Morphogenetic Experiments in Cleft Palate: Mandibular Response

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A concept of the nature of the deformity is significant to prognosis in patients with cleft palate. The concept should include differentiation between the primary defect and the adaptational responses of normal structures to an abnormal environment.

The relative dependence or independence of various components in the orofacial complex contributes to the morphogenesis of the face. This is apparent in individuals with acquired defects as well as those with congenital malformations. Otherwise normal components of the face may develop different shapes when growing in an abnormal position. In birth defects, it may be difficult to distinguish those contributions to facial morphogenesis which are due to inadequate cell potential from those which are simply normal responses to certain distortions or dysfunctions in related systems (*4*). If this differentiation can be made, it may be possible to focus attention on the primary defect and to prevent the development of secondary deformation.

For the past few years, a series of experiments has been undertaken in efforts to clarify some of these adaptational reactions and response systems. In this report the response of the mandible to the maxillary deformity is presented.

In 1949 Graber (*3*) reported that the mandible in children with cleft palate was characterized by a more obtuse gonial angle than was found in unaffected children. Harvold (*5*) demonstrated that with increase of the palatal vault during treatment of cleft palate children, the tongue was allowed to assume a normal position and the gonial angle decreased significantly. The difference between cleft palate and unaffected children was then reduced. Ross and Johnston (*8*) made similar observations on the shape of the mandible in children with unilateral and bilateral cleft lip and palate.

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These clinical investigations have suggested that the shape of the mandible is secondary to the cleft palate deformity. In order to examine these observations further, an experiment was designed to test the hypothesis that a normal mandible would change shape in response to maxillary deformity. Enlow (*2*) described mechanisms of structural remodeling of the mandible and found that the fundamental principles were generally similar in the human being and the rhesus monkey.

Materials

Forty-two rhesus monkeys, 10 females and 32 males, were included in the experiment. The birthdates of the animals were unknown, and ages were assessed on the basis of the dentition according to data obtained by Hurme and Van Wagenen (*7*). The animals were estimated to range in age from one and one-half to six years. The monkeys were maintained in cages, each accommodating two animals, and were fed a standard diet of nutritional biscuits commercially prepared for primates.

The health of the animals was monitored daily, and their weights were recorded monthly. On the basis of increase in weight during the experimental period of one year, it was determined that the animals remained healthy and continued to grow.

Method

The technique pertinent to this paper has been previously reported along with certain findings on the upper face (*1*). Cephalometric x-rays and dental models were made of all animals at the beginning of the experiment. Twenty-one animals were subjected to a surgical procedure which produced a complete cleft of the bony palate extending from the piriform aperture to the posterior border of the hard palate. The nasal septum was not surgically disturbed nor were the lips and soft palate included in the operation. An appliance was used to induce medialward movement of the maxillary segment on the operated side (Figure 5).

Following recovery, periodic cephalograms and dental models were obtained during the one-year experimental period. Subsequently, selected dimensions of the mandibles were measured on the x-rays and also on the corresponding dental models.

The length of the mandible was measured from the condyle to the symphysis on the profile cephalogram. The face height was measured on the profile x-ray from the lower border of the orbit to the symphysis, with teeth in occlusion (Figure 1).

The gonial angle of the mandible was measured on the oblique cephalogram (Figure 2). The mandibular plane was represented by a line drawn through the symphysis and extending posteriorly through the deepest point of the concavity anterior to the attachment of the masseter muscle on the lower border of the mandible. A second line, tangent to the posterior

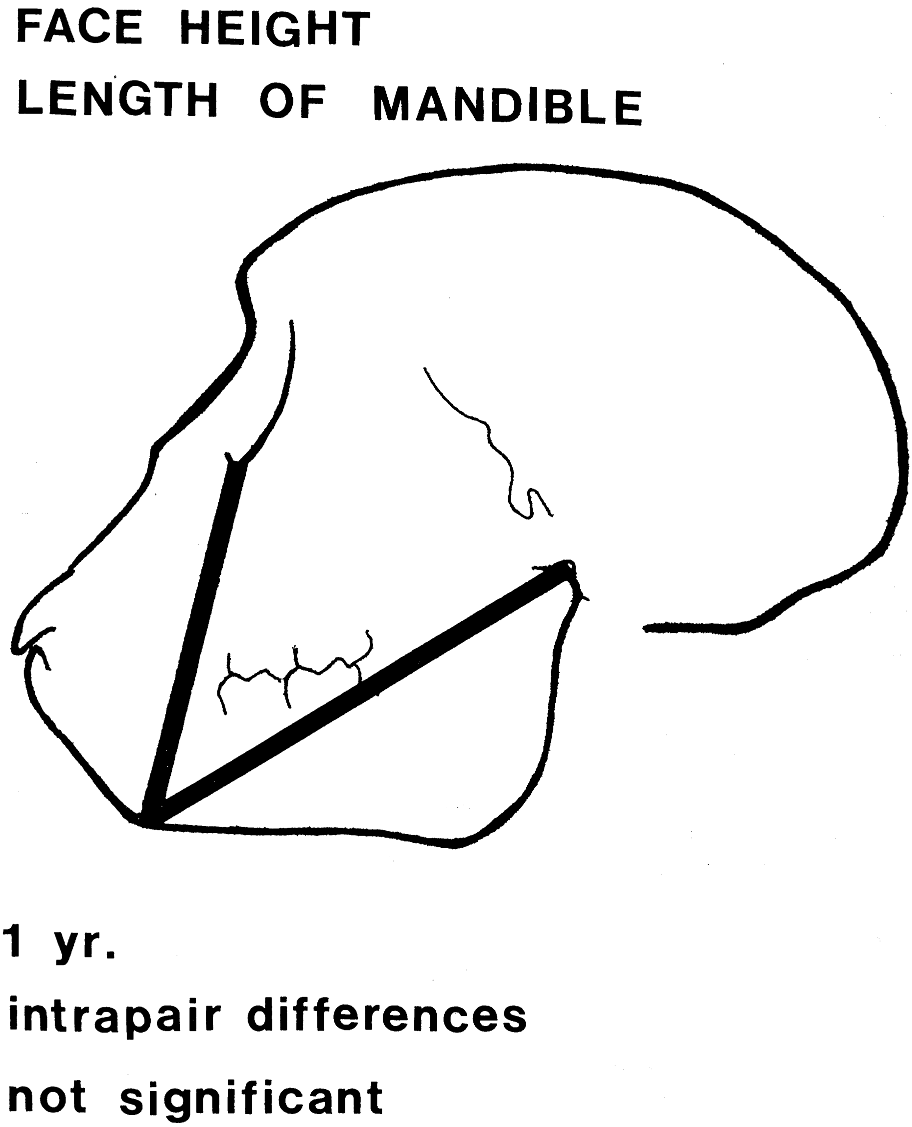

FIGURE 1. Tracing of a profile cephalometric film showing the dimensions measured to assess face height and length of mandible.

contour of the ramus and condyle, was drawn. The angle between these lines were recorded as the gonial angle.

The inclination of the lower incisors was measured on the profile film as the angle enclosed by a line through the longitudinal axis of the central incisor, relative to the mandibular plane (Figure 3).

The height of the lower first molar was measured on the oblique cephalogram from the tip of the mesiobuccal cusp to the mandibular plane.

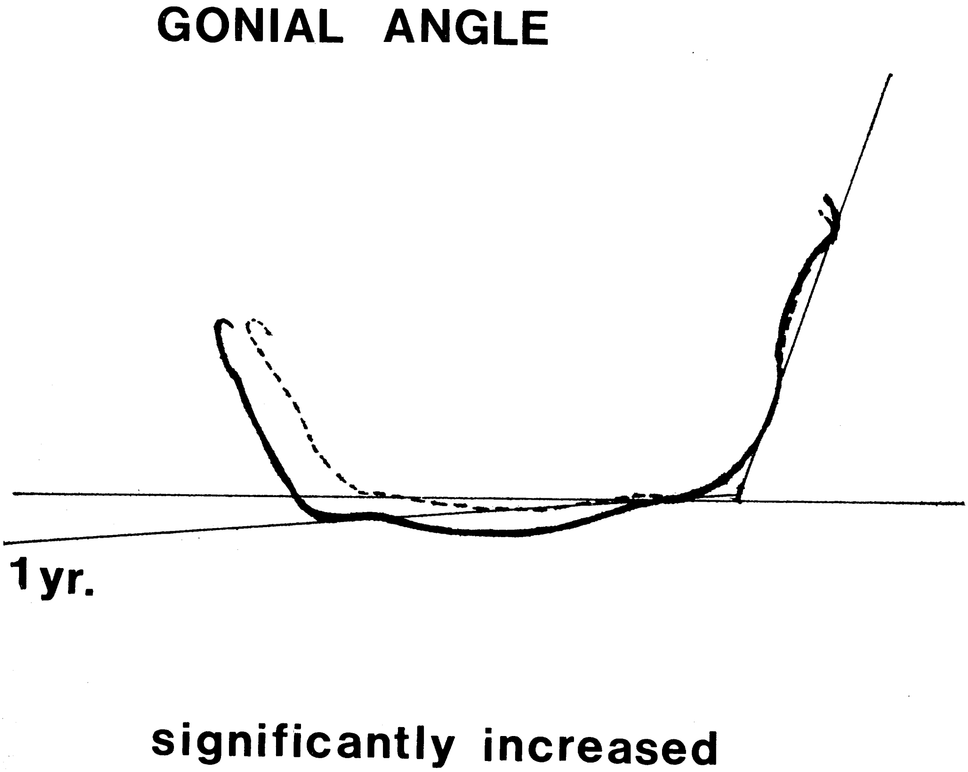

FIGURE 2. Tracing of an oblique cephalometric film depicting the changes observed in an experimental animal during the 12 month test period. The dotted line traces the shape of the mandible at the beginning of the experiment. The solid line traces the mandibular shape one year later.

Measurements on the dental models of the original 42 animals were limited by the transition from deciduous to permanent dentition, with missing or unerupted teeth in some of the young monkeys. In order to increase this sample, dental models of 28 additional male monkeys in the selected age group were utilized. Half of these animals also had experimental cleft palate.

The intercanine width was measured between the buccal and the lingual surfaces of the right and left canines and the mean of the values was obtained.

The intermolar distance was measured from the lingual developmental grooves of the mandibular first permanent molars.

The length of the arch was measured from a line connecting the central pits of the mandibular first permanent molars to the labial surface of the incisors.

The height of the incisors relative to the occlusal plane was determined on dental models by placing a stiff plastic triangle on the occlusal surface

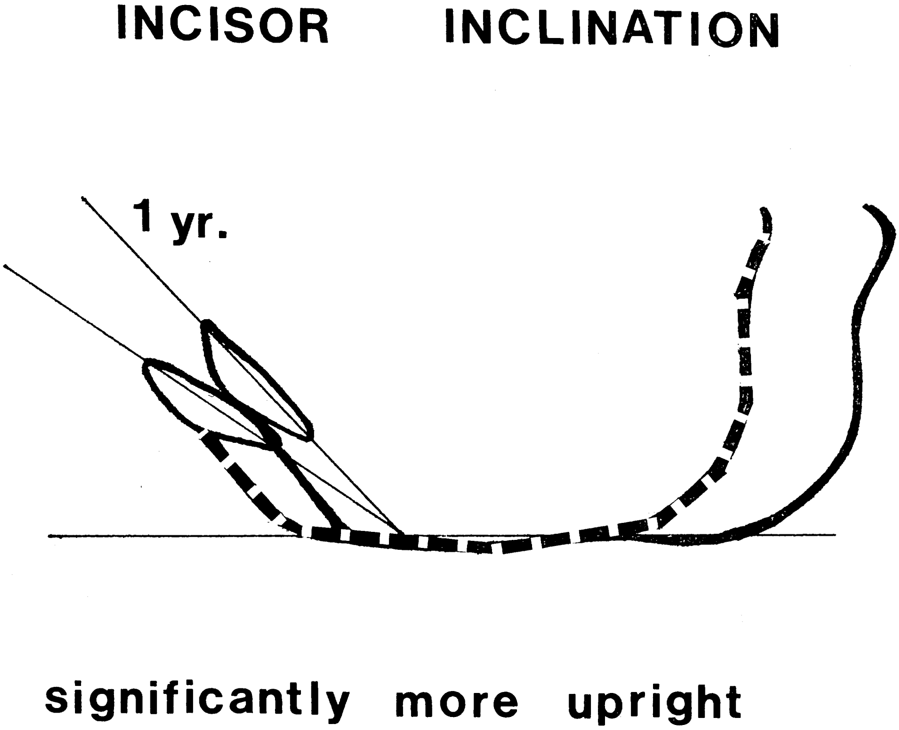

FIGURE 3. Tracing of a profile cephalogram indicating the change in incisor inclination of an experimental animal in the 12 month test period. The dotted line represents the shape of the mandible at the beginning of the experiment. The solid line shows the mandibular shape 12 months later. The tracings were superimposed on the apex of the angle formed by the axis of the incisor and mandibular plane.

of the mandibular second deciduous molar (or second bicuspid, if present) and the first and second permanent molars. The relative position of the incisal edge of the lower anterior teeth to the established plane was measured.

Design

The monkeys were paired according to sex and age. The data obtained from x-rays and dental models were analyzed by intrapair observation tests in order to randomize the effect of uncontrolled variables. The mean difference, the standard error of the mean, the standard deviation and the "t" value were determined.

Intrapair tests were used on the data derived at the beginning of the experiment. No statistically significant differences in the pertinent measurements were present between the control and experimental animals.

The same statistical analysis was made on the data obtained after six months and again after twelve months of the experiment. Statistically significant intrapair differences occurring after six or twelve month periods would be due to experimentally induced changes and would determine whether the formulated hypotheses should be rejected.

Findings

MEASUREMENTS ON THE CEPHALOMETRIC FILMS. Table 1 shows the results on the data derived from the cephalometric films.

1. There was no significant difference in mandibular length between the experimental and control animals.
2. There was no significant difference in face height between the paired control and experimental animals.
3. The gonial angle increased in the experimental monkeys, whereas the gonial angle usually decreased in the control group and the intrapair difference was significant at .01 level of confidence.
4. The uprighting of the incisors in the experimental animals was significant at the .01 level when compared to the control monkeys.

TABLE 1. Intrapair observation tests on selected measurements of cephalometric x-rays.

change during 12 months experimental period	*mean difference* $\bar{D}$	*standard error of mean* $s_{\bar{D}}$	*standard deviation* $s_{\bar{d}}$	*"t" value* "t"	*degrees of freedom* n–1	*number of pairs* n
length of mandible	−.905 mm	.799	3.659	−1.133	20	21
face height	.190 mm	1.011	4.633	.188	20	21
gonial angle	4.625 degrees	.600	2.685	7.704*	19	20
inclination of incisors	11.547 degrees	1.500	6.539	7.697*	18	19
height of lower first molar	−1.447 mm	.597	2.603	−2.424†	18	19

$$\bar{D} = \frac{1}{n}\sum_{i=1}^{n} D_i$$

$$S_D = \sqrt{\frac{\Sigma D_i^2 - \frac{(\Sigma D_i)^2}{n}}{n-1}}$$

$$S_{\bar{D}} = \frac{S_D}{\sqrt{n}}$$

$$t \text{ (test statistic)} = \frac{\bar{D}}{S_{\bar{D}}}$$

$$\gamma \text{ (degrees of freedom)} = n - 1$$

* Significant at .01 level of confidence.
† Significant at .05 level of confidence.

TABLE 2. Intrapair observation tests on selected measurements of dental models.

average monthly change during experimental periods	*mean difference (mm)*	*standard erorr of mean*	*standard deviation*	*"t" value*	*degrees of freedom*	*number of pairs*
intercanine width						
0–6 months	.063	.043	.226	1.480	27	28
6–12 months	.036	.033	.175	1.098	27	28
intermolar width						
0–6 months	.154	.033	.176	4.647*	27	28
6–12 months	.061	.029	.154	2.100†	27	28
arch length						
0–6 months	.116	.037	.193	3.164*	27	28
6–12 months	.027	.140	.107	4.018*	27	28
extrusion of incisors						
0–6 months	.229	.038	.217	6.068*	32	33
6–12 months	.106	.026	.149	4.103*	32	33

* Significant at .01 level of confidence.
† Significant at .05 level of confidence.

5. Outward tilting of the molars was observed in the experimental monkeys. The height of the lower first molars relative to the mandibular plane was smaller in the experimental animals than in the control animals at the end of the test period. This difference was significant at the .05 level of confidence when the intrapair test was employed.

Measurements on the dental models. Table 2 presents the statistical analysis of the available data from the dental models of the original 21 pairs of monkeys combined with the data from the supplemental pairs. The average monthly differences in the experimental monkeys were compared with similar data on the control animals. Thus, the changes occurring in the first six months of the experiment could be examined in relation to those differences appearing in the second six month period.

1. The changes in dimension between the mandibular canines of the experimental animals were not significantly different from those changes observed in the control monkeys.

2. The increases in width between the left and right mandibular first molars were significantly greater in the experimental monkeys than in the control animals. The greater width was significant at the .01 level in the first six months of the experiment and at the .05 level in the second six months.

3. The mandibular arch length was significantly greater at the .01 level of confidence in the experimental animals. Increases in arch length observed in the initial six month period continued during the last six months of the experiment.

4. The height of the incisors relative to the occlusal plane was significantly greater in the experimental animals than in the control animals.

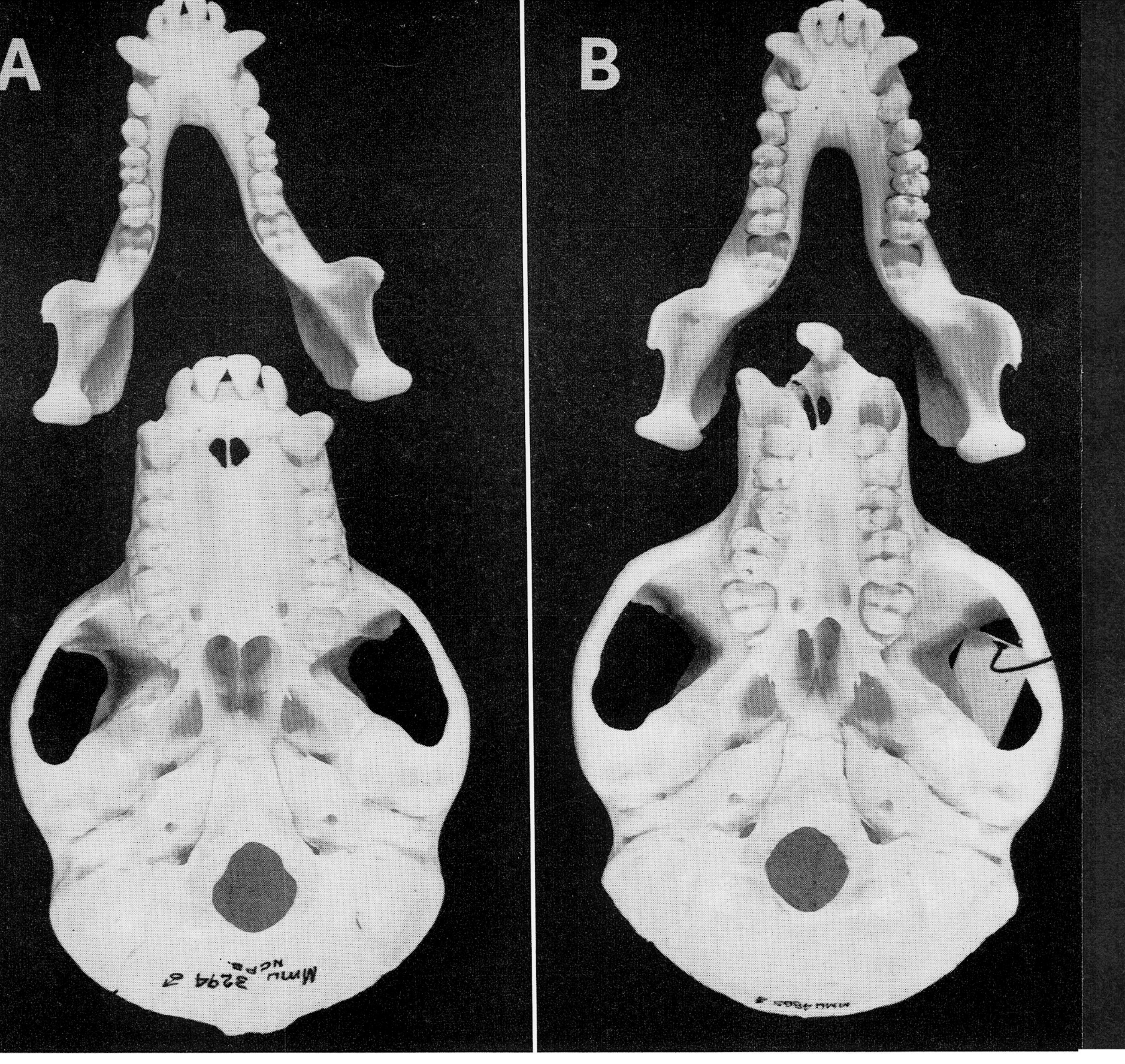

FIGURE 4. A. The skull of a control rhesus monkey. B. The skull of an experimental animal with maxillary deformation.

Extrusion of the incisors in the experimental animals was significant at the .01 level in the consecutive six month period of data collection.

Discussion

The initial hypothesis to be tested held that deformation of the maxilla would elicit adaptational responses in the mandible. Under conditions of the test, failure of a normal mandible to respond by statistically significant changes in shape would warrant rejection of the hypothesis. Comparison of the 21 pairs of rhesus monkeys at the end of the experiment showed that the hypothesis could not be rejected. Deformation of the maxilla resulted in changes in mandibular shape (Figure 4).

This then led to a series of theories which might account for the observed changes.

1. THE MAXILLARY DEFORMITY INFLUENCED GROWTH IN LENGTH OF THE MANDIBLE. This possibility was rejected since there was no significant difference in mandibular length between the experimental and control pairs at the end of the test period of twelve months.

2. THE CHANGE IN SHAPE OF THE MANDIBLE WAS DUE TO INCREASED FACE HEIGHT AS A RESULT OF EXTRUSION OF POSTERIOR TEETH. No significant difference in face height was revealed when the teeth were in occlusion. This contrasts with findings reported by the authors *(6)* in experiments which induced a lowered position of the mandible through stimulation of the tongue with an acrylic block in the palate. The block did not interfere with the teeth, and extrusion of the molar teeth could occur. Data from those experiments showed an increase in lower face height when the teeth were occluded. In the present experiment, extrusion of the

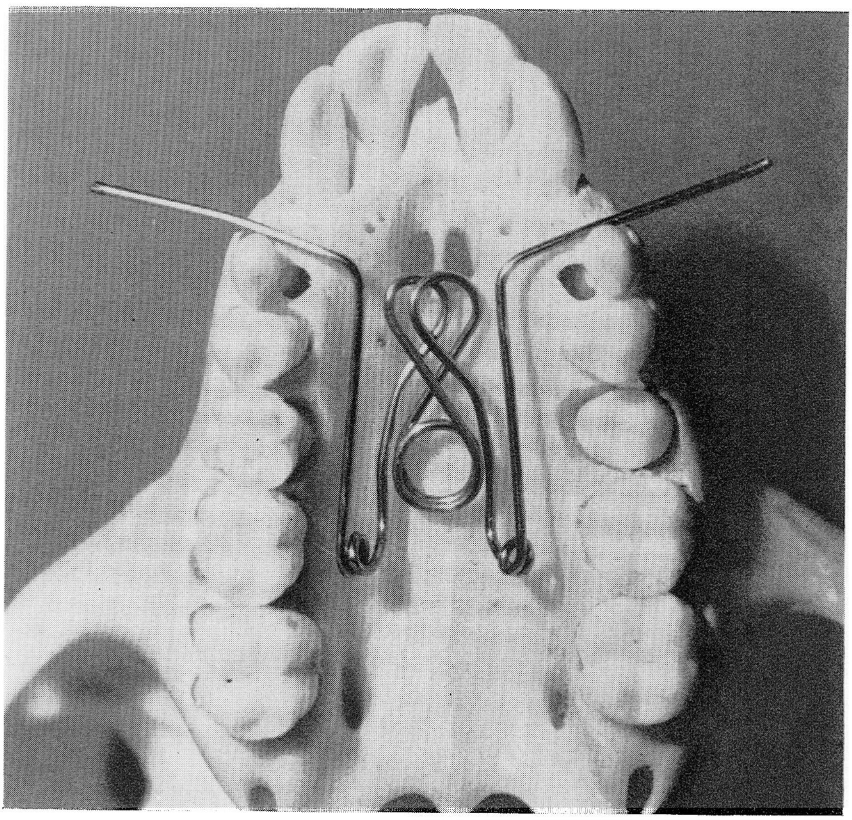

FIGURE 5. A model of the appliance used to produce medialward deformation of the maxilla is shown on the prepared skull of a normal rhesus monkey. The long extensions are cut after the appliance is fitted to the cleft palate of the experimental animal.

posterior teeth did not occur. In fact, vertical development of the lower first molars relative to the lower border of the mandible was inhibited in the experimental animals, and no significant change in face height appeared when measured with the teeth in occlusion. This second theory was therefore rejected as an explanation for the observed changes in mandibular shape.

3. The Change in Shape Resulted from an Altered Postural Position of the Mandible without Compensating Increase in Alveolar Height. A change in postural position of the mandible could be induced by displacement of the tongue after surgery, since the upper dental arch became very narrow. There was a reduction in the height of the palatal vault, and the tongue could not maintain its usual position in the palate. The nature of the resulting horizontal and vertical changes in the dental arches was dependent on the new position of the tongue. In this experiment, the distance between the right and left molars became significantly greater in the animals with deformed upper jaws. The width of the lower arch in the canine area was unaffected.

The lower incisors tipped upward in response to altered tonus in the lip musculature, which in turn resulted from the new mandibular position. Despite uprighting of the incisors, the length of the arch increased, as the result of extrusion of the incisors above the level of the occlusal plane of the molars. The extrusion was significantly greater in the experimental animals than in the control pairs.

At present no reliable method of measuring the postural position of the mandible or freeway space is available to us. However, it is not justified to reject the hypothesis that adaptational changes in mandibular shape are related to altered postural position of the mandible under conditions of maxillary deformation.

The theory emerging from this and previously reported morphogenetic experiments postulates that under conditions of maxillary deformity, the postural position of the mandible is lowered and the shape of the jaw alters. Due to the deformation, the tongue rests between the maxillary and mandibular arches and prevents further eruption of the posterior teeth. Therefore, lower face height is not necessarily increased when measured with the teeth in occlusion.

In the treatment plan for patients with cleft palate, the prevention, utilization, or reversal of these secondary adaptations should be considered. When a patient with a malformation is examined, certain aspects of the observed facial form may reflect normal responses to an abnormality in a collateral system. Inadequate cell potential may provide a more reliable basis for characterizing a malformation or syndrome than do similarities in appearance due to normal response systems.

Summary

An experiment was designed to test the response of the mandible to maxillary deformity. Forty-two rhesus monkeys were paired according to sex

and to age, as determined by dental development. A complete cleft of the bony palate was surgically produced in one animal in each pair, and maxillary constriction was induced by an appliance. Cephalometric x-rays, dental models and photographs were obtained before the experiment and at three month intervals thereafter. At the end of one year, data from the records were analyzed, using intrapair observation tests. No significant differences in the length of the mandible or in face height were found between paired experimental and control animals. Significant differences were disclosed in the gonial angle of the mandible, the inclination and extrusion of the incisors, mandibular intramolar width, and arch length. Extrusion of the mandibular molars was less in the experimental animals than in the control monkeys.

The hypothesis that the observed changes in mandibular shape were due to the lowered postural position of the mandible under conditions of maxillary deformity could not be rejected.

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