Experiments on the Influence of Oriented Stress on Bone Formation Replacing Bone Grafts

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A cleft maxilla is healed when it has the attributes of a normal maxilla. Experimental and clinical observations suggest that bone perimeters can be extended by biophysical stimuli induced through functional forces when the tissue is under tension. An experiment was designed to test whether the establishment of bone across the cleft is similarly influenced. Bone most consistently replaced split-rib grafts when tension was applied to the segments of surgically produced maxillary clefts. Additional observations on this model indicate that a suture can be developed in the bone bridge across the cleft margins. While the parameters are not established, the hypothesis cannot be rejected that tension facilitates the extension of bone inducing stimuli and influences the differentiation of tissue in intra-alveolar transplants.

Clinicians treating cleft palate patients recognize the need for stabilizing the upper jaw at some time during habilitation. The appropriate time for this treatment is dependent on the specialist’s perception of the relative significance of the different growth areas for facial development: 1) at sutures between the maxilla and adjacent bones, 2) between the maxilla and teeth through the periodontium, and 3) through surface apposition of bone on the maxilla and margins of the cleft.

The accepted method of permanent stabilization of the upper jaw is to establish bone between the cleft margins of the maxilla. Various transplant materials have been employed to induce new bone formation, and the techniques of transplantation are well established (Albee, 1923; Burwell, 1969; Boyne, 1973).

However, clinical observations indicate that, despite excellent surgical techniques and the absence of infection and irrespective of the source of the transplant, bone is not always established across the cleft. Clinical observations have also indicated that bridging of the cleft sometimes occurs spontaneously without direct surgical intervention (Skoog, 1966). The minimum requirements for bone formation are cells with osteogenic potential, adequate nutrition, and appropriate stimuli (Bassett, 1962, 1972). Predominant attention has been directed to the first two requirements. Yet, it is apparent that bone formation depends on more...
than the cellular and biochemical resources. That a relationship exists between the shape of bone and function has been well established. In previous experiments we have demonstrated that existing functional forces will alter the shape of a normal maxilla when this bone is experimentally moved to a new position (Chierici et al., 1973a). It is also recognized that bone forms in response to certain forces. This is the basis for clinical orthodontics, whereby force applied to a tooth results in bone formation in a tooth socket. The distribution of the force is influenced with the result that bone forms on the alveolar surface which is subjected to tension.

Our experiments have demonstrated that bone deposition can be confined to one border or extended to both sides of the zygomatico-maxillary suture when tension is applied and the distribution of normal functional stimuli is controlled (Harvold, 1975b). In additional experiments on animal models and in subsequent clinical trials, the controlled application of forces has been shown to induce bone apposition on normal mandibles and to extend the perimeter of malformed mandibles (Harvold, 1975a).

The question arises as to whether similar conditions are significant to the development of bone continuity across the margins of the cleft maxilla. Forces acting on the maxilla are numerous, variable, and probably conflicting. It is postulated that bone will be established only in those environments in which bone-inducing stimuli dominate for a sufficient time and that tension facilitates transmission of appropriate stimuli.

The following experiment was designed to test the hypothesis that bone-inducing stimuli can be transmitted beyond the margins on the cleft maxilla if the intervening connective tissue is placed under tension.

**Methods and materials**

In each of 15 adolescent rhesus monkeys, a unilateral cleft of the palate was produced according to previously reported techniques (Chierici et al., 1970). The parasagittal cleft extended from the piriform aperture to the end of the hard palate. The lips and soft palate were not included in the cleft nor was the mucosal lining of the nasal surface of the palate penetrated. An orthodontic appliance was used to rotate the cleft segment medially (Chierici et al., 1973b). Three months later, when maxillary deformation had been established, an autologous split rib graft without periosteum was placed into a soft tissue bed prepared between the margins of the cleft below the piriform aperture in each of the animals. The bed did not include a periosteal layer. Three groups of five animals each were distinguished.

Group I: The appliance used to induce the maxillary deformation was removed, and the cleft maxilla was not artificially supported in any way. All stimuli acting on the maxilla during function, favorable or unfavorable to bone induction, were transmitted to the graft area.

Group II: The original appliance was left in place after bone grafting.
This appliance, although passive, was presumed to be sufficient to protect the graft environment from shearing movements of the cleft maxillary segments.

Group III: After bone grafting, the action of the appliance was reversed to expand the deformed maxilla and to stretch the soft tissue bed of the graft. The intent was to orient the connective tissue between the bone margins to conduct the stimuli which induce new bone.

Antibiotics were not administered, and after the operation the monkeys were returned to their cages and maintained on their usual diet. Four months after grafting, x-rays were taken of the graft area. Additional information was obtained by examination of skull preparations from animals 18 months after the experiment and from histologic preparations of biopsy material from other monkeys three, eight, and ten weeks and 18 months after bone grafting.

The biopsies included margins of the host bone and the intervening soft tissue of the transplant environment. The specimens were fixed in 10 per cent buffered formalin and decalcified in formic acid and citrate solution. The tissue blocks were embedded in paraffin and cut on a sledge microtome. The sections were prepared according to techniques standard for hematoxylin and eosin and modified Van Gieson stains.

Results

Group I: None of the clefts showed evidence of development of new bone (Figure 1).

Group II: Radiographic evidence of bony continuity was observed in three of the five animals.

FIGURE 1. X-ray of the cleft upper jaw of a rhesus monkey four months after an intra-alveolar bone transplant. New bone has not replaced the resorbed transplant.

FIGURE 2. X-ray of the upper jaw of a rhesus monkey four months after an intra-alveolar bone transplant was placed and tension applied by the appliance shown. New bone has replaced the transplant and a bone bridge is established between the cleft margins.
Group III: All five animals showed radiographic evidence of an established bony bridge between the margins of the cleft maxilla (Figure 2).

Histologic preparations of biopsy material from the graft area at three weeks (Figure 3) revealed new bone trabeculae attached to the surface of the transplant. The new trabeculae were characteristically joined almost perpendicularly to the surface and were turned abruptly in the direction of the host margins along the plane of stress orientation. Resorption of the grafted bone was already in progress.

At eight weeks (Figure 4), the transplant was surrounded by new bone trabeculae. Some of the trabeculae fused and were in continuity with a network of bone spicules developing from the edges of the host bone. No islands of new bone were found within the transplant, and the graft showed continued resorption.

Preparations at ten weeks showed a trabecular arrangement of new bone extending across the formerly cleft margins (Figure 5). Transplanted bone was no longer identifiable, and resorption was apparently complete. The spaces between the trabeculae were wide, and the labial and palatal borders of new bone were defined by an irregular trabecular system.

Histologic examination of established bone at 18 months showed compact bone across the margins of the former cleft (Figure 6). The trabecular spaces were now reduced to small openings for blood vessels. The bone bridge was narrow and thin in the middle portion.

A previously unreported finding in this experiment was the devel-
opment of a suture in the area of a former transplant (Figure 7). The interdigitating suture displayed morphology similar to that observed in the midline suture of a normal maxilla.

Skull preparations demonstrated different forms of established bone between the maxillary segments. A thin bridge accompanied a wide span where the canine was missing, and more substantial bone was found where the canine was fully erupted. In some preparations a new suture was clearly evident in addition to the existing median suture (Figure 8). New suture formation was also found in preparations in which the median suture was missing and presumed to be obliterated during the surgical procedures involving production of the cleft or placement of the transplant.

Discussion

It has been established that injury and the regeneration of nerve tissue have a significant effect on bone formation (Becker, 1972). Furthermore, close contact between fractured bone segments has a beneficial effect on repair, which suggests that the transmission of biophysical stimuli plays an important part in bone regeneration (Matzen, 1967; Ham and Harris, 1971). In this experiment, no attempt was made to distinguish between the relative significance of these factors. The assumption is that injury to the site was similar in all the animals while the stimuli were altered in the various groups.

The upper jaw is subjected to indeterminate stress during normal
function. In one group of experimental animals, normal forces were transmitted to the graft area without interference. When the maxilla was subjected to all functional forces, no bone replaced the transplant, and the operation "failed." In the remaining two groups, the distribution of

FIGURE 5. Histologic section of the cleft area at ten weeks. There is no evidence of the transplant. New trabeculae with wide spaces form an irregular network between the margins of host bone. (6605 Van Gieson X 100.)

FIGURE 6. Histologic section of the bone bridge at one and a half years after an intra-alveolar graft was placed. The established bone is compact with small openings for blood vessels. In this preparation, the bridge of bone was narrow and thin. (6536 Van Gieson X 40.)
FIGURE 7. Histologic section in the area of a former transplant in a rhesus monkey. A suture has formed with morphology similar to that observed in the midline suture of the normal maxilla. (6525 Van Gieson × 40.)

FIGURE 8. Skull preparation of rhesus monkey (5907) with bone established across the former cleft margins. New suture formation (a) is seen in the bone bridge. The midline suture is labelled (b). The premaxillary suture is located on the alveolar process slightly medial to the canine.

functional stress was altered. The graft environment was protected by the appliance in the second group of monkeys, thus reducing the effect of normal stress. Under this condition, bone formation between the cleft margins was inconsistent. In Group III, tension was applied to the soft tissue bed of the graft with the result that new bone formation occurred and replaced the resorbing transplant in all animals.

The new bone developed on the surface of the host bone and on the
surface of the transplant. No new bone was found to be developing except from the cleft margins or more than a few mm. distant from the graft surface even though the entire maxilla and graft bed were subjected to tension. However, the histologic sections were not entirely serial so that independent sites of new bone development within the connective tissue subjected to tension cannot be definitely excluded.

In orthodontic palate splitting procedures, published studies report new bone adding to the surface but do not mention bone formation within the stretched intervening tissue between bone margins. Bone deposition has also been shown to occur on the surface of alveolar bone subsequent to tension induced by lifting the periosteum (Donnelly et al., 1973).

There is no clear evidence that stretching causes differentiation of certain connective tissue cells to develop as osteoblasts and produce bone. If this were the case, bone surfaces would be expected to extend consistently in the direction of muscle tension. Clinical observations indicate that the mastoid process develops in harmony with the direction of tension in the sternocleidomastoid muscle but that the gonial angle of the mandible develops away from the action of the masseter and internal pterygoid muscles.

An alternative explanation for these observations suggests that tension may not produce bone but that the resultant stretch of the adjacent connective tissue facilitates the transmission of osteogenic stimuli which extend the perimeter of the bone. The nature of the osteogenic stimuli is not known but must be presumed to be produced by forces generated in normal activities. The distribution of functional forces to the graft environment was conditioned in some way by the tension which stretched the intervening tissue, and bone-producing stimuli were dominant.

It is possible, but not yet tested, that prior to resorption, the graft serves to extend further the transmission of appropriate stimuli (Harvold, 1975b; 1976). In the present experiment, bone developed from both margins of the cleft and on the surface of the transplant, which was gradually resorbed and replaced by new bone. The hypothesis that tension facilitates the extension of bone-inducing stimuli between the cleft margins cannot be rejected on the basis of this experiment.

Present clinical methods to establish bone across the cleft have not included efforts to control biophysical forces acting on the transplant environment. The experiments reported here suggest that the application of oriented stress improves the results of intra-alveolar bone graft procedures. Techniques for this purpose have been developed and are the basis of a subsequent report (Vargervik, 1976).

The bone bridge which replaced the resorbed graft developed its shape in response to functional requirements. In some animals, a narrow, compact bony plate formed the lower border of the piriform
aperture. Alveolar bone developed only in association with tooth eruption.

Further observations on the bone bridge established across the cleft in experimental animals demonstrate that a new suture can develop between the extended cleft margins. The functional forces acting on the maxillary segments may distribute bone-inducing stimuli to both sides of the cleft margins. The experiment suggests that a suture forms where these forces reach an equilibrium. Earlier reports on this model (Chierici et al., 1973c; Harvold 1975b) have shown that a new palatal suture can be developed adjacent to the midpalatal suture when the forces acting on the maxilla are altered. The parameters for these factors must be determined and subjected to testing before a complete theory of bone induction and suture formation in the cleft area can be established.

In a series of experiments, the hypothesis now being tested holds that sutures represent areas of conflicting stimuli. With the identification and control of responsible forces, it is reasonable to expect that future intra-alveolar transplants will result in new bone to provide stability and support to overlying soft tissue. It might also be expected that a suture could be developed in the new bone to permit growth adjustment.

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References


