# Histologic Changes Associated With the Herbst Appliance in Adult Rhesus Monkeys (Macaca mulatta)

James A. McNamara, Jr, John E. Peterson, Jr, and Hans Pancherz

Although most Class II orthopedic treatments have been recommended for use in juveniles and adolescents, orthopedic intervention with the Herbst appliance has recently been suggested for use in young adults. Previous experimental studies have suggested that the potential for adaptation in the temporomandibular joint (TMJ) region of the young adult, while diminished compared with that of adolescents, still may be sufficient to allow for the resolution of Class II problems. The purpose of the current study was to evaluate histologically the response of the mandibular condyle, glenoid fossa, and posterior border of the ramus of adult Rhesus monkeys whose mandibles had been positioned forward with a Herbst appliance. Acrylic splint Herbst appliances were bonded to the maxillary and mandibular dental arches of 14 female adult animals. The animals were killed at 3-, 6-, 12-, and 24-week intervals after appliance placement. Seven female adult Rhesus monkeys served as controls. The TMJ regions were removed and analyzed histologically qualitatively and quantitatively by way of the Bioquant IV measuring system (Bioquant Image Analysis Corp, Nashville, TN). Significant variation was observed in the TMJ regions of the control animals, with some animals having identifiable prechondroblastic and chondroblastic layers of condylar cartilage and others with more fibrous coverings of the mandibular condyle. In the experimental animals, adaptive changes in the condylar cartilage were evident as early as 3 weeks, with the dimensions of the condylar cartilage increasing gradually throughout the experimental period. Only minor changes were noted in the articular tissue. All adult control animals had a bony cap, and the bony cap persisted in the experimental animals. Significant bone deposition occurred along the anterior surface of the postglenoid spine only in the 6- and 12-week experimental groups. No significant areas of bone deposition and resorption were noted along the posterior border of the ramus. The result of any study in animals, even in nonhuman primates, obviously cannot be applied directly to human functional orthopedic treatment. Because the tissue types and the morphology of the TMJ generally are similar between monkey and man, however, the findings of the present study may provide some insight concerning the changes occurring within the mandibular condyle and glenoid fossa when a Herbst appliance is used clinically in young adult patients. (Semin Orthod 2003;9:26-40.) Copyright 2003, Elsevier Science (USA). All rights reserved.

From the Department of Orthodontics and Pediatric Dentistry, School of Dentistry, University of Michigan, Ann Arbor, MI; the Department of Pediatric Dentistry, Loma Linda University, Loma Linda, CA; and the Department of Orthodontics, University of Giessen, Giessen, Germany.

Supported in part by United States Public Health Service Grant DE-03610 and by funds made available through the Thomas M. and Doris Graber Endowed Professorship at the University of Michigan.

Address correspondence to James A. McNamara Jr, DDS, PhD, Department of Orthodontics and Pediatric Dentistry, School of Dentistry, University of Michigan, Ann Arbor, MI 48109-1078.

Copyright 2003, Elsevier Science (USA). All rights reserved. 1073-8746/03/0901-0001\$35.00/0 doi:10.1053/sodo.2003.34022

The 28th Annual Moyers Symposium<sup>1</sup> considered the timing of orthodontic and orthopedic interventions used to correct various types of skeletal and occlusal problems. The presentations and discussions at that symposium can be considered representative of the broad spectrum of orthodontic opinion in existence today among practitioners concerning the optimal time for the initiation of orthodontic and orthopedic therapy, with recommendations that extend from initiating treatment in preschool children<sup>2</sup> (Hamilton DC, personal communication, 2001) to those entering young adulthood.<sup>3</sup>

Considerable controversy still remains concerning the most advantageous time to begin orthopedic treatment of Class II malocclusion, with some clinical investigators recommending deferring functional jaw orthopedics until about the time of the pubertal growth spurt. For example, increased increments of mandibular length have been noted in patients who began functional appliance treatment in the late mixed or early permanent dentition ( $\sim 11.5$  years of age) than in those who began treatment in the early mixed dentition ( $\sim 8.5$  years of age).<sup>4</sup> If the maturation of the cervical vertebrae (CVM) is used as a marker, increased growth responses have been observed with functional appliance therapy at about the time of the pubertal growth spurt (CVM stages 3-4) than at earlier stages of maturation (CVM stages 1-2).5,6

Although the major focus of debate about the timing of Class II intervention has been whether juvenile or adolescent intervention is more advantageous, Pancherz and von Bremen<sup>3</sup> and Ruf and Pancherz<sup>7,8</sup> recently have broadened the discussion of the age of intervention considerably, suggesting orthopedic intervention in young adults by way of the Herbst appliance. They summarize the current concept for Class II treatment as growth modification in juveniles and adolescents, camouflage orthodontics in postadolescents, and corrective jaw surgery in adults. These investigators, however, have raised the possibility of orthopedic correction of Class II malocclusion in young adults, recommending such intervention in women 18 to 24 years of age and in men 20 to 25 years of age. Camouflage orthodontics and orthognathic surgery remain treatment options in older adults.

Pancherz and coworkers<sup>7-11</sup> have based their recommendations on the results from roentgen-

ographic cephalometric and magnetic resonance imaging (MRI) studies of the temporomandibular joint performed in adolescent and young adult Herbst patients.<sup>7,12,13</sup> In these studies, it was shown that condylar growth in young adults could be reactivated. The increase in mandibular length accomplished by Herbst therapy in both adolescents and young adults seemed to be a result of condylar and glenoid fossa remodeling.<sup>7,12</sup> Additionally, the mandibular skeletal contribution to Class II molar and overjet correction in young adult Herbst patients amounted to 25% on average.<sup>13</sup>

Furthermore, basic science has disclosed the presence of zones of unmineralized growth cartilage and undifferentiated mesenchymal cells in the adult mandibular condyle.<sup>14,15</sup> Researchers and clinicians also have noted favorable TMJ responses in young adult patients after condylar fracture therapy.<sup>16</sup> corrective jaw surgery.<sup>17,18</sup> and mandibular repositioning in disk displacement therapy.<sup>19-21</sup> During each of these procedures, the mandibular condyle typically is repositioned within the glenoid fossa; however, minimal pathological findings (eg, temporomandibular disorders) have been reported in young adult patients.

# **Previous Clinical Studies**

The general topic of functional appliance therapy in adults has received scant attention during the last few decades, although some clinicians have advocated the use of such appliances to alleviate temporomandibular joint dysfunction or to correct minor or major skeletal and dental discrepancies.

Previous clinical investigations of functional appliance treatment in adults are anecdotal at best. One of the few published clinical studies of functional appliance treatment in young adults was a prospective pilot study by McNamara<sup>22</sup> concerning the efficacy of the function regulator (FR-2) appliance of Fränkel in 5 adult patients. Only 3 of the 5 patients completed a minimum of 1 year of full-time appliance wear. The 3 patients wore a function regulator from a minimum of 1 year to a maximum of 3.5 years. The length of the mandible did not increase significantly in any of the patients. In all patients, however, there were increases in the vertical dimension. McNamara<sup>22</sup> concluded that

only minimal skeletal and dental adaptation occurred and that these adaptations were insufficient to resolve the patients' malocclusions completely. No large-scale prospective clinical trials have addressed the issue of functional appliance therapy in adults.

## **Previous Experimental Studies**

Although numerous experimental investigations have considered the possibility of advancing the mandible therapeutically in juveniles and adolescents,24-32 studies of adaptations within the young adult temporomandibular joint are much more limited. Historically, the temporomandibular joint region of adult animals was regarded as largely unresponsive to changes in occlusal conditions, especially by Ramfjord and coworkers.<sup>33-35</sup> Hiniker and Ramfjord<sup>33</sup> reported that the temporomandibular joints of the adult Rhesus monkey were very stable and resistant to changes in occlusal relations and trauma. They stated that the microscopic adaptations in the joint were "insignificant, non-progressive and possibly reversible without treatment." The predominance of dentoalveolar adaptations led Ramfjord and Ash<sup>36</sup> to state that there is a "need for adapting the occlusion to the joints rather than hoping for the joints to adapt to the occlusion, at least when considering the temporomandibular joint."

The first large-scale experimental study of adaptation of the adult temporomandibular joint comparable to those on growing animals was conducted by McNamara and coworkers in 1982.37 Twelve young adult Rhesus monkeys (precise ages unknown) were fitted with cast functional protrusion appliances for periods ranging from 2 to 24 weeks. Seven other animals were used as controls. Histological analysis of the temporomandibular joint region showed that half of the sample exhibited a tissue response that was similar qualitatively to that noted previously in juvenile animals.<sup>31</sup> They found, however, that the response in young adults was reduced in magnitude from that observed in younger animals. In addition, 3 animals that functioned anteriorly exhibited little or no detectible condylar response, and 3 other animals developed unilateral posterior crossbites after appliance placement by positioning the jaw to one side rather than forward. McNamara and

colleagues<sup>37</sup> concluded that although some adaptive capability still may be present in the temporomandibular joints of young adult animals, the joint response was highly variable in occurrence and modest in magnitude in comparison to juveniles.

The variability in response observed in this 1982 study37 was somewhat unexpected, given that presumably all animals were young, physiologically mature females with third molars in occlusion. To evaluate the relative age of the animals in the study, Hinton and McNamara<sup>38</sup> subsequently analyzed occlusal and interproximal tooth wear data from the sample. Because all animals were housed under the same conditions and were fed an identical diet, fewer assumptions were required than when this method of analysis is applied to human samples.<sup>39,40</sup> Hinton and McNamara<sup>38</sup> concluded that when the experimental animals were ranked by age on the basis of dental attrition data, those animals with evident hypertrophy and hyperplasia of the condylar cartilage were among the youngest in the sample of adult females, supporting the view that although the adaptive potential of the temporomandibular joint may diminish with age, the ability to adapt to altered occlusal function persists in some younger adult animals.

Relatively few experimental studies of forced mandibular protrusion by way of the Herbst appliance have been conducted, with data from only 1 adult animal analyzed. In what amounted to a case report, Woodside and coworkers<sup>41</sup> noted a small amount of remodeling in the superior aspect of the condyle of a juvenile Cynomolgus monkey that wore a Herbst appliance for a 13-week period. The glenoid fossa also showed extensive bone formation in the posterior region. In a follow-up study,42 5 animals wore Herbst appliances for 6 to 13 weeks, and 2 additional animals wore nonactivated appliances as sham controls. The investigators classified 1 animal as a juvenile, 5 animals as adolescents (including the sham controls), and only 1 animal as an adult. No condylar response was observed in the adult animal.

Thus, although tissue responses have been documented in the experimental literature regarding the adaptations within the temporomandibular joint regions of juveniles and adolescents, there is a paucity of information regarding condylar and fossa adaptations in adults. Previous experimental studies have indicated that adaptive responses can occur in young adult animals, although in general the magnitude of the response is diminished in comparison to that observed in younger animals. The response of the adult temporomandibular joint specifically to forced protrusion with the Herbst appliance has not been investigated rigorously. This report describes the tissue responses that occur in adult nonhuman primates subsequent to forced protrusion; a companion study on juveniles is presented elsewhere.<sup>43</sup>

## **Materials and Methods**

Twenty-one adult female Rhesus monkeys (*Macaca mulatta*) were used in this study. The adult female monkey was chosen as the experimental model because the canines of the female more closely resemble those of the human than do those of the male Rhesus monkey. Each of the 14 experimental animals wore an acrylic splint Herbst appliance that was bonded to the maxillary and mandibular dental arches. Three adult animals were terminated after 3 weeks, 5 adults after 6 weeks, 3 adults after 12 weeks, and the remaining 3 adults after 24 weeks. Seven additional adult female monkeys served as controls.

The Herbst appliance was modified for use in the monkey by including full acrylic coverage of the maxillary anterior teeth and palatal region.<sup>43</sup> The appliance was constructed so that the mandibles were advanced an average of 3.3 mm (this average does not include 1 adult animal who was advanced 6.0 mm, which is discussed later). The specific amount of advancement, however, varied slightly among animals. No subsequent reactivation of the appliances was performed. The splint was bonded in place using Excel<sup>TM</sup> adhesive (Reliance Orthodontic Products, Itasca, IL).

#### **Histological Analysis**

The animals were prepared for termination, and the tissue blocks taken from the temporomandibular joint regions subsequently were prepared for histological analysis according to our standard protocols described in detail elsewhere.<sup>43</sup> The tissue sections were evaluated both qualitatively and quantitatively by way of light microscopy. The portions of the study requiring linear measurements were quantified with a Bioquant IV microscopic system (Bioquant Image Analysis Corp, Nashville, TN).

Both central and medial sections of the TMJ region were selected for analysis. The mandibular condyle and the posterior border of the mandible were examined in central sections; the postglenoid spine was studied in more medial sections. Three central sections and 2 medial sections per animal were examined for each joint.

#### **Statistical Analysis**

Differences in condylar articular tissues and cartilage between control and experimented animals were determined by way of paired *t* tests. In addition, a least squares regression analysis was used to detect significant variations for articular tissue and cartilage width within experimental groups.

The presence of a bony cap was judged simply to be present or absent. The postglenoid spine, presence of ossified cartilage in the condyle, and the posterior border of the mandible were evaluated by assigning a degree of expression rating of 0 to 3 (0 = none, 1 = minimal, 2 = moderate,3 = extensive). A chi-square analysis was used to evaluate the postglenoid spine, ossified cartilage, and posterior border of the mandible. To use the chi-square analysis, the combined readings of each joint and ramus were collapsed into 2 categories (0-1 and 2-3). On infrequent occasions, the combined rating for a joint or ramus was in between the 0-1 or 2-3 category; in these instances, the particular joint or ramus was eliminated from the chi-square analysis.

The error of the measurement for the quantitative data was determined by remeasuring 12 sections in the control and 12 more in the experimental groups.<sup>37</sup> The error was within acceptable limits, with the exception of the 24week experimental measurement of superior cartilage width.

#### Results

The temporomandibular joint regions of adult control and experimental animals were analyzed both qualitatively and quantitatively. Of major interest were the mandibular condyle, the glenoid fossa, and the postglenoid spine (Fig 1). Although significant variability was evident even



**Figure 1.** The temporomandibular joint of 2 adult control animals. Lower power view of the mandibular condyle, articular disk, and retrodiscal tissue of the first animal. The inferior surface of the articular eminence can be observed superiorly (A). Higher power view of the same young adult monkey, illustrating abundant prechondroblastic and chondroblastic cells underlying the articular tissue covering the condyle (B). Similar views of another control animal with limited cellular activity in the mandibular condyle. The postglenoid spine can be observed in C (C and D).

among the control animals, their temporomandibular joints shared common characteristics. Importantly, no pathological findings were detected in any of the control or experimental animals analyzed.

#### **Condylar Cartilage**

The condylar cartilage generally can be divided into prechondroblastic and chondroblastic zones, although a precise differentiation into 2 layers was difficult in some control and experimental animals. The quantity of chondrocytes in the adult control condyles was reduced in comparison to untreated juveniles.<sup>15,43-45</sup> The number of hypertrophied chondrocytes within the mandibular condyles varied widely among the control animals, with condylar cartilage hypertrophy obvious in some animals (Fig 1A and B) but not in others (Fig 1C and D). In the latter condyles in particular, collagen fibers typically were visible faintly in the matrix, giving the tissue the appearance of fibrocartilage in many areas. Overall, the condylar cartilage was thickest in the superior region (144  $\mu$ m) and thinnest in the posterior region (104  $\mu$ m, Fig 2).

Adaptive changes in the condylar cartilage were evident as early as 3 weeks (Fig 3). In fact, in all areas measured, the total width of the condylar (prechondroblastic-chondroblastic) cartilage increased significantly over controls, with the greatest increases in width occurring in the posterior (177  $\mu$ m) and posterosuperior (188  $\mu$ m) regions (Fig 2, Table 1). Further condylar cartilage proliferation was evident at 6 weeks (Figs 2 and 4).

The thickness of the condylar cartilage continued to increase with time (Table 2). By 12 weeks (Figs 2 and 5), the average thickness of



**Figure 2.** Graphic representation of the relative thicknesses of the articular and condylar cartilages of the mandibular condyle in the adult monkey, as determined by the Bioquant measuring system. For each condyle, the thicknesses were determined at 3 regions: superior, posterosuperior, and posterior.

the posterior condylar cartilage was 246  $\mu$ m, in comparison to 103  $\mu$ m in the controls. At 24 weeks (Figs 2 and 6), the average thickness was 262  $\mu$ m. Similarly, the average thickness of the posterosuperior region of the 12- and 24-week animals was 277  $\mu$ m and 261  $\mu$ m, respectively, in comparison to 128  $\mu$ m in the controls.

#### Articular Tissue

Articular tissue covered the articulating surfaces of all condyles. This tissue consisted of dense connective tissue, with groups of fibers running parallel to the curvature of the head of the condyle. The thickness of the articular tissue in the controls ranged from 60 to 73  $\mu$ m (Fig 2).

After 3 weeks of wearing the Herbst appliance (Fig 3), hyperplasia of the articular connective tissue had occurred to a significant degree in both the posterior and posterosuperior areas of the condyle (Fig 2, Table 1). The slight increase in superior articular tissue width over the control, however, did not represent a statistically significant change. The articular tissue after 6 weeks of appliance wear (Fig 4) had diminished widths in all areas measured compared with that noted at 3 weeks. The posterosuperior tissue



**Figure 3.** The temporomandibular joint region of a 3-week adult experimental animal. Lower power view of the overall joint morphology (A). Higher power view of the mandibular condyle. Little change in morphology is observed in either view, except for some soft-tissue thickening anterior to the postglenoid spine (B).

	1	7		
	$3 \ wk \ (n = 6)$	$6 \ wk \ (n = 10)$	$12 \ wk \ (n = 6)$	$24 \ wk \ (n = 6)$
Posterior articular cartilage	+++	NS	+++	+++
Posterosuperior articular cartilage	+++	+++	+++	+ + +
Superior articular cartilage	NS	NS	NS	+
Posterior condular cartilage	+ + +	+++	+++	+++
Posterosuperior condylar cartilage	+++	+ + +	+++	+ + +

**Table 1.** Adult Control Versus Adult Experimental (t test)

Abbreviations: +, P < .05; ++, P < .01; +++, P < .001, NS, not significant; n, number of temporal mandibular joints (includes right and left joints).

+++

++

zone was the only area to continue to exhibit statistically significant hyperplasia over controls (Table 1). The articular tissue of the 12-week (Fig 5) and 24-week (Fig 6) animals responded somewhat similarly relative to the controls, in that a slight increase in thickness was recorded in both the posterior and posterosuperior regions over what had occurred previously (Fig 2, Table 1). The superior articular connective tissues, which had remained relatively stable throughout the experimental period, finally showed a minor but statistically significant (P < .05) width increase at the 24th week (Table 1).

#### **Bony Cap**

Superior condylar cartilage

All adult control condyles had what can be termed a bony cap,<sup>37</sup> in that there was a closing off of the cartilage layer from the underlying medullary spaces by a coalescence of bony trabeculae and, in many instances, by a compact layer of what appeared to be lamellar bone (Fig 1). The presence of the bony cap provided a distinct separation between the articular and condylar cartilage and the underlying medullary spaces. Relatively few invaginations occurred at the cartilage-bone interface, an observation in sharp contrast to the zone of hypertrophying and degenerating chondrocytes and the deposition of new bone next to remnants of calcified cartilage matrix observed in young growing Rhesus monkeys.<sup>15,43-45</sup> Remnants of calcified cartilage matrix could be distinguished in the condyles of almost all adult animals, but the number of occurrences was reduced significantly in comparison to juvenile controls. In the experimental animals, the bony cap persisted, with no significant differences between control and experimental groups noted (Tables 3 and 4).

+++

+++

#### **Ossified Cartilage**

Ossified cartilage or calcified cartilage matrix is the last morphologic stage of condylar cartilage before it ossifies into trabecular bone. The presence of calcified cartilage matrix within the condyle can be considered a sign of active bone formation. Only 2 control and one 12-week experimental condyle showed a significant amount of ossified cartilage. Overall, there still were no statistically significant differences between the control and any of the experimental groups (Tables 3 and 4).

#### **Postglenoid Spine**

The anterior and posterior surfaces of the postglenoid spine typically are quiescent in adult control animals, as is shown in Figure 7A. By 3 weeks, some indications of a thickening of the soft tissue immediately in front of the anterior aspect of the postglenoid spine (Fig 7B). At 12 weeks, areas of new bone deposition along the anterior border of the postglenoid spine could be observed (Fig 7C). Overall, significant bone deposition along the anterior surface was observed only in the 6- and 12-week experimental groups; interestingly, increased bone resorption along the same surface was noted as well at 6 weeks, but at no other experimental interval (Tables 3 and 4).

Table 2. Least Squares Regression Analysis (3 Weeks, 6 Weeks, 12 Weeks, and 24 Weeks.)

	Posterior	Post Superior	Superior	Posterior	Post Superior	Superior
	Articular	Articular	Articular	Condylar	Condylar	Condylar
	Cartilage	Cartilage	Cartilage	Cartilage	Cartilage	Cartilage
Adult experiment	+++	+++	+	+	++	+

Abbreviations: +, P < .05; ++, P < .-1; +++, P < .001; NS, not significant.



**Figure 4.** The temporomandibular joint region of a 6-week experimental animal. Lower power (A). Higher power of the mandibular condyle. Some slight cartilage proliferation is observed in the region of the condylar cartilage. Artifact is present in the retrodiscal tissue region (B).

#### Posterior Border of the Ramus

The posterior border of the mandibular ramus was examined for both resorption and apposition. No animals in the control or experimental groups demonstrated significant areas bone deposition or resorption (Tables 3 and 4).

# Discussion

As mentioned at the beginning of this article, one of the more recent recommendations concerning the orthopedic treatment of Class II malocclusion is that of Pancherz and coworkers<sup>3,7,8</sup> who have advocated the use of the Herbst



**Figure 5.** The temporomandibular joint regions of two 12-week experimental animals. Lower power views (A and C). Higher power views. Increased proliferation of the condylar cartilage can be observed in all views (B and D). Deposition of new bone can be observed along the anterior border of the postglenoid spine in C. This animal unintentionally had the largest amount of bite advancement (6 mm).



**Figure 6.** The temporomandibular joint region of a 24-week experimental animal. Lower power view of the temporomandibular joint region that included only the mandibular condyle, articular disk, and retrodiscal tissue (A). Higher power view of the mandibular condyle. A distinct cellular layer of condylar cartilage is present (B).

appliance in young adults. These investigators have based their recommendations on a number of experimental and clinical observations, including the presence of zones of unmineralized growth cartilage and undifferentiated mesenchymal cells in the adult mandibular condyle, as well as the favorable responses clinically in young adult patients after condylar fracture ther-

Table 3. Adult Control and Experimental data Indicating the Presence or Absence of Certain Histological
Characteristics for the Anatomic Areas Listed

	Control		3-wk Experiment		6-wk Experiment		12-wk Experiment		24-wk Experiment	
Anatomical Areas	n	%	n	%	n	%	n	%	n	%
Postglenoid spine-posterior										
surface resorption										
0-12	0	100	6	100	9	100	4	100	5	100
2-3	0	0	0	0	0	0	0	0	0	0
Postglenoid spine-posterior										
0-1	20	100	6	100	9	100	4	100	6	100
2-3	0	0	0	0	0	0	0	0	0	0
Postglenoid spine-anterior surface resorption										
0-1	16	89	5	83	3	38	5	100	3	60
2-3	2	11	1	17	5	62	0	0	2	40
Postglenoid spine–anterior surface reposition										
0-1	20	100	6	100	7	<b>78</b>	3	60	6	100
2-3	0	0	0	0	2	22	2	40	0	0
Presence of bony cap-condyle										
Yes	18	90	6	100	9	90	4	100	6	100
No	2	10	0	0	1	10	0	0	0	0
Ossified cartilage-condyle										
0-1	18	90	6	100	9	100	2	67	6	100
2-3	2	10	0	0	0	0	1	33	0	0
Posterior border of ramus– resorption	-	10								
0-1	20	100	6	100	9	100	5	100	6	100
2-3	0	0	0	0	0	0	0	0	0	0
Posterior border of ramus-	-	-								
apposition	90	100	6	100	0	100	5	100	6	100
0-1	20	100	0	100	9	100	5	100	0	100
2–3	U	U	U	U	U	U	U	U	v	0

Note. Two or 3 slides were evaluated for each joint area and judged collectively to be either in the 0-1 or 2-3 category. If they were judged to be between the 2 categories, they were omitted from the above data compilation and chi-square analysis. Abbreviations: n, number of temporal mandibular joints for each category (includes right and left); 0-1, none-minimal; 2-3 moderate-extensive.

	Chi-Squa	2×4 Chi-square All 4 Experimental Groups			
Anatomical Areas	3-wk Experiment	6-wk Experiment	12-wk Experiment	24-wk Experiment	Compared Among Themselves
Post glenoid spine-posterior surface resorption	NA	NA	NA	NA	NA
-	NS	NS	NS	NS	NS
Post glenoid spint-posterior surface apposition	NA	NA	NA	NA	NA
	NS	NS	NS	NS	NS
Post glenoid spine-anterior surface resorption	NS	++	NS	NS	NS
Post glenoid spine-anterior surface apposition	NA	+	++	NA	NA
	NS			NS	NS
Presence of bony cap-condyle	NS	NS	NS	NS	NS
Ossified cartilage-condyle	NS	NS	NS	NS	NS
Post border of ramus	NA	NA	NA	NA	NA
Resorption	NS	NS	NS	NS	NS
Post. border of ramus	NA	NA	NA	NA	NA
Apposition	NS	NS	NS	NS	NS

Table 4. Chi-Square Test for Statistical Significance for Individual Anatomic Areas in Adult Animals

Abbreviations: n, number of temporal mandibular joints for each category (includes right and left); +, P < .05; ++, P < .01; +++, P < .001; NS, not significant; NA chi-square not appropriate to calculate because of excessive zeros in the 2 × 2 configuration.

apy, corrective jaw surgery, and mandibular repositioning in disk displacement therapy. The recommendation of Pancherz and coworkers<sup>3.7.8</sup> obviously raises the issue of the potential for clinically significant condylar adaptations in young adult patients. This question can be addressed by both experimental and clinical studies.



**Figure 7.** Postglenoid spine of a control adult Rhesus monkey. Neither the anterior (right) nor posterior (left) surfaces of the spine show evidence of bone deposition or resorption (A). Postglenoid spine of a 3-week experimental animal. Note the thickening of the soft tissue anteriorly (B). Deposition of new bone is occurring along the anterior aspect of the postglenoid spine; the posterior border appears quiescent (C).

#### **Experimental Investigations**

The current study considered the structural adaptations occurring in the temporomandibular joint regions of adult female Rhesus monkeys that had worn a specially designed acrylic splint Herbst appliance for variable time periods (ie, 3-24 weeks). In many respects, the present investigation is similar to the adult functional protrusion study conducted previously by the Michigan group in which cast Ticonium (Ticonium Co, Albany, NY) splints were used to produce a forward position of the lower jaw.37 In both studies, considerable variation was observed in the temporomandibular joint region of those animals used as controls. Some animals had easily identifiable areas of condylar cartilage that could be differentiated into prechondroblastic and chondroblastic zones. In other control animals, the condylar cartilage underlying the articular tissue either was reduced substantially in thickness or absent altogether. The outer condylar layers in these animals looked more like dense irregular connective tissue or fibrocartilage rather than the type of condylar cartilage typically seen in juveniles.15,42-45

The differences in adaptive potential within the temporomandibular joint appear to be age related, with the mandibular condyle gradually losing the capability of adapting as the individual matures. A simple comparison of the thickness of the condylar cartilage in adults controls used in the current study (104-144  $\mu$ m) to the controls used in the companion study of Herbst treatment in juvenile Rhesus monkeys<sup>43</sup> (248-312  $\mu$ m) may show that the potential for adaptation in adults is reduced in comparison to younger animals. Further, Hinton and Mc-Namara,<sup>38</sup> when evaluating the maturational level of the animals used in the original adult functional protrusion study,37 concluded that when the monkeys were ranked by age based on dental attrition data the younger animals tended to have condylar cartilage with evident hypertrophy and hyperplasia, whereas older adult animals tended to have much less defined areas of condylar cartilage. These observations support the view that although the adaptive potential of the temporomandibular joint may diminish with age, the ability to adapt to altered occlusal function still may persist in some younger adult animals.

Both the current study and the original adult functional protrusion study<sup>37</sup> support this concept, in that most of the temporomandibular joints examined showed evidence that structural adaptations had occurred after an alteration in occlusal function. For example, in both studies, an increase in the number of cells in the prechondroblastic-chondroblastic layers was noted as was deposition of new bone at the cartilagebone interface. The precise nature of the appliance worn (ie, acrylic splint Herbst vs cast ticonium splint) probably made little difference in the nature of the tissue response with the temporomandibular joints because the result of the intervention was a forward repositioning of the mandible in both instances.

The current study of Herbst appliance therapy in adult Rhesus monkeys also can be compared with the companion study of the Herbst appliance in juvenile Rhesus monkeys.43 Although not as pronounced, the response of the adult animals to the Herbst appliance was qualitatively similar to the response of the juvenile monkeys to the same type of appliance. It should be noted that the magnitude of response in the adult monkeys, however, was reduced. For instance, in the juvenile study,43 the average thickness of the posterior region of the condylar cartilage in the controls was 272  $\mu$ m, whereas the maximum thickness of the same region occurred in the experimental animals at 3 weeks after appliance placement (512  $\mu$ m). By 24 weeks, the thickness of the posterior condylar cartilage was 336  $\mu$ m. In contrast, the thickness of the same region in the adult controls was 104  $\mu$ m. During the experimental period, there was a gradual increase in thickness of the posterior condylar cartilage from 177  $\mu$ m at 3 weeks, 227  $\mu$ m at 6 weeks, 246  $\mu$ m at 12 weeks, and 262  $\mu$ m at 24 weeks. In other words, the condylar cartilage of the juvenile monkeys responded immediately (within 3 weeks) to the change in occlusal function, then gradually decreased in thickness with time. The condylar cartilage in the adult animals diminished in thickness before treatment compared with the juveniles and responded more gradually to the change in occlusal function-reaching a maximum thickness at the end of the 24-week experimental period. Similar differences in maturational levels have been observed when adult monkeys treated with a functional protrusive appliance37 were compared with juveniles wearing the same type of cast device.<sup>31</sup>

A basic assumption underlying any discussion of orthopedic correction of Class II malocclusion is that ultimately the length of the mandible will be increased. The assumption is made that the increased proliferation of the condylar cartilage will be followed by increased bone deposition at the cartilage-bone interface. This supposition has been supported by a serial cephalometric study that evaluated long-term mandibular adaptations to induced protrusive function.<sup>32</sup> At the end of the 144-week experimental period, the mandibles of the treated animals were 5 to 6 mm longer than those of the control animals. The results of this study indicate that at least in growing animals, new bone formation follows experimentally produced condylar cartilage hypertrophy; similar findings have been observed in rats after induced protrusive function.46 Related studies in adult animals have not been published.

The discussion thus far has focused on the response of the mandibular condyle to changes in occlusal function. Another clinically relevant area of adaptation is within the glenoid fossa. The first investigator to suggest this type of adaptation was Breitner,<sup>23,24,47</sup> who noted significant adaptive changes in the temporal bone after functional protrusion. He concluded that "a mesial migration of the glenoid fossa" had occurred. Similar findings were reported by Häupl and Psansky,<sup>25</sup> but other investigators<sup>27,48,49</sup> have not observed evidence of significant forward migration of the glenoid fossa.

Woodside and coworkers<sup>42</sup> have noted changes in the temporal bone after Herbst treatment in 7 Cynomolgus monkeys. Five of the animals wore Herbst appliances for 6 to 13 weeks; 2 additional animals wore inactivated appliances as sham controls. The bonded appliances were activated 2 mm initially and then were reactivated every 2 weeks for an additional 1 to 2 mm, with a total activation of 7 to 10 mm. One of the primary findings noted by Woodside and coworkers<sup>42</sup> was a progressive anterior remodeling of the glenoid fossa produced by continuous and progressive mandibular protrusion, thus leading to an anterior repositioning of the mandible.

The amount of bite advancement may be a critical issue with regard to inducing changes within the glenoid fossa, including the postglenoid spine in monkeys. In the current study, the appliances were constructed so that the mandibles were advanced 3 to 4 mm. Each animal was radiographed after appliance insertion, and the actual amount of advancement was 3.3 mm, not including 1 animal whose mandible was advanced 6 mm inadvertently. The postglenoid spines of the adult control animals tended to be quiescent, with little deposition or resorption noted. Increased bone deposition was noted only in some of the 6- and 12-week experimental animals. Interestingly, the animal whose mandible was advanced 6 mm showed the most dramatic increase in bone deposition along the anterior aspect of the post glenoid spine (Fig 7C). It may be that an aggressive advancement of the mandible may produce not only condylar adaptations but also clinically relevant changes within the glenoid fossa.

#### **Clinical Investigations**

The results of this experimental investigation of adult Rhesus monkeys in general are in agreement with those in young adult Class II malocclusion subjects treated with the Herbst appliance.<sup>7</sup> In the Herbst patients, magnetic resonance images (MRIs) were taken before placement of the appliance, 6 to 12 weeks after appliance placement, and after treatment after appliance removal. In the 14 adult subjects analyzed, signs of condylar remodeling were seen at the posterior border after 6 to 12 weeks of Herbst treatment. This finding was noted in 26 of the 28 condyles analyzed. Bilateral remodeling of the mandibular ramus could be detected in 2 subjects. Signs of glenoid fossa remodeling at the anterior surface of the postglenoid spine were noted in 22 joints.

The increase in MRI signal intensity on the posterosuperior aspect of the condyles found in the MRIs of the young adult Herbst patients at 6 to 12 weeks of treatment presumably would be the result of reactivation of the cells in the prechondroblastic zone, thus representing an area of active condylar growth. This picture represents the histologically proven hyperplasia of the prechondroblastic-chondroblastic area in monkeys. Furthermore, the changes in MRI signal of the patients treated with the Herbst appliance correspond in time to the histological changes observes in the experimental animals.

MRI signs of ramus remodeling were seen in only 2 of the 14 adult Herbst subjects; distinct remodeling along the posterior border of the ramus was not noted in any of the experimental or control animals. In some respects, these findings in 2 different species, although in agreement, are surprising. Logically some increased bone deposition along the posterior border of the ramus might be expected, especially with increased growth at the mandibular condyle. Because the prechondroblastic cells in the condyle are very similar to the preosteoblasts of the periosteum of the mandible,30 they should react in a similar way to mechanical stimuli.<sup>31</sup> Such a response along the posterior border of the ramus, however, was not evident in the experimental animals.

Fossa remodeling as visualized by MRI in 22 of the 28 temporomandibular joints of the young adult Herbst subjects occurred at a later treatment stage than condylar remodeling. A similar delay in temporomandibular bone response was observed histologically in the Herbst monkeys. Furthermore, fossa adaptations in the Herbst patients, as seen in the MRIs, seemed less intensive than in some of the Herbst monkeys, which may be because of the relative size of the postglenoid spine in the 2 species. The human postglenoid spine is reduced in size in comparison to that of the monkeys.<sup>50</sup>

## **Summary and Conclusions**

The purpose of this study was to evaluate histologically the mandibular condyle, glenoid fossa, and the posterior border of the ramus in adult female Rhesus monkeys whose mandibles had been positioned forward with a Herbst appliance. Acrylic splint Herbst appliances were bonded to the maxillary and mandibular dental arches of 14 female adult animals. The animals were terminated at 3-,6-,12-, and 24-week intervals after appliance placement. Seven female adult Rhesus monkeys served as controls. The temporomandibular joint regions were removed en bloc and were prepared for qualitative and quantitative histological analysis.

The results of this study indicate that structural adaptations occurred in most of the joints removed from the experimental animals. The following observations were noted.

- 1. No evidence of pathology was noted in any of the control or experimental temporomandibular joints examined.
- 2. Increased proliferation of the condylar cartilage was noted in the experimental animals. The thickness of the cartilage increased as the study progressed.
- 3. Some thickening occurred in the articular tissue covering the mandibular condyle, particularly at 12 and 24 weeks after appliance placement.
- 4. Minimal adaptations were observed along the anterior surface of the postglenoid spine, particularly at 6 and 12 weeks.
- 5. No evidence of bony apposition or resorption on the posterior border of the mandibular ramus was noted.

The current study did not consider another component of Class II correction, that being the role of dentoalveolar compensation. Herbst appliance therapy is known to produce roughly equal skeletal and dentoalveolar adaptations in adolescent patients.<sup>51,52</sup> Recent data on young adult Herbst patients indicates that the skeletal contributions to Class II correction may be closer to 25%.<sup>13</sup>

The result of any study in animals, even in nonhuman primates, obviously cannot be applied directly to human functional orthopedic treatment. Because the tissue types and the morphology of the TMJ generally are similar between monkey and man, however, the findings of the present study may lead to a better understanding of the changes occurring within the mandibular condyle and glenoid fossa when the Herbst appliance is used clinically in young adult patients.

## Acknowledgments

The authors wish to thank Dr Barbara Nesbitt Emerick for her invaluable technical support during the experimental phase of this project.

#### References

- McNamara JA Jr, Kelly KA. Treatment timing: Orthodontics in four dimensions. Ann Arbor, MI: Monograph 39, Craniofacial Growth Series, Department of Orthodontics and Pediatric Dentistry and Center for Human Growth and Development, the University of Michigan, Ann Arbor, 2002.
- 2. Wieslander L. Intensive treatment of severe Class II mal-

occlusions with a headgear-Herbst appliance in the early mixed dentition. Am J Orthod 1984;86:1-13.

- 3. Pancherz H, von Bremen J. Efficiency of Class II, division 1 therapy in relation to treatment timing and modality. In: McNamara JA Jr, Kelly KA, eds. Treatment timing: Orthodontics in four dimensions. Monograph 39, Craniofacial Growth Series. Ann Arbor, MI: Department of Orthodontics and Pediatric Dentistry and Center for Human Growth and Development, The University of Michigan, 2002.
- McNamara JA Jr, Bookstein FL, Shaughnessy TG. Skeletal and dental changes following functional regulator therapy on Class II patients. Am J Orthod 1985;88:91-110.
- Baccetti T, Franchi L, Toth LR, et al. Treatment timing for twin block therapy. Am J Orthod Dentofac Orthop 2000;118:159-170.
- 6. Baccetti T, Franchi L. Maximizing esthetic and functional changes in Class II treatment by appropriate treatment timing. In: McNamara JA Jr, Kelly KA, eds. Frontiers of dental and facial esthetics. Monograph 38, Craniofacial Growth Series. Ann Arbor, MI: Department of Orthodontics and Pediatric Dentistry and Center for Human Growth and Development, The University of Michigan, 2001.
- Ruf S, Pancherz H. Temporomandibular joint remodeling in adolescents and young adults during Herbst treatment: A prospective longitudinal magnetic resonance imaging and cephalometric radiographic investigation. Am J Orthod Dentofac Orthop 1999;115:607-618.
- 8. Ruf S, Pancherz H. When is the ideal period for Herbst therapy-carly or late? Semin Orthod 2003;9:47-56.
- Pancherz H. Dentofacial orthopedics or orthognathic surgery: Is it a matter of age? Am J Orthod Dentofac Orthop 2000;117:571-574.
- Pancherz H, von Bremen J. Efficacy of early and late Class II treatment. In: McNamara JA, Jr, Kelly KA, eds. Treatment timing: Orthodontics in four dimensions. Monograph 39, Craniofacial Growth Series. Ann Arbor, MI: Department of Orthodontics and Pediatric Dentistry and Center for Human Growth and Development, The University of Michigan, Ann Arbor, 2002.
- Ruf S, Pancherz H. Dentoskeletal effects and facial profile changes in young adults treated with the Herbst appliance. Angle Orthod 1999;69:239-246.
- Ruf S, Pancherz H. Temporomandibular joint growth adaptation in Herbst treatment: a prospective magnetic resonance imaging and cephalometric roentgenographic study. Eur J Orthod 1998;20:375-388.
- Pancherz H, Ruf S. The Herbst appliance: Researchbased updated clinical possibilities. World J Orthod 2000;1:17-31.
- Blackwood HJ. Adaptive changes in the mandibular joints with function. Dent Clin North Am 1966;10:539-566.
- Carlson DS, McNamara JA Jr, Jaul DH. Histological analysis of the growth of the mandibular condyle in the Rhesus monkey (Macaca mulatta). Am J Anat 1978;151: 103-117.
- Jacobsen PU, Lund K. Unilateral overgrowth and remodeling processes after fracture of the mandibular condyle. Scand J Dent Res 1972;80:68-74.

- Edlund J, Hansson T, Willmar K. Sagittal splitting of the mandibular ramus. Scand J Plastic Reconstr Surg 1979; 13:437-443.
- Hollender L, Ridell A. Radiography of the temporomandibular joint after oblique sliding ostcotomy of the mandibular rami. Scand J Dent Res 1974;82:466-469.
- Hellsing G, Hollender LG, Carlsson GE, et al. Temporomandibular joint adaptation to mandibular repositioning in adult occlusal rehabilitation. Cranio 1985;3:273-279.
- Sato S, Fugii T, Uetani M, et al. Anterior mandibular repositioning in a patient with temporomandibular disorders: A clinical and tomographic follow-up case report. J Craniomand Pract 1997;15:84-88.
- Westesson PL, Lundh H. Temporomandibular joint disk displacement: Arthrographic and tomographic follow-up after 6 months treatment with disk-repositioning onlays. Oral Surg Oral Med Oral Pathol 1988;66:271-278.
- McNamara JA Jr. Dentofacial adaptations in adult patients following functional regulator therapy. Am J Orthod 1984;85:57-71.
- Breitner C. Experimental change of the mesio-distal relations of the upper and lower dental arches. Angle Orthod 1933;3:67-76.
- Breitner C. The influence of moving deciduous teeth on permanent successors. Am J Orthod 1940;26:1152-1177.
- Häupl K, Psansky R. Experimentelle Untersuchungen über Gelenktransformation bei Verwendung der Methoden der Funktionskieferorthopädie. Deutsche Zahn Mund Kieferheilkd 1939;6:439-448.
- Derichsweiler H. Experimentelle Tieruntersuchungen über Veränderungen des Kiefergelenkes bei Bisslageveränderung. Fortschr Kieferorthop 1958;19:30-44.
- Baume LJ, Derichsweiler H. Is the condylar growth center responsive to orthodontic therapy? An experimental study in *Macaca mulatta*. Oral Surg Oral Med Oral Path 1961;14:347-362.
- Stöckli PW, Willert HG. Tissue reactions in the temporomandibular joint resulting from anterior displacement of the mandible in the monkey. Am J Orthod 1971;60: 142-155.
- McNamara JA Jr. Neuromuscular and skeletal adaptations to altered function in the orofacial region. Am J Orthod 1973;64:578-606.
- 30. Petrovic A, Stutzmann JJ, Oudet C. Control process in the postnatal growth of the condylar cartilage. In: Mc-Namara JA Jr, ed. Determinants of mandibular form and growth. Monograph 4, Craniofacial Growth Series. Ann Arbor, MI: Center for Human Growth and Development, The University of Michigan, 1975.
- McNamara JA Jr, Carlson DS. Quantitative analysis of temporomandibular joint adaptations to protrusive function. Am J Orthod 1979;76:593-611.
- McNamara JA Jr, Bryan FA. Long-term mandibular adaptations to protrusive function: an experimental study in *Macaca mulatta*. Am J Orthod Dentofacial Orthop 1987;92:98-108.
- Hiniker J, Ramfjord S. Anterior displacement of the mandible in adult rhesus monkeys. J Pros Dent 1966;16: 503-512.
- 34. Ramfjord S, Enlow R. Anterior displacement of the man-

dible in adult rhesus monkeys: Long term observations. J Pros Dent 1971;26:517-531.

- 35. Ramfjord SP, Walden JM, Enlow RD. Unilateral function and the temporomandibular joint in rhesus monkeys. Oral Surg 1971;32:236-247.
- Ramfjord SP, Ash MM. Occlusion. Philadelphia, PA: Saunders, 1971.
- McNamara JA Jr, Hinton RJ, Hoffman DL. Histologic analysis of temporomandibular joint adaptation to protrusive function in young adult rhesus monkeys (*Macaca mulatta*). Am J Orthod 1982;82:288-298.
- Hinton RJ, McNamara JA Jr. Effect of age on the adaptive response of the adult temporomandibular joint. A study of induced protrusion in Macaca mulatta. Angle Orthod 1984;54:154-162.
- Miles AEW. Assessment of the ages of a population of Anglo-Saxons from their dentitions. Proc Roy Soc Med 1962;55:881-886.
- Helm S, Prydso U. Assessment of age-at-death from mandibular molar attrition in medieval Danes. Scand J Dent Res 1979;87:79-90.
- Woodside DG, Altuna G, Harvold E, et al. Primate experiments in malocclusion and bone induction. Am J Orthod 1983;83:460-468.
- Woodside DG, Metaxas A, Altuna G. The influence of functional appliance therapy on glenoid fossa remodeling. Am J Orthod Dentofacial Orthop 1987;92:181-198.
- Peterson JE Jr, McNamara JAJ. Temporomandibular joint adaptations associated with Herbst appliance treatment in juvenile rhesus monkeys (*Macaca mulatta*). Semin Orthod 2003 (in press).

- 44. Zimmermann HI. The normal growth and remodeling of the temporomandibular joint of *Macaca mulatta* [master's thesis]. Seattle, WA: Department of Orthodontics, University of Washington, 1971.
- 45. McNamara JA Jr. Neuromuscular and skeletal adaptations to altered orofacial function. Monograph 1, Craniofacial Growth Series. Ann Arbor, MI: Center for Human Growth and Development, The University of Michigan, 1972.
- 46. Petrovic A, Stutzmann J, Gasson N. The final length of the mandible: Is it genetically determined? In: Carlson DS, ed. Craniofacial biology. Monograph 10, Craniofacial Growth Series. Ann Arbor, MI: Center for Human Growth and Development, The University of Michigan, 1981.
- Breitner C. Experimentelle Veränderung der mesiodistalen Beziehungen der oberen und unteren Zahnreihen. Ztschr f Stomatol 1930;28:343-356.
- Hoffer O, Colico GL. Le modificazioni dell'A.T.M. conseguenti a spostamento mesiale della mandibola. Rass Int Stomatol Prat 1958;9 (suppl 4):27-40.
- Lieb G. Application of the activator in rhesus monkey. Trans Eur Orthod Soc 1968;44:141-147.
- Hinton R, Carlson DS. Histologic changes in the articular eminence and mandibular fossa during growth of the rhesus monkey. Am J Anat 1983;166:99-116.
- Pancherz H. The mechanism of Class II correction in Herbst appliance treatment. A cephalometric investigation. Am J Orthod 1982;82:104-113.
- Pancherz H. The Herbst appliance—Its biologic effects and clinical use. Am J Orthod 1985;87:1-20.