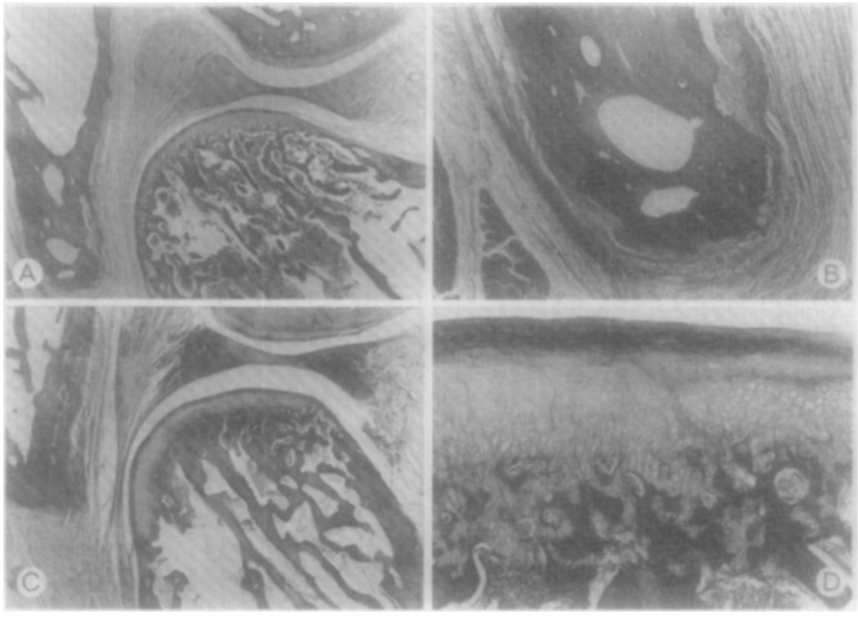

Fig. 8. Condylar adaptation in a 4-week cross-bite animal in which the mandible deviated to the right. **A,** Right temporomandibular joint region with resorption of bone along the anterior border of the postglenoid spine. Note the lack of cartilage proliferation along the posterior border of the mandible. **B,** Resorption of bone along the anterior border of the right postglenoid spine. **C,** Left temporomandibular joint region in same animal. Note the deposition of new bone along the postglenoid spine and the proliferation of the condylar cartilage. **D,** Proliferation of condylar cartilage along the superior surface of the left condyle. (Magnifications: **A** and **C,** ×12; **B** and **D,** ×40.)

chondroblastic layer together with a highly invaginated cartilage-bone interface in both joints.* The right temporomandibular joint, which had cartilage thicknesses from 14 to 110 percent greater than those on the left side at comparable locations, displayed distinct evidence of new bone formation on the anterior aspect of the postglenoid spine, while the left postglenoid spine contained foci of resorption along its anterior border (Fig. 8). The 6-week cross-bite animal showed little difference in condylar morphology from that seen in controls, but there were distinct areas of resorption on the anterior surface of the postglenoid spine in both joints. The 2-week animal with a cross-bite presented no notable differences from controls; in light of the tissue responses noted in cross-bite animals at later stages, it is possible that the lack of response in the 2-week animal may be due to the abbreviated time interval.

*Although a cycling female, this animal was perhaps a little less mature than the others. While the mandibular third molar had reached the level of the occlusal plane, the maxillary third molar, although erupted, had not quite reached this level. Thus, the vitality of the condylar cartilage, rivaling that of any animal in either the control or experimental groups, may be due in part to its slight developmental immaturity.

Quantitative analysis

In order to test whether changes in the condylar cartilage display a diminished response over time as seen in juvenile animals,[11] thickness of the prechondroblastic-chondroblastic cartilaginous layer was measured by means of a reticule inserted into the eyepiece of a Zeiss Photomicroscope III. The thickness of the cartilage layers was measured perpendicular to the articular surface at the posterior, posterosuperior, and superior regions along the circumference of the condyle.[11] Linear regressions* were computed for each region of the condyle to determine the association between cartilage thickness and duration of treatment (Fig. 9, Table I). Although cartilage thickness appears to undergo a slight decrease with treatment duration, no significant relationship could be detected comparable to that found in juvenile animals. However, Fig. 9 substantiates the qualitative assessment that the adaptive response is more pronounced in the superior and posterosuperior regions of the condyle, with less response in the posterior region. Thickness of the condy-

*Regressions were performed for right side measurements, left side measurements, and both sides combined. Data from animals who developed cross-bites were excluded from the analyses.

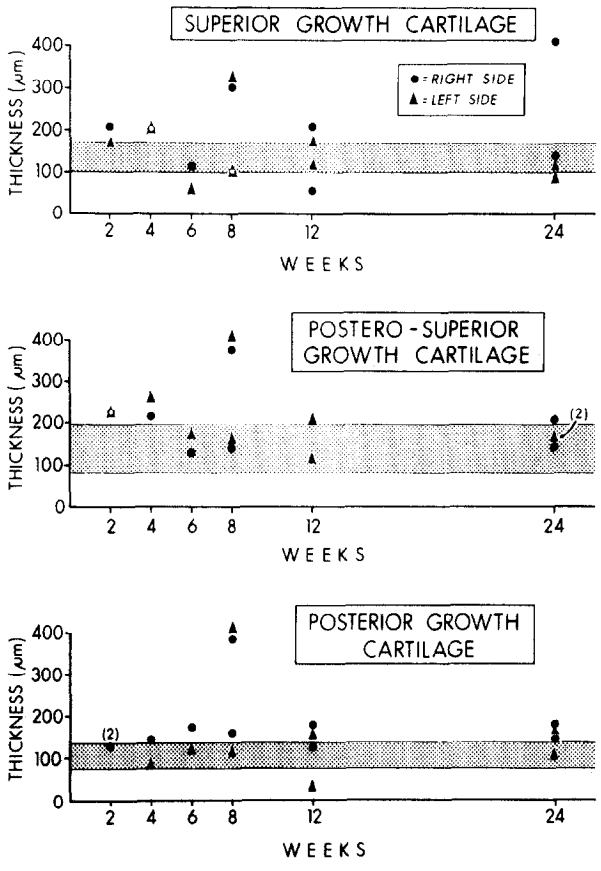

Fig. 9. Least squares regression analysis of adaptive responses in the thickness of condylar cartilage relative to duration of treatment. Data points for each experimental animal are indicated by side. Stippled area indicates the range of condylar thickness to the first standard deviation in the control animals.

lar cartilage was consistently greater in experimental animals relative to controls at all locations studied (Table I), although the differences were not significant, perhaps because of the large amount of variation in the experimental sample.

DISCUSSION

The results of this study provide evidence that in the majority of the experimental animals the condylar cartilage in young adult monkeys was affected by alteration of the biomechanical environment of the temporomandibular joint. Functional protrusion of the lower jaw resulted in an increase in the number of cells in the prechondroblastic-chondroblastic layer accompanied by a deposition of new bone at the cartilage-bone interface. Although not as pronounced, this response is qualitatively very similar to that documented in growing monkeys that were fitted with a similar protrusive appliance. While the magnitude of the response (as assessed by thickness of the prechondroblastic-chondroblastic layer) decreased somewhat as the duration of treatment increased, the time-dependent nature of the adaptive response in adult animals was not nearly as marked as that seen in juvenile monkeys. (Regressions of adult cartilage thickness on treatment duration were *not* significant.) However, the density of chondroblasts in most experimental animals was consistently greater than that in the control sample, suggesting that a true change in condylar morphology had taken place in the experimental animals. Apart from the magnitude of the response, the other main difference observed between growing and young adult animals concerned the *localization* of the response along the circumference of the condyle. In the growing (juvenile) animals, cartilage proliferation was maximum in the posterior, and to a lesser extent, the posterosuperior regions of the condyle.[11] In contrast, the most pronounced changes in the adult animals tended to occur primarily on the superior and posterosuperior aspects of the condyle, although there was perhaps more variability in location than in young animals. Assuming that the adaptive response is of the same sort as in juvenile animals (that is, a compensatory change to reposition the condyle back within the mandibular fossa), then these data would suggest that the adjustment in the adult condylar response was predominantly to the *vertical* displacement introduced by the appliance and only secondarily to the horizontal (protrusive) displacement. Such an assessment is admittedly subjective and demands replication and further study.

It is interesting that cross-bites were developed in one fourth of the experimental sample in response to appliance placement. Since cross-bites were never noted in juvenile animals fitted with appliances of similar construction, their occurrence in a substantial percentage of the adult animals is worthy of note. While the reasons for this situation are unclear, it may indicate a diminution in adults of the capability to habitually posture the lower jaw forward to the extent required by the appliance. Support for this inference derives from the fact that aberrant and even painful jaw postures, including constantly keeping the mouth open or penetration of the palate by the prongs of the appliance, were tolerated as apparent alternatives to protrusion of the lower jaw during occlusion. Whatever the case, tissue responses noted in the cross-bite animals may be explicable as adaptations induced by the asymmetric occlusion. In the 4-week cross-bite animal, the persistent distraction of one condyle from the mandibular fossa and the retrusion of the other condyle prompted by the nature of the cross-bite occlusion are consistent with the histologic findings: relatively greater cartilage thickness and bone deposition on the postglenoid spine

Table I. Mean thickness (in microns) of the condylar cartilage in the control and experimental samples

	Right						*Left*					
	Superior		*Posterosuperior*		*Posterior*		*Superior*		*Posterosuperior*		*Posterior*	
	Mean	*S.D.*	*Mean*	*S.D.*	*Mean*	*S.D.*	*Mean*	*S.D.*	*Mean*	*S.D.*	*Mean*	*S.D.*
Control (n = 7)	128.7	30.9	132.9	45.5	101.7	31.3	136.9	45.7	149.3	71.4	110.0	27.8
Experimental (n = 9)	191.9	108.7	198.3	94.2	179.0	76.3	158.0	71.5	201.7	88.8	137.2	110.6

Differences between means are not significant.

in one joint and the relatively reduced cartilage thickness (especially posteriorly) and postglenoid bone resorption at the contralateral joint. The resorption noted on the anterior surfaces of both postglenoid spines in the 6-week cross-bite animal may also be related to the presence of a cross-bite, since the animal seemed to adapt to the appliance by keeping its mouth open and shifting the lower jaw laterally to minimize the degree of opening. It has been suggested on various grounds[22, 28] that contact between the postglenoid spine and condyle may take place in monkeys, especially during gapes of some magnitude. In view of several studies linking habitual retropositioning of the condyle in the fossa with resorption on the anterior surface of the postglenoid spine,[7, 30–32] the association of postglenoid remodeling changes with this animal's particular adaptation to the protrusive appliance does not seem unreasonable.

In the juvenile animal, it has been suggested that the proliferative chondrogenic response to altered function is explicable in light of certain distinctive features of the condylar cartilage. Several workers[29, 33] have noted that the articular layer is continuous with the outer fibrous periosteum of the neck of the condyle, while the prechondroblastic-chondroblastic layer corresponds to the inner osteogenic periosteal layer of the condylar neck. This fact has led to the assertion[3, 4] that the cells of the prechondroblastic zone are homologous with the preosteoblasts of the remainder of the periosteum of the mandible. On this basis, we have previously suggested that, just as mechanical forces may stimulate or inhibit periosteal osteogenesis they may act in similar fashion on the prechondroblasts of the condylar cartilage to produce the adaptive response.[11] Studies employing autoradiography in growing animals have confirmed the primary role played by proliferation of prechondroblasts during normal growth of the condyle[34–36] and in response to altered occlusal relationships.[2, 4, 20, 37] However, there is little consensus concerning the potential for differentiation of prechondroblasts into chondroblasts in adult animals. Kanouse and associates[36] have noted that the activity of cells at the cartilage-bone interface was much higher than the activity in the prechondroblastic zone in a young adult female monkey, in contrast to the greater activity in the prechondroblastic zone in younger animals. It seems reasonable that the chondrogenic response noted in this study involving adult animals may be the result of a *reactivation* of the cells of the prechondroblastic zone, with their subsequent differentiation into chondrocytes in deeper layers. This interpretation is supported by the work of Lindsay,[19] who used autoradiographic techniques to study cellular activity in the condylar cartilage of mature rats fitted unilaterally with a bite-raising splint. He found a threefold increase in cellular proliferation on the splinted side, with higher labeling of cells in the prechondroblastic zone than in the hypertrophic zone. Using a similar experimental protocol on adult rats, Ehrlich and colleagues[21] observed that occlusal changes introduced by the bite splint also preferentially altered the staining pattern for the cyclic nucleotides cAMP and cGMP in the prechondroblastic and hypertrophic zones. Staining for the cyclic nucleotides, which have been postulated to act as mediators between mechanical stimuli and cellular proliferation,[38] was greatly intensified in the prechondroblastic zone of treated animals but almost unaffected in the hypertrophic zone. In contrast, staining in control animals was uniform in both zones.

The implications of this study that a significant adaptive response may take place at the temporomandibular joint in some adult monkeys are in disagreement with the conclusions of several previous reports. Perhaps the best known of these are the series of studies performed by Ramfjord and co-workers.[13, 14, 16] They were unable to detect significant adaptive changes in the temporomandibular joints of adult monkeys subjected to functional protrusive and other appliances, and they attributed the adaptive response which did occur to compensatory changes in the dentoalveolar region. However, a number of factors make comparison of their results with those of the present study difficult. For instance, the control and experimental samples used in the various studies cited above were not

always well matched for sex and age (to the extent that the latter can be determined in adult monkeys). Since young adult *male* monkeys continue to grow at a rate that is several times that seen in young adult females,[39] our study included *only* young adult females in both control and experimental samples in an effort to minimize the amount of growth not associated with experimental intervention. Also, since third molars in females erupt, on the average, 4 to 8 months *later* than in males,[27] the use of female animals with third molars in occlusion tended to bias the sample in favor of *older* animals, thereby making any results more conservative. In the Ramfjord studies, the experimental groups comprised either adult *males* of unknown age[13] or very old females.[14] It may very well be the case that the potential for cellular response of the sort studied here is diminished in individuals considerably beyond young adulthood, a possibility which might be a mitigating circumstance in the lack of response noted by Ramfjord and associates. Second, the amount of functional protrusion introduced by the appliance was appreciably greater in our experiment (5 mm.) than in those of Ramfjord and associates (1.5 mm.). Conceivably, the greater occlusal imbalance created in the former instance could elicit an adaptive response of larger magnitude. Finally, previous studies of this problem have not, for the most part, undertaken detailed histologic analyses of the temporomandibular joint tissues. However, it is interesting to note that Hiniker and Ramfjord,[13] working with adult *males*, describe "some cartilage [covering] the bone on the articular surfaces" in a 2-week experimental animal and note that "these structures did not have a well-defined layer of cortical bone," characteristics which they attribute to the relatively young adulthood of the animal but which also resemble the morphology observed in 2-week experimental monkeys in this study. In addition, in the 6-week experimental animal they figure and describe a "narrow zone of newly-formed bone" on the distal aspect of the condylar neck as well as a thin layer of new bone on the anterior surface of the postglenoid spine and inferior surface of the mandibular fossa. Similarly Adams and co-authors[7] comment that in the "youngest adult monkey" exposed to Class II intermaxillary forces on one side and Class III on the other side (see also Meikle[40]), the condyle subjected to Class II force "demonstrated a more posteriorly directed endochondral ossification . . . compared to the control animals," and they liken this pattern to growth "to that seen in the younger [growing] experimental animals."

To varying degrees, the earlier studies cited above have concluded that condylar adaptive response in the *adult* temporomandibular joint, if it exists, is of such minimal magnitude as to be of no importance. The results of our study suggest that an adaptive response does indeed occur in most *young adult* animals, although its magnitude and even its presence may be considerably more variable than in growing animals. The question of *magnitude* of the response remains unresolved and may depend on a number of factors, including the age and sex of the individual, amount of condylar distraction produced by the appliance, and duration of treatment. For example, a recent cephalometric study of the effect of a bite-opening appliance on mandibular growth in adult female monkeys by two colleagues[41] provides additional (quantitative) evidence of the potential for adaptive growth at the temporomandibular joint in young adults. In their study, distraction of the condyle from the mandibular fossa, brought about by the appliance, resulted in the deposition of an average of 1.5 mm. of new bone along the posterosuperior aspect of the condyle in the experimental animals after 48 weeks. Thus, while dentoalveolar adaptations are undoubtedly of primary importance in adults,[8] there are indications that compensatory changes at the temporomandibular joint may also contribute to the over-all accommodation to occlusal alterations, at least in young adults.

Clinical implications

The results of this study seem to indicate that in many instances the temporomandibular joint of the young adult animal is capable of some functional adaptation. This should not be surprising to the reader, even in light of previous studies which seemed to report contrary findings. The usefulness of this adaptive capability of the adult TMJ is perhaps best observed in patients following various orthognathic procedures of the mandible.[42, 43] In many of these cases, the mandibular condyle is repositioned or rotated to a moderate extent and TMJ pathosis is not a routine finding. By inference (and by radiographic indications of remodeling documented in such cases), this seems to indicate that some adaptive responses in the temporomandibular joint are elicited to accommodate to the new structural relationships within that region.

The relevance of this study to the use of functional jaw orthopedic appliances in adults must be stated with great caution. First, while in the majority of instances the qualitative response of the young adult condyle was similar in many respects to that observed in the juvenile animals, the magnitude of the response was greatly reduced in the adults. The amount of cartilage proliferation in the young adult animals was not nearly as great as observed in the young monkeys. Thus, it must be kept in mind that the *biologically* significant changes

documented in this study may or may not be *clinically* significant.

The second reason for caution is that it must be noted that in our previous experiments with juvenile animals, condylar responses were observed in every animal studied from 2 to 12 weeks following appliance placement.[11] In contrast, in three of the nine animals that functioned anteriorly (excluding the three additional cross-bite animals), the morphology of the condyles in the experimental animals could not be distinguished from controls. These nonresponding animals tended to have reduced cartilage thickness overlying a solid bony cortex similar to those control animals with a limited cartilage thickness without treatment (Fig. 2,*E* and *F*). Since the exact age of the animals used was not known, it is not possible to directly evaluate whether the lack of response was primarily attributable to a more advanced age or to variation in responsiveness among individual animals. However, use of relative chronological ages obtained from assessment of occlusal and interproximal attrition indicates that the three nonresponding animals are all among the oldest in the experimental sample.[44] Thus, it may be that as individuals age the condyle gradually loses the ability to respond functionally as the cartilage cells are lost. The problem facing the clinician is the prediction of which patients have sufficient capability to adapt to functional orthopedic treatment. A few millimeters of increased mandibular growth may be a reasonable goal in some patients. However, the correction of a mandibular deficiency that would otherwise require orthognathic surgery does not seem possible in the light of our experiments with adult monkeys.

SUMMARY AND CONCLUSIONS

The primary aim of this study has been to analyze histologic changes in the condylar cartilage of young adult monkeys (*Macaca mulatta*) in response to induced protrusive function. In the majority of animals in the experimental sample, a proliferative chondrogenic response accompanied by deposition of new bony trabeculae at the bone-cartilage interface was evident. These morphologic changes in the condylar cartilage resemble in form, although not in magnitude, the changes previously documented in growing monkeys undergoing a similar experimental protocol. In the growing monkeys, this chondrogenic response has been generally interpreted as an indication of the potential of the condylar cartilage to undergo compensatory growth as a means of re-establishing functional equilibrium. Although dentoalveolar adaptations are very likely the primary mechanism of occlusal adjustment in adults, the documentation of a qualitatively similar response in young adult monkeys suggests that the ability of the young adult condylar cartilage to participate in the over-all craniofacial adaptation to functional perturbations has been underestimated. Since all animals used in this study were physiologically mature adults with third molars in occlusion (thereby perhaps corresponding to human beings in their late teens to mid-twenties), the results reported here indicate that the assumption that the temporomandibular joints of young adults are stable and resistant to clinical intervention should be re-examined.

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