Histologic Evaluation of Tissue Response to Hydroxylapatite Implanted on Human Mandibles

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Histologic Evaluation of Tissue Response to Hydroxylapatite Implanted on Human Mandibles

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The tissue response to hydroxylapatite implants was examined histologically in samples taken from four patients three to six months after the material had been used to augment deficient mandibular alveolar ridges. Minimal inflammation was found, but the implants had not induced new bone formation and were instead surrounded by a fibrous connective tissue scar.

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Introduction.

Hydroxylapatite, a calcium phosphate ceramic, has been intensively investigated as a bone substitute (Jarcho, 1981; Larsen *et al.*, 1983; Kent *et al.*,1983; Rothstein *et al.*, 1984a,b). Early studies in animals demonstrated that bone bonds directly to hydroxylapatite without intervening fibrous tissue (Boyne and Szutz, 1981; Osborn and Newesely, 1982; Piecuch *et al.*, 1983; Chang *et al.*, 1983). Examination of experimental defects in dog femurs filled with particulate dense hydroxylapatite revealed an intimate contact of the bone with the ceramic implant at the light and electron microscopic levels (Jarcho, 1981). When porous hydroxylapatite manufactured from coral was placed on dog mandibles, it formed a bond with bone without intervening soft tissue (Piecuch *et al.*, 1983).

These promising results in animals led to the clinical testing of particulate, dense, non-resorbable hydroxylapatite in humans. This material was successfully used to augment deficient alveolar ridges (Kent *et al.*, 1983; Larsen *et al.*, 1983; Rothstein *et al.*, 1984a,b), fill periodontal defects (Rabalais *et al.*, 1981), and maintain the alveolar ridge after tooth extraction (Denissen and DeGroot, 1979). While these reports described the clinical results of these uses of hydroxylapatite in humans, the microscopic response to hydroxylapatite has only been described for its use in filling periodontal defects, and in this situation a bone-to-implant interface did not develop (Froum *et al.*, 1982; Moskow and Lubarr, 1983). Because the periodontal defect is chronically inflamed, the tissue response to hydroxylapatite placed in such an area may be different from the response to the implant used, for example, to augment the alveolar ridge. When four patients who had undergone mandibular alveolar ridge augmentation with hydroxylapatite needed a vestibuloplasty several months later, we had the unusual opportunity to examine samples of the implant microscopically. This report describes the tissue response to the hydroxylapatite obtained from these patients.

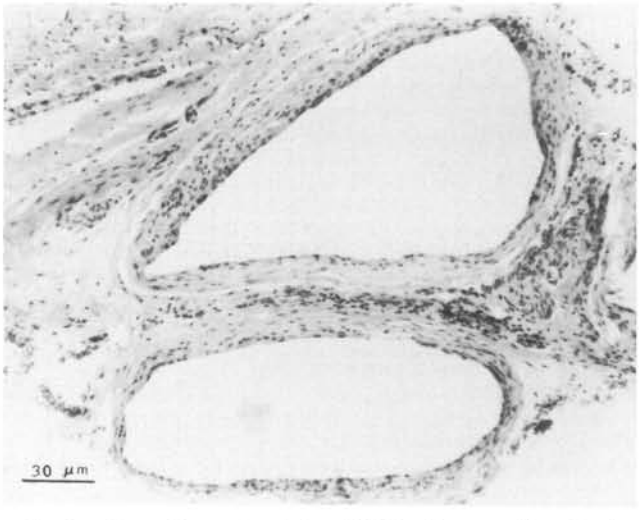

Fig. 1 — Photomicrograph of a decalcified and hematoxylin and eosin-ained sample taken from a 70-year-old patient three months after augmentation with hydroxylapatite. The white areas represent the hydroxylapatite particles which were removed during decalcification.

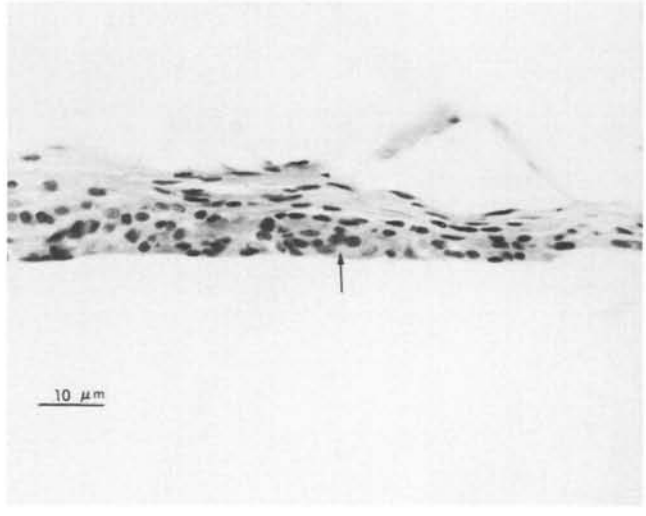

Fig. 2 — Photomicrograph of a decalcified and hematoxylin and eosin-stained sample taken from a 70-year-old patient three months after augmentation with hydroxylapatite. Arrow indicates a typical multi-nucleated giant cell. The white areas represent the hydroxylapatite particles which were removed during decalcification.

Materials and methods.

Four female patients with deficient mandibular ridges chose to undergo ridge augmentation with hydroxylapatite to improve denture retention. Two patients were 70 years old, a third patient was 55 years old, and a fourth patient was 49 years old (mean, 59 years). One patient received an implant of Calcitite 2040*, and three were given implants of Alveograf†.

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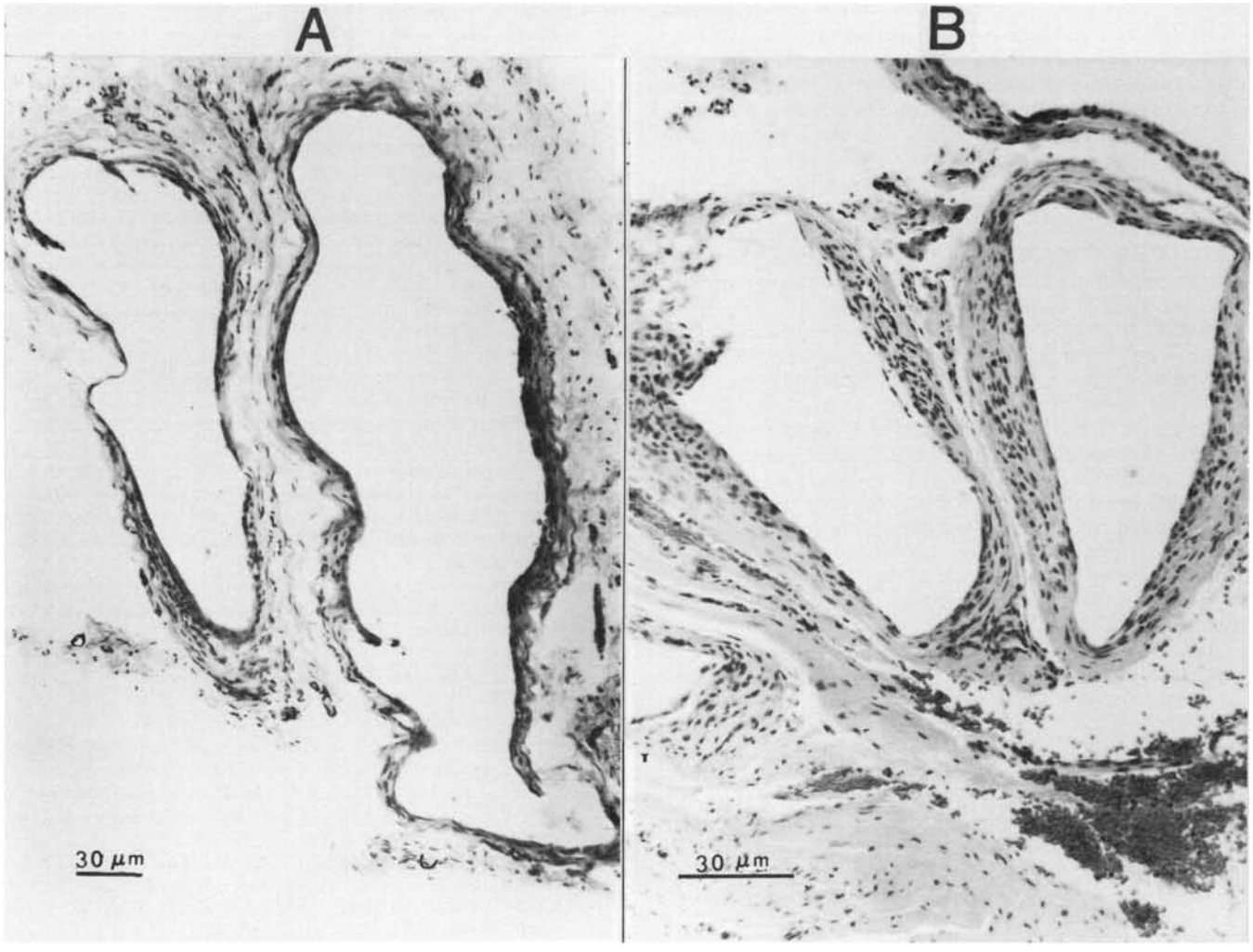

Fig. 3 — Photomicrographs of decalcified hematoxylin and eosin-stained samples. White areas represent the hydroxylapatite particles which were removed during decalcification. A. Sample of spherical hydroxylapatite particles (Calcitite 2040) taken from a 70-year-old patient six months after augmentation. B. Sample of multi-faceted hydroxylapatite particles (Alveograf) taken from a 70-year-old patient three months after augmentation.

Because the patients had inadequate vestibular depth after ridge augmentation, a vestibuloplasty was done for two patients at three months, a third patient at five months, and a fourth patient at six months (mean, 4.2 months). At the time of the vestibuloplasty, we were able to remove a 3-mm-diameter specimen of hydroxylapatite from the superior border of the implant without compromising the surgical results. The samples were fixed in formalin, decalcified, and stained with hematoxylin and eosin.

Results.

Fig. 1 shows an example of the tissue reaction that was observed in all the specimens. The hydroxylapatite was surrounded by a fibrous scar, with occasional epithelial macrophages in the area immediately adjacent to the implant. An occasional multi-nucleated giant cell was seen adjacent to the implant (Fig. 2). Although the thickness of the fibrous border surrounding the Alveograf and Calcitite 2040 was different because the hydroxylapatite particles could not be packed together the same amount for each patient, no obvious differences were seen in the inflammatory reactions to Alveograf and Calcitite 2040 (Fig. 3).

Discussion.

The samples of hydroxylapatite obtained from the patients in this study showed a very mild inflammatory response. The implants were surrounded by epithelial macrophages in a fibrous connective tissue scar, but we did not find the bone-to-implant interface observed in animals. One possible reason why bone did not surround the implant may be that, because bone migrates from the basilar bone to the superior aspect of the implant rather than from the periosteum (Chang *et al.*, 1983), bone may not have reached the superior border at the time of the biopsies. Another possibility is that because these patients were older, they may lack the osteogenic potential needed to surround the hydroxylapatite with bone.

The mild inflammatory response we observed is similar to the response to hydroxylapatite used to fill periodontal defects in humans. Froum *et al.* (1982) reported minimal inflammatory response to hydroxylapatite filling periodontal defects, and the

implants were surrounded by fibrous connective tissue but no bone. Moskow and Lubarr (1983) examined an extracted tooth with a defect in its bifurcation that had been filled with dense hydroxylapatite nine weeks before removal, and found fibrous connective tissue surrounding the implant with a few inflammatory cells and no new bone. The response we observed also resembled the response to hydroxylapatite placed in the soft tissue of animals. Dense or porous hydroxylapatite implanted into soft tissue was surrounded by fibrous tissue with minimal inflammation and no bone (Piecuch, 1982; Drobeck *et al.*, 1984; Misiek *et al.*, 1984). In all of these studies, the hydroxylapatite failed to induce bone formation, but was compatible with the tissue in both humans and animals.

Misiek *et al.* (1984) reported that inflammation resolved more slowly with multi-faceted hydroxylapatite (Alveograf) implanted in dogs than with spherical hydroxylapatite (Calcitite 2040). Even after six months, the spherical implants were associated with fewer inflammatory cells than were the multi-faceted implants. In our study, the one patient whose mandible was augmented with spherical hydroxylapatite showed no obvious difference in the inflammatory response from that of the three patients who received multi-faceted hydroxylapatite, even though the spherical implant was biopsied six months after ridge augmentation, while two of the multi-faceted implants were biopsied three months and one five months after augmentation.

This study shows that hydroxylapatite stimulates minimal inflammation and induces no bone formation when used to augment alveolar ridges in humans. Because a bone-to-implant interface does not develop, the dentures rest on a more resilient base than when placed on a bony alveolar ridge, making it more difficult to fabricate the dentures. However, even though denture fabrication is more difficult, denture retention can be clinically improved by augmentation of alveolar ridges with hydroxylapatite (Beirne and Curtis, 1985).

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