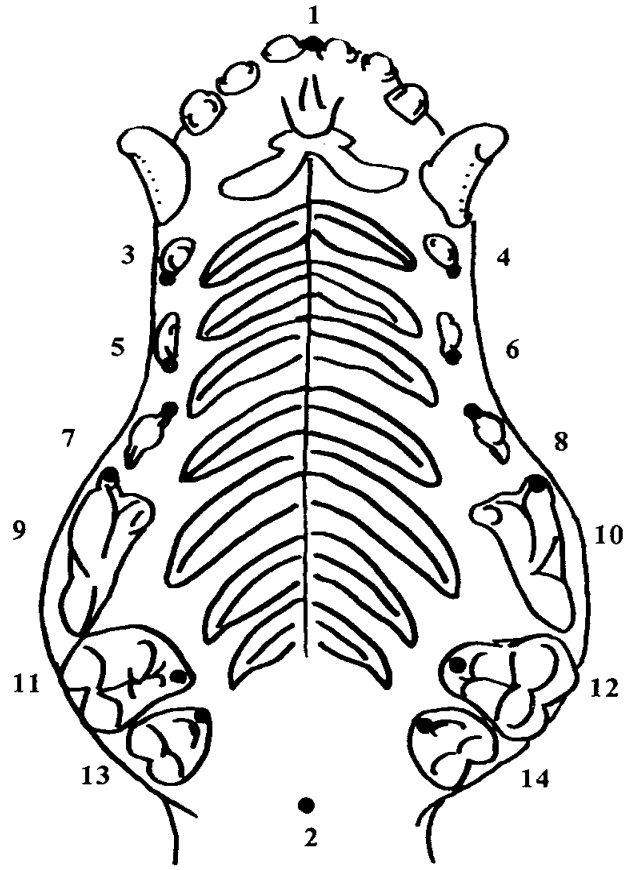

FIGURE 3 Schematic diagram of the points selected for the model analysis. Maxillary length: points 1–2; first bicuspid width: points 3–4; second bicuspid width: points 5–6; third bicuspid width: points 7–8; fourth bicuspid width: points 9–10; first molar width: points 11–12; second molar width: points 13–14.

tologic and radiographic evaluations following repair were performed to determine the regenerative capacity of the palatal tissues.

Materials and Methods

Eighteen purebred male Beagle pups (51 to 58 days old)* were used in this study. Three groups were established to separate the variables of the different surgical interventions. No littermates were placed in the same group.

Control group: No surgical procedure was performed (mean age, 54.8 ± 0.8 days); N = 6.

Cleft group: An isolated, partial cleft of the hard palate was created at the age of 8 weeks (mean age, 54.5 ± 2.1 days). The surgical defect was not subsequently repaired; N = 6.

Repaired group: An isolated, partial cleft of the hard palate was surgically created at 8 weeks and subsequently repaired 4 weeks later, using the von Langenbeck procedure (mean age for cleft creation, 54.5 ± 2.2 days; mean age for repair, 82.5 ± 2.2 days); N = 6.

Surgical Procedure to Create Cleft

The dogs were anesthetized with halothane, using a pediatric anesthesia unit. After local anesthetic was applied, a midline incision was made extending from the level of the first primary molar posteriorly to the edge of palatine bone of the hard palate. Bilateral, full-thickness mucoperiosteal flaps were raised. With a high-speed handpiece, using water coolant, a section of bone 3 × 13 mm was removed from the center of the posterior edge of the hard palate. Crescent wedges, approximately 10 mm × 1 mm were bilaterally excised from the edges of the incised oral mucosa to assure postoperative patency of the cleft (Fig. 1). The size of the cleft was measured to the nearest 0.05 mm. The nasal and oral mucosa were sutured to each other, to also prevent spontaneous closure, with

* Supplied by Marshall Research, North Rose, NY.

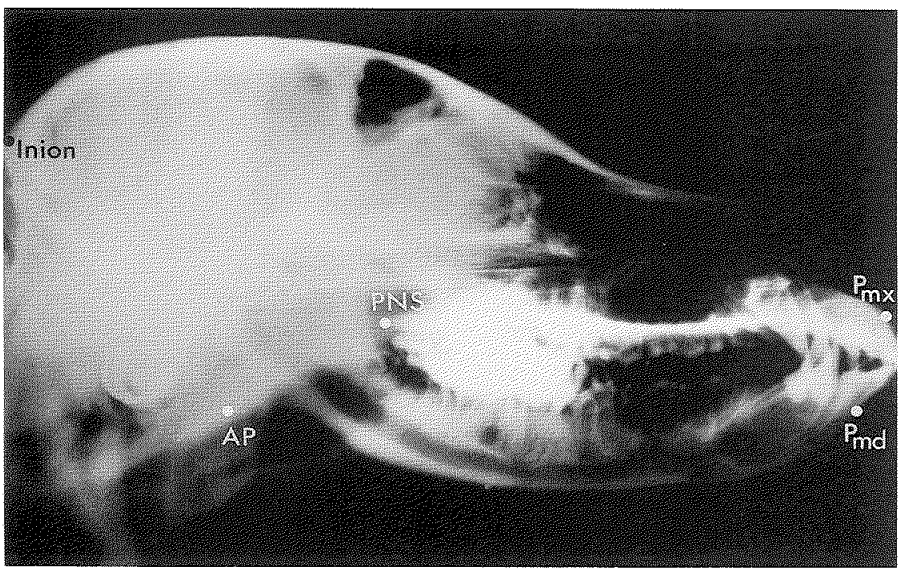

FIGURE 4 Lateral cephalogram with landmarks used to evaluate craniofacial growth: PNS (posterior nasal spine); AP (angular process); P_{mx} (prosthion-maxillary); P_{md} (prosthion-mandibular); Inion (external occipital protuberance). Maxillary length: PNS–P_{mx}; mandibular length: AP–P_{md}; craniofacial length: Inion–P_{mx}.

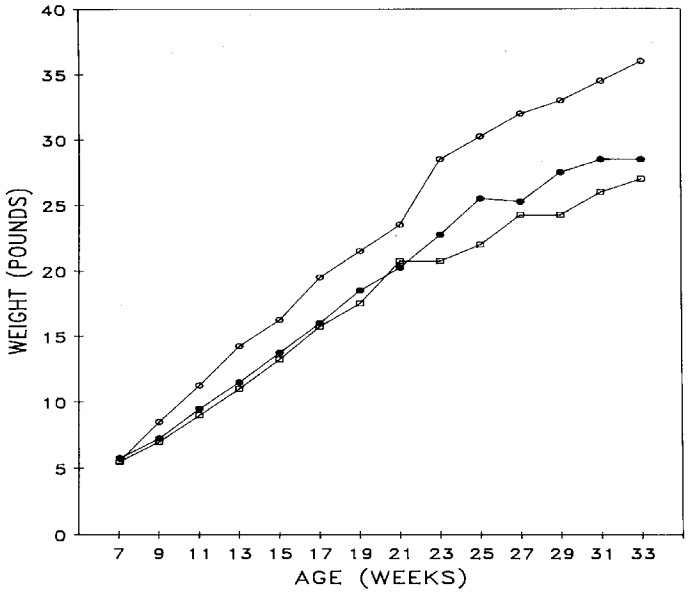

FIGURE 5 Graph of the body weight recordings. The body weight values of the cleft and repaired group were significantly different from those in the control group (8–24 and 8–36 weeks; $p \leq 0.02$).

4–0 gut sutures. The dogs were given 100% oxygen until fully recovered (see Fig. 1). The size of the cleft created was determined by pilot studies to be of a size that did not permit spontaneous closure by the mucoperiosteum and yet did not interfere with the vomer, which was shown by Latham (1975) to interfere with facial growth (see Fig. 1).

To maximize food intake, all the dogs were fed Purina Puppy Chow mixed with an equal volume of water to achieve a softened consistency. There were two feedings daily: one in the morning and one in the evening. The dogs were inspected twice daily for signs of infection, dehydration, and eating deficiencies. Housing consisted of kennels kept at a constant temperature of 72°C with 14/10 hours of light and darkness, respectively.

Cleft Palate Repair Procedure

After a 4-week interval, the dogs were anesthetized and a palatal closure procedure was performed by the method of von Langenbeck (Fig. 2). To assure closure, two full-thickness mucoperiosteal flaps were raised and lateral releasing incisions made. The size of the cleft was measured with calipers (Helios) with a 0.05-mm resolution. At this time, a two-layered palatoplasty was performed. To be considered a successful repair, two criteria had to be met: (1) Only one, two-layered palatoplasty procedure should be required to close the defect, and (2) no fistulae should develop after the repair procedure.

Growth and Development Evaluation

At 24 and 36 weeks, three animals from each group were sacrificed by anesthetic overdose. All animals were weighed weekly. Records were taken, with the dog under general anesthesia, according to the following schedule: 8, 12, 24, 30, and 36 weeks of age. Records consisted of standardized lateral cephalographs, occlusal radiographs, dental casts, and intraoral photographs.

TABLE 1 Model Analysis: Maxillary Arch Width Between the Maxillary Second Molars (Points 13–14)*

	Group		
	Control	*Cleft*	*Repaired*
Weeks			
24	42.6 ± 1.9	40.7 ± 1.3	38.7 ± 2.7†
30	45.9 ± 2.3	42.1 ± 0.7	39.5 ± 3.0†
36	46.7 ± 2.9	42.7 ± 0.6	39.8 ± 2.8†

* Mean ± standard deviation in millimeters. 24 weeks: n = 6; 30 and 36 weeks: n = 3.
† Repeated measures one-way analysis of variance revealed significant differences from control group; $p \leq 0.05$.

TABLE 2 Model Analysis: Maxillary Arch Width Between the Maxillary First Molars (Points 11–12)*

	Group		
	Control	*Cleft*	*Repaired*
Weeks			
24	34.1 ± 2.5	33.1 ± 2.5	31.7 ± 1.0
30	35.3 ± 2.1	34.4 ± 2.5	32.8 ± 1.3
36	35.4 ± 2.1	34.7 ± 2.1	33.4 ± 0.9

* Mean ± standard deviation in millimeters. 24 weeks: n = 6; 30 and 36 weeks: n = 3.
Repeated measures one-way analysis of variance revealed no significant differences.

TABLE 3 Model Analysis: Maxillary Arch Width Between the Maxillary Fourth Bicuspids (Points 9–10)*

	Group		
	Control	*Cleft*	*Repaired*
Weeks			
24	41.6 ± 1.6	40.6 ± 2.3	39.3 ± 0.3
30	44.0 ± 1.2	42.5 ± 2.6	40.2 ± 0.3
36	47.0 ± 1.9	43.2 ± 2.4	41.1 ± 0.5

* Mean ± standard deviation in millimeters. 24 weeks: n = 6; 30 and 36 weeks: n = 3.
Repeated measures one-way analysis of variance revealed no significant differences.

Model Analysis

The maxillary cast analysis was performed by measuring the distances between the points with calipers (Fig. 3). The casts were evaluated for the incidence of malocclusion—in particular, the prevalence of anterior crossbites.

Cephalometric Analysis

The radiographs were taken at fixed cathode–film distances. The landmarks used to assess craniofacial growth are presented in Figure 4. The cephalometric films were traced and the designated landmarks transformed into sets of coordinates, using a two-dimensional digitizer (e.g., Tectronix no. 4953) that has a 0.01-inch resolution. The distances were calculated, taking into account the individual magnification.

Histologic Examination

The dissected palate of the dog was placed in 10% phosphate-buffered formalin (pH 7.4) for 24 hours at room temperature and decalcified in Perenyi's solution. After decalcification, the tissue sections were neutralized in a saturated solution of lithium carbonate in 75% ethanol. Standard histologic embedding procedures were followed, and the palate was sectioned at 6-μm thickness. Sections were stained in hematoxylin and eosin.

TABLE 4 Model Analysis: Maxillary Arch Width Between the Maxillary Third Bicuspids (Points 7–8)*

	Group		
	Control	*Cleft*	*Repaired*
Weeks			
24	38.4 ± 1.9	37.1 ± 2.1	35.4 ± 0.9
30	41.4 ± 1.8	38.5 ± 2.4	37.3 ± 1.3
36	41.9 ± 2.4	39.1 ± 2.1	38.0 ± 1.8

* Mean ± standard deviation in millimeters. 24 weeks: n = 6; 30 and 36 weeks: n = 3.
Repeated measures one-way analysis of variance revealed no significant differences.

TABLE 5 Model Analysis: Maxillary Length (Points 1–2)*

	Group		
	Control	*Cleft*	*Repaired*
Weeks			
8	54.0 ± 2.1	54.2 ± 2.1	53.4 ± 2.1
12	64.7 ± 2.1	63.4 ± 2.9	63.5 ± 2.1
18	77.8 ± 1.4	75.5 ± 4.0	74.8 ± 2.5
24	83.4 ± 0.2	82.0 ± 5.6	80.6 ± 1.2
30	88.9 ± 0.4	83.7 ± 4.8	83.4 ± 1.9
36	89.9 ± 0.6	84.5 ± 5.2	87.9 ± 0.6

* Mean ± standard deviation in millimeters. 24 weeks: n = 6; 30 and 36 weeks: n = 3.
Repeated measures one-way analysis of variance revealed no significant differences.

Alkaline Phosphate Activity

Selected regions of the palate were placed in 10% phosphate-buffered formalin (pH 7.4) at 4°C for 1 hour. After fixation, the tissues were washed in deionized water for 1 hour and then placed in 10% EDTA (pH 6.2) at 4°C. Once decalcified, the tissues were immersed in 1% $MgCl_2$ at 4°C for 24 hours. Four-micron sections were cut on a cryostat and stained according to the method of Gomori (1952). Alkaline phosphatase activity was used to monitor bone regeneration in the palate.

Statistical Analysis

A repeated measures analysis of variance was performed on all longitudinal data, and a one-way analysis of variance was performed on all cross-sectional data. If the levels of significance were determined to be less than 0.05 level of

TABLE 6 Cephalometric Analysis: Mandibular Length (AP-Pmd)*

	Group		
	Control	*Cleft*	*Repaired*
Weeks			
8	71.4 ± 1.8	70.2 ± 2.3	69.9 ± 1.9
12	85.9 ± 3.3	81.8 ± 3.0	82.6 ± 2.4
18	102.5 ± 2.2	96.6 ± 3.0†	97.9 ± 2.4†
24	112.7 ± 3.3	108.0 ± 4.8†	107.5 ± 2.2†
30	118.3 ± 2.8	113.1 ± 1.5	112.9 ± 1.3
36	121.5 ± 4.5	114.2 ± 5.4	114.9 ± 3.1

* Mean ± standard deviation in millimeters. 8 through 24 weeks: n = 6; 30 and 36 weeks: n = 3.
† Repeated measures one-way analysis of variance revealed significant differences from control group: $p \leq 0.05$.

TABLE 7 Cephalometric Analysis: Maxillary Length (PNS-Pmx)*

	Group		
	Control	*Cleft*	*Repaired*
Weeks			
8	55.0 ± 1.3	54.1 ± 1.8	54.5 ± 1.9
12	65.5 ± 2.3	63.8 ± 2.0	63.8 ± 1.9
18	78.5 ± 3.1	75.0 ± 4.4	75.9 ± 2.7
24	85.2 ± 3.7	81.0 ± 4.7	81.9 ± 3.5
30	88.2 ± 1.3	81.8 ± 4.4	83.4 ± 4.4
36	89.2 ± 1.1	82.4 ± 4.6	83.8 ± 4.6

* Mean ± standard deviation in millimeters. 8 through 24 weeks: n = 6; 30 and 36 weeks: n = 3.
Repeated measures one-way analysis of variance revealed no significant differences.

probability, a test of least significant differences was performed, using the pooled mean sum of squares due to error.

RESULTS

Weight Gain

The weekly weight gain of the dogs is presented in Figure 5. The weight gain showed a significant difference among the three groups. The repeated measures analysis of variance indicated that the line representing the weight gain of the control group was significantly different from the lines representing the cleft or repaired groups ($p \leq 0.05$). No significant difference was found between the cleft and repair groups.

Growth and Development

The results of the model analysis are presented in Tables 1 to 5. The results of the cephalometric analysis are presented in Tables 6 to 9. Although all dimensions were reduced in the cleft and repaired groups, only two dimensions were significantly different: mandibular length and the width of the palate at the level of the second molars. The cleft and repaired groups were significantly different from the control group but not from each other ($p \leq 0.05$).

Histologic Findings

At 24 weeks, the cellular activity of the maxilla was considerably greater than at 36 weeks. This was true in all three groups. The cephalometric data substantiated the histologic picture with the finding that the greatest amount of facial growth occurred between 8 and 24 weeks.

Control Group

The anatomy of the control group suture at 36 weeks is presented in Figures 6 and 7. The suture at this time presents in a curved rather than a linear configuration, as seen in the 7-week-old dog. Alkaline phosphatase activity of the suture shows a distinctive banding pattern: the enzyme is greatly reduced in the central region of the suture. Consequently, the histochemical staining pattern displays three layers. From this observation, one can distinguish between a regenerated suture that has reformed and a site where fusion is occurring.

Cleft Group

With few exceptions, the radiographic contour of the cleft was very smooth and regular; only isolated areas displayed an irregular contour (Fig. 8). A widened opening at the major palatine foramina was a consistent finding in the cleft group. This widening of the foramen often extending anteriorly to include the transverse palatine suture (see Fig. 8). The results of the bone measurements of the cleft dimensions are presented in Table 9. Originally rectangular in shape, the cleft became irregular, with a rounded contour (see Fig. 8). The results indicate that the area of the cleft increased by 4.08 times. No difference was seen in the size of the cleft at 24 and 36 weeks in the cleft group.

A consistent finding at 24 weeks was the appearance of resorptive activity along the medial border of the palatal shelf. Osteoclasts and associated Howship's lacunae were routinely observed. This resorption always extended inferiorly from the nasal surface of the palatal shelf along the medial edge. This histologic picture indicated that the size of the bony cleft was actively enlarging. Bone formation along the

TABLE 8 Cephalometric Analysis: Craniofacial Length (Inion-Pmx)*

	Group		
	Control	*Cleft*	*Repaired*
Weeks			
8	106.4 ± 2.4	104.1 ± 4.2	105.9 ± 3.2
12	126.1 ± 3.3	120.0 ± 5.6	121.8 ± 3.3
18	146.5 ± 4.5	137.2 ± 6.8	140.3 ± 5.1
24	160.6 ± 5.0	150.9 ± 9.2	153.3 ± 4.8
30	170.3 ± 4.2	158.1 ± 8.3	157.5 ± 5.4
36	173.1 ± 1.4	159.3 ± 8.4	160.5 ± 7.9

* Mean ± standard deviation in millimeters. Eight through 24 weeks: n = 6; 30 and 36 weeks: n = 3.
Repeated measures one-way analysis of variance revealed no significant differences.

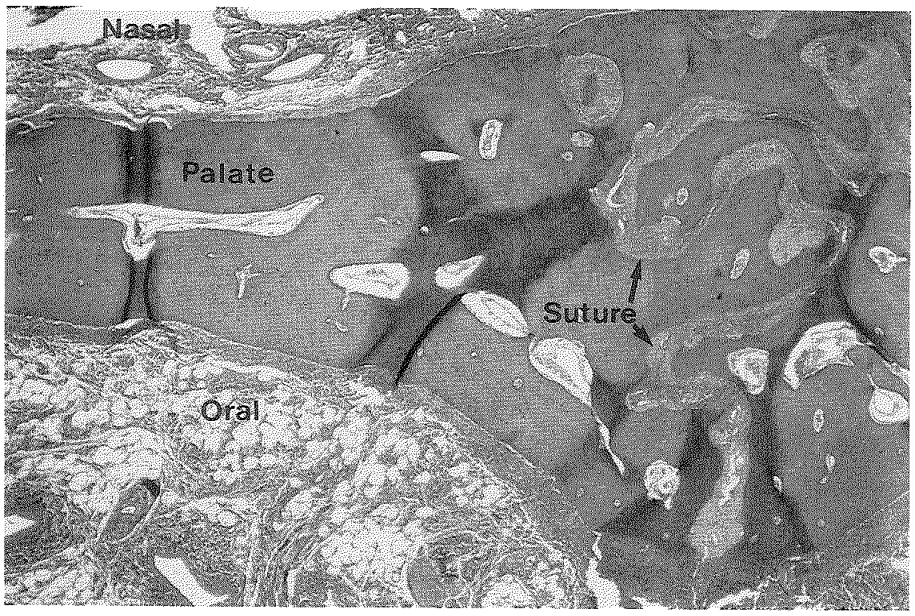

FIGURE 6 Photomicrograph of the control group palate at 36 weeks at the region of the midpalatal suture. Note the appearance of the suture (*Suture*), with its interlocking configuration. At 36 weeks, the suture is narrow. Note the thickness of the palatal shelf (*Palate*). The nasal connective tissue (*Nasal*) and oral connective tissue (*Oral*) are labeled for orientation. (Hematoxylin and eosin ×49.1.)

medial edge of the cleft was not seen (Fig. 9). The resorption seen at 24 weeks accounted for the fact that the palatal shelves were thinner at 36 weeks than in the control group. By 36 weeks, no appreciable osteoclastic activity was seen in the cleft group.

A common characteristic of the cleft group was the curling—up into the nasal cavity—of the oral mucosa bordering the cleft. In this region, an accumulation of dense irregular, collagenous fibers could be observed just beneath the mucosa (Fig. 10). In three dogs, metaplastic transformation of the epithelium was noted. In these areas, stratified squamous epithelium had replaced the normal pseudostratified, ciliated, columnar epithelium. In one dog, heterotopic calcification was detected in the nasal turbinates.

Repaired Group

In the repaired group, the amount of bone regeneration was variable. Complete regeneration did not occur in any of the dogs. Both the 24- and 36-week time periods revealed similar amounts of bone formation. This finding indicated that most of the bone repair occurred during the first 12 weeks after the palatoplasty. The anterior region of the palate demonstrated greater bone regeneration than did the posterior region. Always, new bone formation proceeded from margins of the palatal shelves (Fig. 11). In the region of the lateral releasing incisions, callus formation was frequently observed. Associated with the callus were thick, long strands of collagenous fibers with deep insertions into the bone. Fiber insertions of this length and thick-

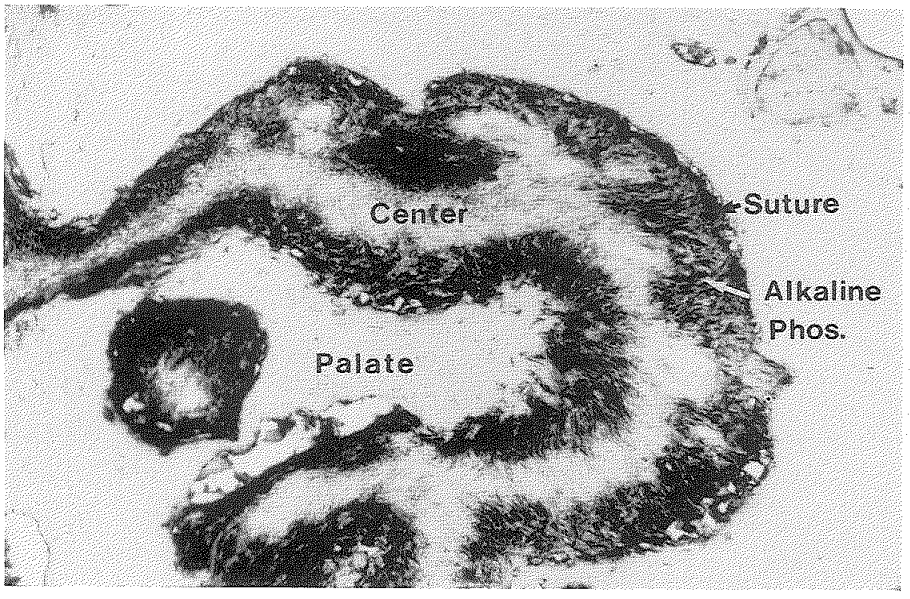

FIGURE 7 Histochemical photomicrograph, staining for alkaline phosphatase (*Alkaline Phos.*) activity, of the suture (*Suture*) of the control group palate in the region of the suture at high magnification. Note pattern of staining in the suture showing three bands: the bands adjacent to the bone stain for enzyme, whereas the central band (*Center*) is almost enzyme free. The bony regions characteristically are unstained. (Azo dye ×196.4.)

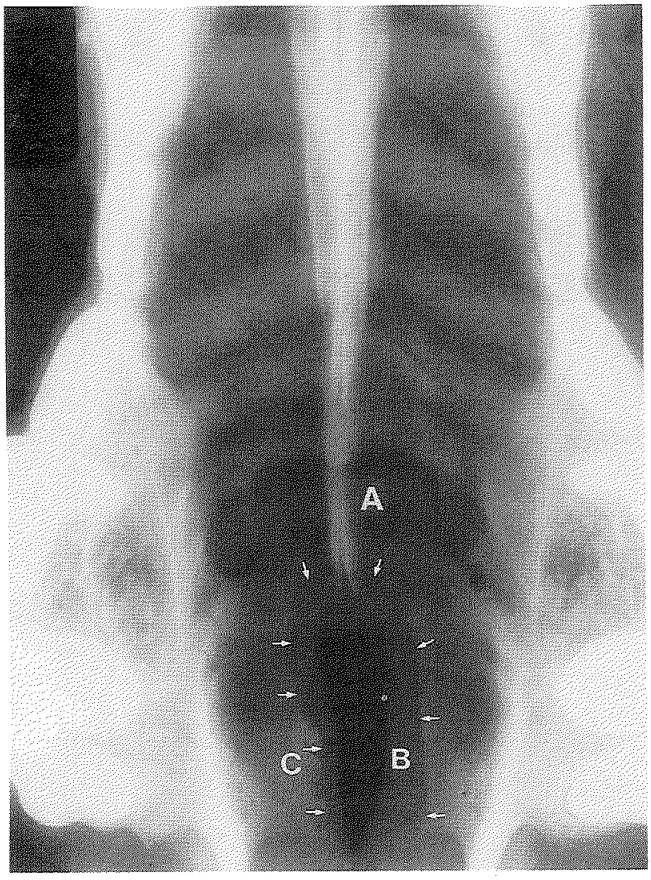

FIGURE 8 Palatal radiograph from the cleft group showing the osseous contour (*white arrows*) of a dog at 36 weeks of age. The transverse palatine foraminae (*A*) are widened. Note that the osseous contour of the cleft is rounded with generally smooth margins, except in the region of (*C*). Note also that the bony cleft is significantly greater than the soft tissue cleft (*B*).

ness were not found in other regions of the palate.

Basically, two patterns of palatal regeneration were observed in the repaired group: (1) The palatal shelf demonstrated localized complete regeneration, including the suture (Fig. 12). (2) No new bone formation was seen. Instead, at 24 weeks, osteoclastic activity was observed and the appearance of the shelf was similar to the cleft group (Fig. 13).

In most instances, when the shelf had regenerated, a suturelike structure had also regenerated. However, the morphologic features of the regenerated suture varied from dog to dog. Most frequently, the regenerated sutures that exhibited normal morphology were located in the anterior region of the cleft. The suture had a more juvenile architecture, showing a linear configuration rather than a complex pattern as is normal for dogs of 24 weeks (see Fig. 12).

Contributions from both sides of the palatal shelves were not always equal. Occasionally, the suture formed unilaterally, extending from one of the shelves, rather than joining the two shelves. In some areas, the bony shelf extensions were very close to approximating and forming a suture. Possible fusion of the palatal shelves was noted in a few regions of the palate. Rather than showing a zone lacking in alkaline phosphatase, these sites had a continuous band of enzyme staining (Fig. 14).

DISCUSSION

The cleft creation procedure appeared to have an irreversible effect on weight gain. One week after the surgical procedure, reduced weight gain was apparent. A similar but smaller reduction was found after the repair procedure. With the closure of the cleft, the repair group did not recover to control values. Although the cleft was small, it had a large impact on the animals' body weight. Ranalli et al (1975) also found no correlation between the size of the cleft and the amount of reduction of body weight in children.

In addition to the discomfort of the surgery, the decrease in the dogs' weekly weight gain following the surgery may reflect an altered ability to eat. Paradise et al (1974) and Avedian et al, (1980) reported impaired weight gain in children with cleft palate whose body weight increased until the sixth month. In laboratory studies, Freng et al (1976, 1979), Bardach et al, (1980, 1987), and Schultz (1964) reported reduced weight gain in rabbits after surgery to the soft palate alone.

In the present investigation, every attempt was made to ensure that the dogs maintained a steady intake of food. Nonetheless, their body weight-gain readings suggest that the dogs with the artificial clefts experienced some difficulty

TABLE 9 Cleft Dimensions: Measurements* of the Surgically Created Cleft in the Cleft and Repaired Groups

	Group			
	8 Weeks Cleft	*8 Weeks Repaired*	*12 Weeks Repaired*	*24–36 Weeks Cleft†*
Width	3.3 ± 0.2	3.1 ± 0.2	5.4 ± 1.0	7.9 ± 1.6
Length	11.8 ± 0.5	11.7 ± 0.7	13.1 ± 0.5	18.8 ± 0.7

* Measurements were taken directly from the palate at the 8- and 12-week time periods. At the 24- and 36-week time periods, measurements were taken from an occlusal radiograph of the dissected palate. Adjustments were made for magnification. Mean ± standard deviation in millimeters; n = 6.

† Statistical analysis (Student's *t* test) indicated that there were no differences between the 24- and 36-week time periods for the cleft dimensions; $p < 0.2$.

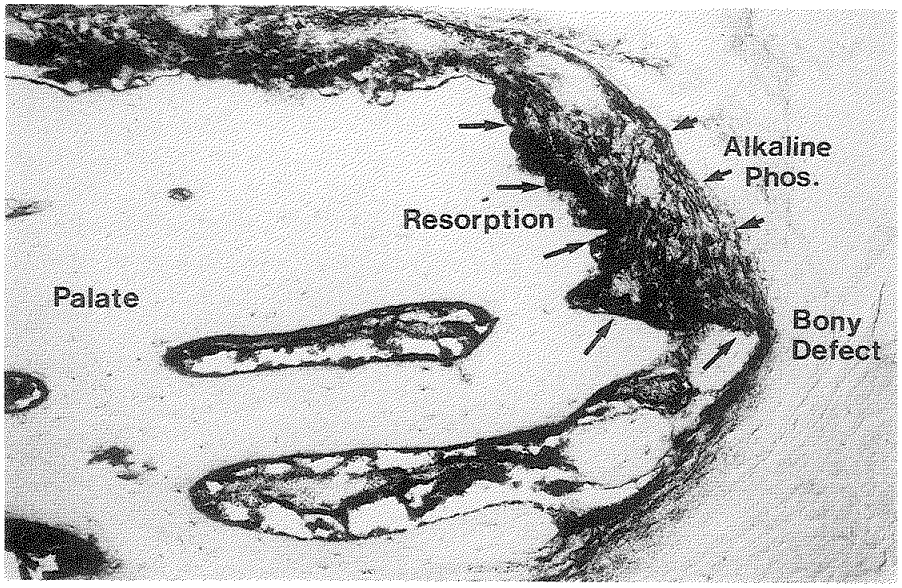

FIGURE 9 Histochemical photomicrograph of the cleft group at 18 weeks, showing alkaline phosphatase activity (*Alkaline Phos.*) in the region of the bony cleft. Note that the alkaline phosphatase activity is principally localized to the periosteum and the marrow spaces of the bone. No alkaline phosphatase activity is observed in the connective adjacent to the periosteum (*Bony Defect*). Note the ragged border of the palatal shelf, indicating active osteoclastic activity (*Resorption*) occurring along this margin (*Arrows*). (Azo dye ×49.1.)

in eating. Misdirection of the food was a chronic problem and was substantiated by the findings of heterotopic calcification of the maxillary turbinates and by impacted food in the anterior region of the nasal cavity in one dog at the time of sacrifice. This constant misdirection against the palate and up into the nasal cavity may possibly explain some of the histologic findings seen in the cleft group. The connective tissue beneath the cleft margin showed signs of chronic irritation: the marginal edges of the cleft commonly had a buildup of dense collagenous fiber bundles. The marginal edge also showed signs of osteoclastic activity. Both of these findings could have been the result of continual operculation of the soft connective tissue against the bony palate. This decreased ability of the dogs in the cleft and repaired groups to gain weight was reflected in the growth and development assessment of this study. Overall values in the maxilla and the mandible, although not significantly different, were nonetheless consistently reduced. This reduction was most likely the result of the dogs' failure to thrive.

In contrast to the cleft group, which demonstrated a fairly uniform response, members of the repaired group did not. A broad range in regenerative potential was displayed. One area of the palate showed complete regeneration, whereas an adjacent area exhibited degenerative changes or minimal osteogenic activity. This variable response was also reported by Barro et al, (1981), Mors et al, (1975), Chierici et al, (1970), and Lynch and Peil (1966). However, in most dogs, the size of the palatal bony defect, was smaller than the original defect.

This finding raises considerable doubt about the regenerative potential of transposed periosteum. In this investigation, a layer of perioste-

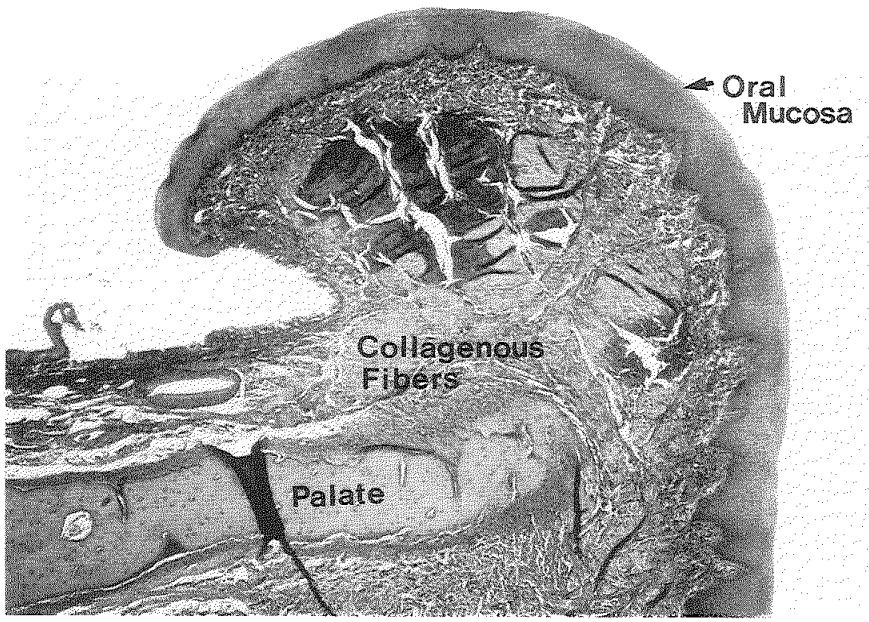

FIGURE 10 Photomicrograph of the cleft group at 36 weeks showing the inversion of the oral mucosa (*Oral Mucosa*) and accumulation of collagenous fibers (*Collagenous Fibers*) above the palatal shelf (*Palate*). Note the thinness of the palatal shelf as compared with the 18-week period. (Hematoxylin and eosin ×49.1.)

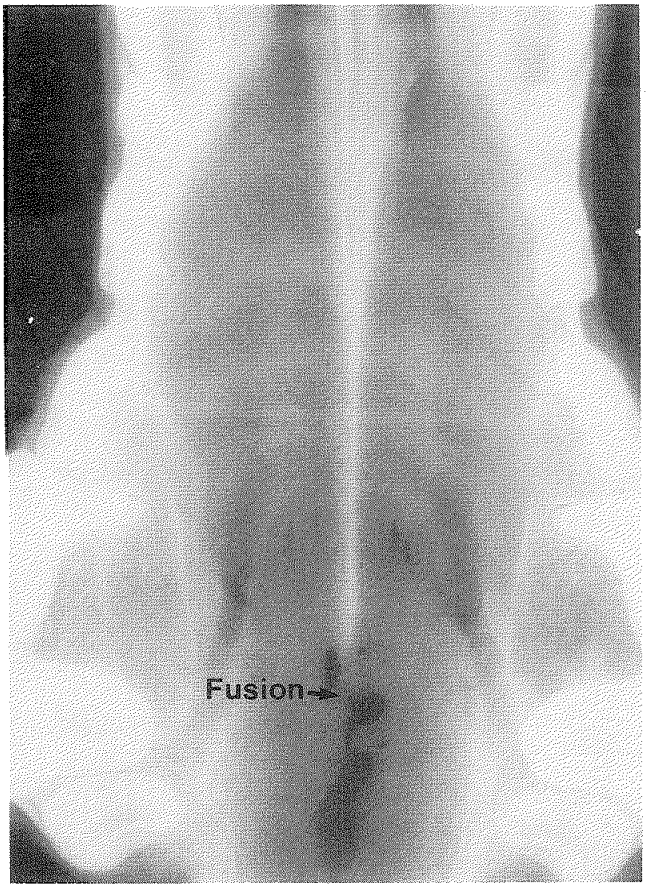

FIGURE 11 An occlusal radiograph showing amount of regeneration in the repaired group at 36 weeks. Note that fusion (*Fusion*) in one site had occurred (*Arrow*) but only in the anterior region. Although partial regeneration occurred, the palatal bone was less well organized when compared with the control.

um was placed over the surgical defect, but bone formation occurred only along the margins of the bone defect. Latham et al (1975) also observed this. Controversy exists over the osteogenic capacity of transplanted periosteum. Most investigators have found that transplantation of autogenous periosteum from young animals achieved bone formation. However, Uddstromer (1978) observed that the osteogenic response of the periosteum varied with the donor site. Alhopuro (1978) reported weaker bone formation from periosteal grafts taken from the calvarium than from the tibia. Melcher (1969) observed a limited osteogenic response by the periosteum when a millipore filter was wedged between the periosteum and a calvarial bone of growing rats. Castero and Salyer (1975), and Melcher and Accursi (1971) found similar lack of bone formation following transplantation of calvarial periosteum. The differential response of new bone formation between the periosteum of long and flat bones may account for the inability of the transplanted periosteum to produce bone that was repositioned during the repair procedure.

The unique feature of this study was the intervening 4-week period between the cleft creation and the repair. By establishing this temporal separation, time was provided to allow the tissues of the surgical defect to heal; this measure permitted a more accurate assessment of the regenerative capacity of the palate. The results showed clearly that the presence of a cleft adversely affected the remaining palatal architecture. These tissues revealed degenerative adaptations as a consequence of the artificial cleft: the size of the bone cleft increased during the first 24 weeks; the mucosa neighboring the cleft curled up into the cleft site; epithelial metaplasia occurred in several areas; heterotopic calcification of the nasal turbinates occurred; and at 24 weeks, the palatal bone demonstrated mainly resorption along the cleft margin. This study also demonstrated the limited capacity of the palatal tissues to regenerate. Although the size of the original cleft was small (3.1 × 11.7 mm), only partial regeneration occurred. When bone

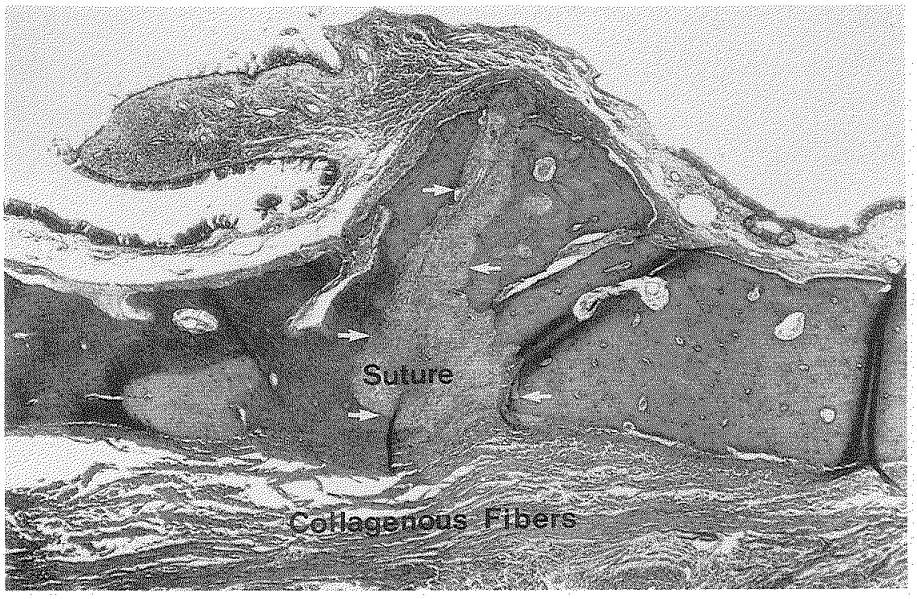

FIGURE 12 Photomicrograph of the repaired group at 36 weeks in the region of the repair. Note that regeneration of the palate has occurred. The configuration of the suture (suture outline marked in white arrows) is linear, reflecting a simpler, less mature type of suture when compared with control. Beneath the palate are dense bands of collagenous fibers (*Collagenous Fibers*), which represent part of the repair process. (Hematoxylin and eosin ×49.1.)

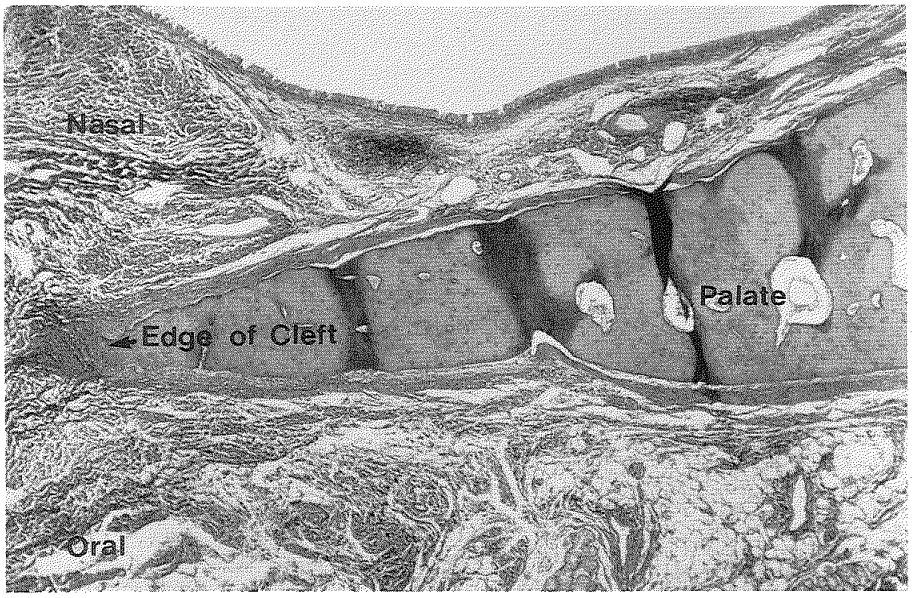

FIGURE 13 Photomicrograph of the repaired group at 36 weeks in the region of the cleft. Note that the palatal shelf (*Palate*) did not totally regenerate. Instead, resorption occurred, resulting in tapered shelf (*Edge of Cleft*). The *Nasal* and *Oral* connective tissues are labeled for orientation. (Hematoxylin and eosin ×49.1.)

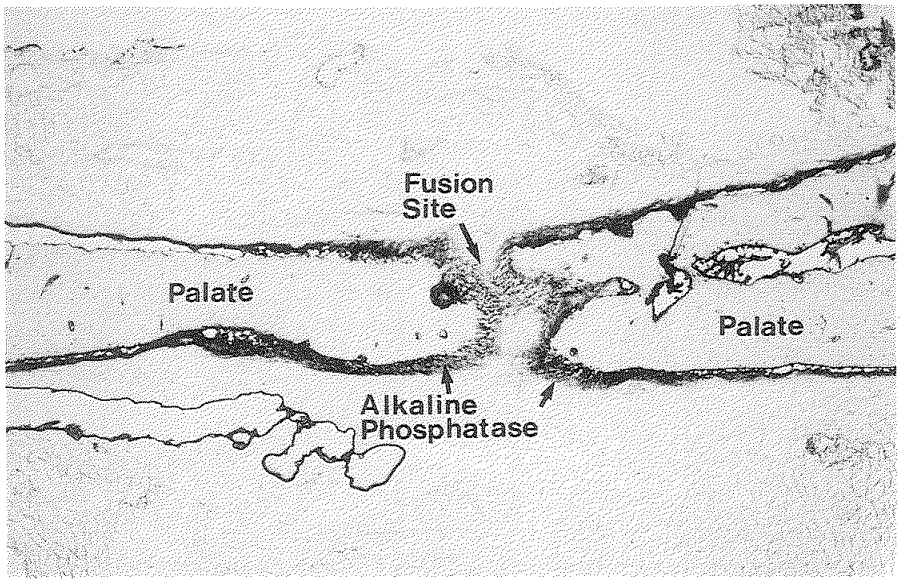

FIGURE 14 Histochemical photomicrograph of the repaired group at 36 weeks showing alkaline phosphatase activity (*Alkaline Phosphatase*) in the region of the repair of the palate (*Palate*). Note that nearly total regeneration occurred. The alkaline phosphatase activity indicates continued osseous activity in the site of the suture. There is indication of fusion (*Fusion Site*) occurring, because alkaline phosphatase is normally absent in the central region of the suture. (Azo dye ×49.1.)

did form, it was irregular and unpredictable in extent. In several sites, suture regeneration or fusion resulted from the new bone growth. This latter consequence—fusion—also adversely affects maxillary growth.

References

ALHOPURO S. (1978). Premature fusion of facial sutures with free periosteal grafts. An experimental study with special reference to bone formation with free periosteal grafts from the tibia, the scapula, and the calvarium. Scand J Plast Reconstr Surg Suppl. 17, 12:1–68.

ATHERTON JD, WHITE SS, MAISELS D. (1970). Histological changes following the surgical closure of a canine cleft palate. Br J Plast Surg 23:365–370.

AVEDIAN LV, RUBERG RL. (1980). Impaired weight gain in cleft palate infants. Cleft Palate J 17:24–26.

BARDACH J. (1985). Facial growth following cleft lip and palate repair: experimental studies in rabbits and beagles. In: Jackson IT, Sommerlad BC, eds. Recent advances in plastic surgery. Edinburgh: Churchill Livingstone.

BARDACH J. (1987). Discussion on the papers: Antonyshyn O, Colcleugh RG, Anderson C. Growth potential in suture bone inlay grafts: a comparison of vascularized and free calvarial bone grafts. Plast Reconstr Surg 79:1–11 and Antonyshyn O, Colcleugh RG, Anderson C. (1987). Growth potential in suture bone onlay grafts: a comparison of vascularized and free calvarial bone and suture bone grafts. Plast Reconstr Surg 79:12–20. Plast Reconstr Surg 79:21–23.

BARDACH J, ROBERTS DM, KLEUSNER EC. (1980). Influence of two-flap palatoplasty on facial growth in rabbits. Cleft Palate J 17:309–318.

BARDACH J, MOONEY M, BARDACH E. (1982). The influence of two-palatoplasty on facial growth in beagles. Plast Reconstr Surg 69:745–753.

BARRO WB, LATHAM RA. (1981). Palatal periosteal response to surgical trauma. Plast Reconstr Surg 67:6–16.

CASTERO J, SALYER E. (1975). Regenerative potential of bone and periosteum. Surg Forum 26:555–556.

CHIERICI G, HARVOLD EP, DAWSON WJ. (1970). Morphologic adaptation secondary to the production of experimental cleft palate in primates. Cleft Palate J 7:59–67.

CHIERICI G, HARVOLD E, VARGERIK K. (1973). Experimental development of a new palatal suture. J Dent Res 52C:248.

FRENG A. (1981). Growth of the middle face in experimental early bony fusion of the vomeropremaxillary, vomeromaxillary, and midpalatal sutural system: a roentgen-

cephalometric study in the domestic cat. Scand J Plast Reconstr Surg 15:117–125.

FRENG A. (1979). The restorative potential of double layered muco-periosteum. A study on experimental midpalatal clefts in the cat. Scand J Plast Reconstr Surg 13:313–320.

FRENG A. (1976). Single layered palatoplasty in experimental midpalatal clefts. A histological study in the cat. Scand J Plast Reconstr 21:339–344.

FRENG A. (1979). Transversal maxillary growth in experimental submucous mid-palatal clefts. Scand J Plast Reconstr Surg 13:409–416.

FRENG A, VOSS R. (1982). Bony or connective tissue union of operated experimental palatal clefts: implications on growth of the dentomaxillary complex; a biometrical study in the domestic cat. Scand J Plast Reconstr Surg 16:233–238.

GOLAN J, SHAPIRO Y, BENTTUR N, DOLBERG I. (1976). Bone formation from periosteal grafts and investigation on the possible effect of calcitonin. J Surg Res 21:339–344.

GOMORI G. (1952). Microscopic histochemistry Chicago: University Press.

HERFERT O. (1954). Microscopic experimenteller Beitrag zur Frage der Schädigung der Oberkiefer-wachstums durch vorzeitige Gaumenspaltoperation. Dtsch Zahn Mund Kieferheilkd 20:369–381.

HERFERT O. (1958). Fundamental investigations into problems related to cleft palate surgery. Brit J Plast Surg 11:97–105.

JONSSON G, STENSTROM SL. (1978). Maxillary growth after palatal surgery. An experimental study on dogs. Scand J Plast Reconstr Surg 12:131–137.

KREMENAK CR, HUFFMAN WC, OLIN WH. (1962). Growth of maxillae in dogs after palatal surgery: I. Cleft Palate J 7:719–736.

KREMENAK CR, HUFFMAN WC, OLIN WH. (1970a). Growth of maxillae in dogs after palatal surgery: II. Cleft Palate J 7:719–736.

KREMENAK CR, HUFFMAN WC, OLIN WH. (1970b). Maxillary growth inhibition by mucoperiosteal denudation of palatal shelf bone in non-cleft beagles. Cleft Palate J 7:817–825.

KREMENAK CR, SEARLS JC. (1971). Experimental manipulation of midfacial growth: A synthesis of five years of research at the Iowa Maxillofacial Growth Laboratory. J Dent Res 50:Suppl. to No. 6:1488–1491.

KREMENAK C, OLIN W JR, SEARLS J, SQUIER C, MORRIS J, MATHEWS J, MOORE C, RUSSELL L. (1980). Factors affecting postsurgical maxillofacial growth: width of regions of denuded palatal bone. J Dent Res 59B:903.

LATHAM RA, DEATON TG, CALABRESE CT. (1975). A question of the role of the vomer in the growth of the premaxillary segment. Cleft Palate J 12:351–355.

LYNCH JB, PEIL R. (1966). Retarded maxillary growth in experimental cleft palates; mechanical binding of scar tissue in puppies. Am Surg 32:507–511.

MELCHER AH. (1969). Role of the periosteum in repair of wounds of the parietal bone of the rat. Archs Oral Biol 14:1101–1109.

MELCHER AH, ACCURSI GE. (1971). Osteogenic capacity of periosteal and osteoperiosteal flaps elevated from the parietal bone of the rat. Archs Oral Biol 16:573–580.

MORS WA, KAMINSKI EJ. (1975). Osteogenic replacement of tricalcium phosphate ceramic implants in the dog palate. Archs. Oral Biol 20:365–366.

PARADISE JL, MANGUBAT OV, JOSEFCZYK P. (1974). Undernutrition in young infants with cleft palate: a prevailing but remediable problem. Presented at the American Cleft Palate Association, Boston.

RANALLI DN, MAZAHIRI M. (1975). Height-weight growth of cleft children, birth to six years. Cleft Palate J 12:400–404.

SCHULTZ RC. (1964). Surgically produced cleft palates in rabbits. A study of resulting middle ear infections. Plast Reconstr Surg 33:120–131.

SEARLS JC, KREMENAK CR, RITTMAN BRJ. (1979). Quantitative characterization of changes in cellularity and collagen fiber size in contracting palatal wounds. Cleft Palate J 16:373–380.

UDDSTROMER L, RITSILIA V. (1978). Osteogenic capacity of periosteal grafts. A qualitative and quantitative study of membranous and tubular bare periosteum in young rabbits. Scand J Plast Reconstr Surg 12:207–214.

URIST MR, MCLEAN FC. (1952). Osteogenetic potency and new bone formation by induction in transplants to the anterior chamber of the eye. J Bone Jt Surg 34A:443–476.

VERWOERD CD, VERWOERD-WERHOEF HL, URBANUS NA. (1976). Skulls with facial clefts; Experimental surgery on the facial skeleton. Acta Otolaryngol 81:249–256.