Hydroxyapatite as a bone substitute in the jaws

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Densely sintered calcium hydroxyapatite has previously been shown to be biocompatible and stable. Its possible role in jaw surgery was investigated using a clinically analogous animal model. The apatite was implanted into the mandible of twelve dogs for 12 weeks, and the healing assessed radiologically and histologically. The new bone which was deposited directly onto the surface of the implants bonded them firmly to the adjacent tissues. There was no fibrous tissue between implant and bone. This material appears to be a suitable substitute for autogenous bone when used as an inert 'space filler' in maxillo-facial surgical procedures.

Autogenous bone grafts are utilised in a variety of surgical procedures in the jaws, including augmentation of the mandible which has been resorbed excessively following extraction of the natural dentition. Since patients requiring this treatment are often elderly, the surgical intervention on the donor site often causes additional pain which is unacceptable. The use of a bone substitute benefits the patient and shortens the operating time.

Recently there have been several papers published on the chemistry, preparation, and biocompatibility of calcium phosphate ceramics, in both solid and porous forms[1-10]. Porous ceramics allow ingrowth of soft tissue and bone which enhances retention of the implant and produces a more satisfactory interface layer[11]. However, the strength of porous materials decreases exponentially with the degree of porosity[12]. In addition, porosity can lead to degradation of the implant and possible loss of its functional value[9, 10]. Thus, when the implant has to be permanent and withstand large functional forces, a more dense, solid form is indicated. This is the situation in the jaws where the implant is subject to masticatory forces. There is little information available on the radiological and histological features of bone healing around hydroxyapatite when used as a substitute for autogenous bone grafts in the maxillofacial region. Healing was evaluated in the present investigation using an animal model which simulates the clinical conditions.

MATERIALS AND METHODS

The ceramic most suitable for this application was densely sintered calcium hydroxyapatite. It was prepared in Philips Research Laboratories, Eindhoven, by sintering hydroxyapatite powder (Merck Co., Darmstadt, W. Germany) at 1200°C for 6 h to produce a dense ceramic which is 97% solid[6]. The compressive strength is 400 MN/m^2, modulus of elasticity 1.2×10^4 MN/m^2, and Vickers hardness 4500 MN/m^2.

Although the biocompatibility of this material has been studied previously[6, 8], only small specimens were implanted and they were not subjected to functional forces. In the present investigation the hydroxyapatite was used instead of autogenous bone grafts to augment the edentulous mandible in dogs.

Edentulous ridges were prepared in the mandible and maxilla of 15 month old beagle dogs by extracting the third and fourth premolars and first molar on each side of the mouth. After three months, when the tooth sockets had healed, the edentulous part of the mandible was divided horizontally on each side and the apatite interposed between the superiorly displaced block of ridge bone and the remainder of the mandible on one side *(Figures 1 and 3)*. To act as control, the other side of the mandible received an autogenous bone graft of similar size, taken from the iliac crest. The implants measured $22 \times 8 \times 5$ mm. and were stabilised by a loop of stainless steel wire passing through the basal bone and the block of ridge bone. In order to improve stability of the hydroxyapatite, grooves 0.5 mm. wide and 0.5 mm. deep were cut into their superior and inferior surfaces. A small sample of apatite measuring $10 \times 10 \times 3$ mm. was placed into a hole cut in the iliac crest to allow a comparison of the behaviour of the material in the mandible and in the more protected environment of the hip. The other side of the hip received an autogenous bone graft. The animals were observed for

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Figure 1 Hydroxyapatite used to increase the height of the edentulous jaw. The implant is interposed between the superiorly displaced block of bone and the remainder of the mandible.



Figure 2 Implant site in the jaw after surgery, showing the increase in ridge height.

twelve weeks, and healing assessed radiologically and histologically. Radiographs were taken using a standardised technique pre-operatively, immediately post-operatively, after two weeks, four weeks and every fourth week until the end of the experiment. During the first week following surgery the animals were fed on a soft diet, and thereafter a normal laboratory diet of meat and biscuits.

RESULTS

The mandibular sites healed well, the augmented ridges, both apatite and autografts being well formed and firmly fixed to the adjacent tissues. The new ridges were stable and the apatite appeared to have bonded firmly with the new bone *(Figure 2)*. Two autografts became infected and were undergoing exfoliation into the mouth. All the implant sites in the hip healed satisfactorily.

Radiographs of the mandible showed good bony healing around the apatite. Immediately after surgery a gap was present between the implant and the adjacent mandible *(Figure 3)*. However, there was rapid deposition of new bone around and onto the surface of the implant, so that by twelve weeks it had become fully incorporated within the host bone *(Figure 4)*. In addition, the superiorly repositioned mandibular ridge had become re-attached to the adjacent jaw bone. Radiologically the new bone had a normal trabecular pattern, and there was no evidence of surrounding infection or bone resorption. There was no reduction in size of the implants. Although the apatite in the iliac crest could be demonstrated clearly, it was more difficult from the radiographs to assess healing.

The autografts on the other side underwent rapid remodelling and incorporation into the host bone. Details of the radiological features of the autografts have been described previously[13].

The histological appearances of the healing process around the grafts in the mandible and iliac crest were similar. The hydroxyapatite was well accepted and rapidly incorporated into the host bone. Sections cut transversely across the mandible showed the close adaptation of the tissues to the implant *(Figure 5)*. The new bone had been deposited directly onto the surface without any intervening fibrous tissue *(Figure 6)*, and closely followed the contours of the implant. This feature is clearly demonstrated on those surfaces of the grafts into which grooves had been cut prior to surgery in order to improve their retention *(Figures 7 and 8)*. The bone which had grown into the small depressions in the implants assisted their anchorage. The surrounding bone contained healthy haematopoietic marrow with only one specimen showing some minor inflammatory cell infiltration. There was no evidence of foreign body reaction. The trabeculae of bone adjacent to the implant did not show any sign of past or present resorption. On those

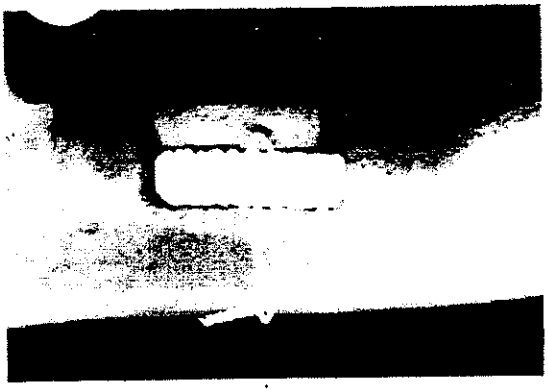


Figure 3 Radiograph of the dense hydroxyapatite implant in the jaw immediately post-operatively. A loop of stainless steel wire is used for stabilisation.

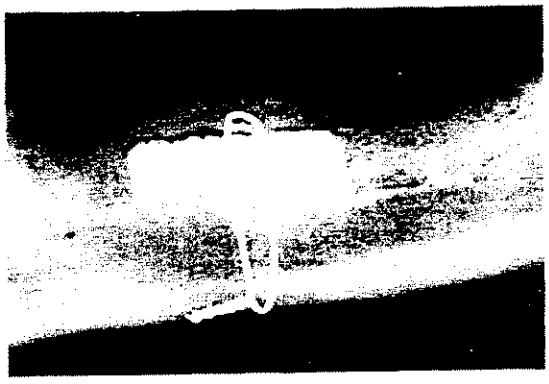


Figure 4 Radiograph of hydroxyapatite twelve weeks after implantation, showing its incorporation within the host bone.



Figure 5 Coronal section through the mandible illustrating the close adaptation of the tissues to the implant.



Figure 6 Ground section showing deposition of new bone (A) directly onto the surface of the hydroxyapatite (x150).

surfaces of the apatite which had not been in contact with bone at the time of implantation (i.e. lateral and medial in the mandible, and superior in the hip grafts) less new bone had deposited, although it was beginning to spread along these surfaces. In none of the specimens was there evidence of resorption or disintegration of the hydroxyapatite.

The autografts were rapidly incorporated into the host bone, so that by twelve weeks it was often difficult to identify the original graft trabeculae. The histological appearances have been recorded elsewhere[3].

DISCUSSION

The new bone which grew onto the surface of the hydroxyapatite implants bonded them firmly to the adjacent tissues. This confirmed previous studies when the material was implanted into dogs' femurs[1-4], and fresh extraction sockets in dogs and humans[3]. Grooves cut into the surface of the implants increased their retention and stability since the new bone was deposited directly into these surface indentations. The histological studies demonstrated the good biocompatibility of the apatite, and the absence of fibrous tissue between implant and bone.

In this investigation the apatite implants were well incorporated after twelve weeks. However, bone healing in dogs occurs about 2½ – 3 times more rapidly than in man[3]. Therefore in humans a longer healing time may be anticipated. After interpositional hydroxyapatite augmentation of the edentulous mandible, it may be advisable for the patient not to wear dentures for 6 months after surgery. However, the rate of bone healing around apatite implants in humans will have to be confirmed by clinical studies. This initial investigation has shown that bone deposition in dogs occurs less rapidly on the lateral and medial aspects of the implants. If this occurs similarly in humans, it will be important to ensure that the denture flanges do not traumatise and ulcerate the mucosa in these sites, possibly leading to infection around the exposed apatite.

The results of these preliminary animal experiments indicate that densely sintered calcium hydroxyapatite may be used as a substitute for autogenous bone in selected operations in the maxillofacial region. This material is suitable as an inert and permanent 'space filler', for example in augmentation of the atrophic mandible. A clinical trial is under way to evaluate the long term behaviour of the material in



Figure 7 Bone growth into groove on implant surface. Ground section (x150).

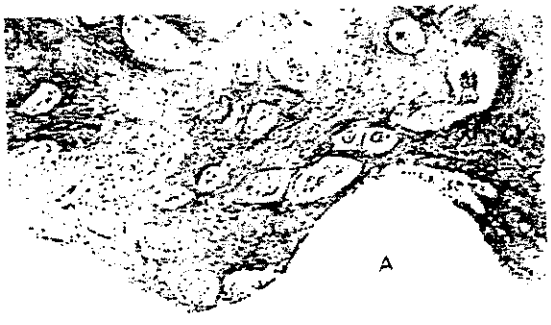


Figure 8 Decalcified section. The hydroxyapatite has been lost during processing (A). The new bone has grown into the surface grooves. H & E (x150).

this situation. Hydroxyapatite may also be of value in some types of jaw osteotomies where a graft is required to mechanically stabilise bones, for example interposed between the pterygoid plates and the posterior aspect of the maxilla when the maxilla is being surgically advanced. However, apatite is a brittle material with a high modulus of elasticity, and is unsuitable for use in situations where it will be subjected to large bending forces.

Further animal and clinical studies are in progress to assess the role of densely sintered calcium hydroxyapatite as a substitute for autogenous bone in other maxillo-facial surgical operations.

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Tricalcium phosphate (TCP), a biodegradable artificial bone substitute, was used to study the following questions: i) can TCP be vascularized; ii) do ectopically placed implants have osteoinductive capacity; and iii) does vascularization affect implant resorption?
Implants were placed in dogs in several areas: i) subcutaneous controls; ii) wrapped with latissimus dorsi muscle; iii) wrapped in omentum; iv) saphenous and thoracodorsal av pedicles threaded through implant. Prior to harvest, animals were given tetracycline and implants were harvested at 3, 6, and 9 weeks. Microfil was injected prior to sacrifice and specimens were xeroradiographed. Histology and computerized axial tomography were obtained. From this study, we conclude that 1) TCP can be vascularized; 2) the most effective method of vascularization was by an AV pedicle threaded through the implant; 3) vascularized implants did not have osteoinductive properties per se, and 4) in the time observed no difference in implant resorption was demonstrated between the test groups.

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VASCULARIZATION OF TRICALCIUM PHOSPHATE, AN ARTIFICIAL BONE SUBSTITUTE: PRELIMINARY OBSERVATIONS

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Large segmental bone defects secondary to major oncologic surgery or trauma are major clinical problems. Free bone grafts presently are an accepted treatment modality; however, they are complicated by resorption and nonunion and require a highly vascular bed for graft take. Vascularized bone grafts obviate many of these problems but donor sites are limited. In such situations an artificial bone substitute could be of practical clinical use.

Revascularization of tissue has been achieved by various methods in the experimental and clinical setting. Creation of an arteriovenous (av) pedicle has been shown to be effective in revascularizing the lunate and femoral head in avascular necrosis.[1] Moreover, an axial pattern flap has been created by placing an av pedicle beneath randomly vascularized skin.[2] Latissimus dorsi muscle with rib as an osteomyocutaneous flap has been utilized to provide circulation to the bone in dogs[3] and man.[4] This muscle wrapped around free bone grafts has, in rabbits, provided vascularization to the graft.[5] In the past 20 years, omentum has shown increasing versatility in providing a blood supply for a wide variety of reconstructive procedures.[6–9] Experimentally, it has demonstrated the ability to vascularize free bone grafts.[10,11] Using these techniques, vascularization of an artificial bone implant may be possible.

Tricalcium phosphate (TCP) is a polycrystalline ceramic ($CA_3\{PO_4\}_2$) possessing osteoconductive properties that has been used to bridge bone defects both experimentally [12–17] and clinically.[18–20] Using this material, we addressed ourselves to the following questions:

1. Can TCP be vascularized; if so, what is the most efficacious mode?
2. Does vascularized TCP in the absence of bone have osteoinductive properties?
3. Does vascularization have any effect on the rate of implant resorption?

MATERIALS AND METHODS

Animals

Seven female dogs, 17–20 kg, individually housed and given food and water ad libitum were used in the study.

Division of Plastic and Reconstructive Surgery (M.F.A., W.M.S., S.S.R., M.L.B.), and Department of Orthopedics (E.N.H.), and Department of Radiology (D.L.H.), School of Medicine, University of Pittsburgh, Pittsburgh, PA.

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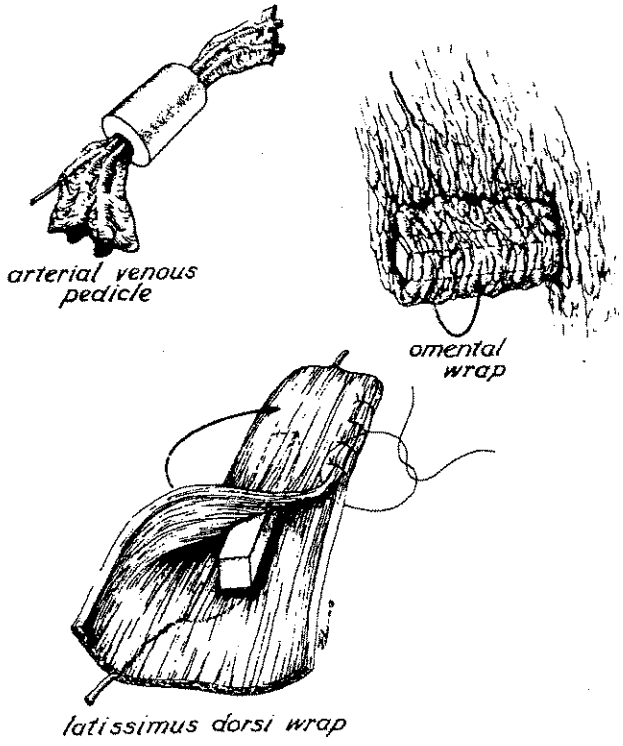


Figure 1. Modes of vascularization. Implants were wrapped in omentum and latissimus dorsi muscle as depicted above. In addition, av pedicles were threaded through the central bore.

Implants

Tricalcium phosphate implants (Miter Corp., Northington, OH) in two shapes were used: a solid 5-×-1-×-1-cm block and a 2-×-2-cm cylinder with a 0.7-cm central bore. The implants were prepared from highly purified calcium phosphate powder which was isostatistically pressed. The powder was mixed with naphalene, which evaporated during the pressing process, leaving in its wake a random pattern of interconnecting pores 100–300 μm in size throughout the implant. (The thin but dense layer of compacted ceramic on all implants was scraped under low-power dissecting microscope control to ensure adequacy of removal.)

Procedure

All animals were anesthetized with sodium pentobarbital (35 mg/kg). At the time of surgery and at 12-hour intervals, 1 gm cefamandole was administered IM for 3 days.

Thirty-one implants were placed as follows (Fig. 1):

1. TCP block placed subcutaneously (controls).
2. TCP block wrapped in omentum and placed subcutaneously.
3. TCP block wrapped in latissimus dorsi muscle.
4. TCP cylinder with the thoracodorsal av pedicle threaded through the central bore and implanted in the flank.
5. TCP cylinder with the saphenous av pedicle threaded through the central bore and implanted in the flank.

Av pedicles were created in the following manner: In both the latissimus dorsi muscle and groin, the artery and vein were isolated from the surrounding tissue gently, so as not to disturb the thin tissue investing both structures. Two 4-0 silk ties were placed distally; a cut was made between the ties and the pedicle was threaded through the central bore of the implant. Flow was presumably maintained by the adventitial tissue surrounding the main vessels.

Implants were harvested at three intervals postoperatively (3 weeks, 6 weeks, 9 weeks). All tissue was placed in 10% formalin for fixation.

EVALUATION OF VASCULAR INGROWTH

Microfil

Prior to sacrifice, the animals were again anesthetized. Microfil (Canton Bio-Medical Products, Inc., Boulder, CO) was injected into the omentum (10 cc through an omental artery), the latissimus dorsi muscle (20 cc through the thoracodorsal artery), and the saphenous artery (10 cc). The animals were then sacrificed and specimens harvested.

Xeroradiography

Specimens were imaged by a Picker Mammorex unit (32 kV, 0.5 sec, 200 mA). All specimens were radiographed within their soft tissue envelopes; in addition, in the first three groups of specimens, the implants were cut in cross section and radiographed after fixation in formalin.

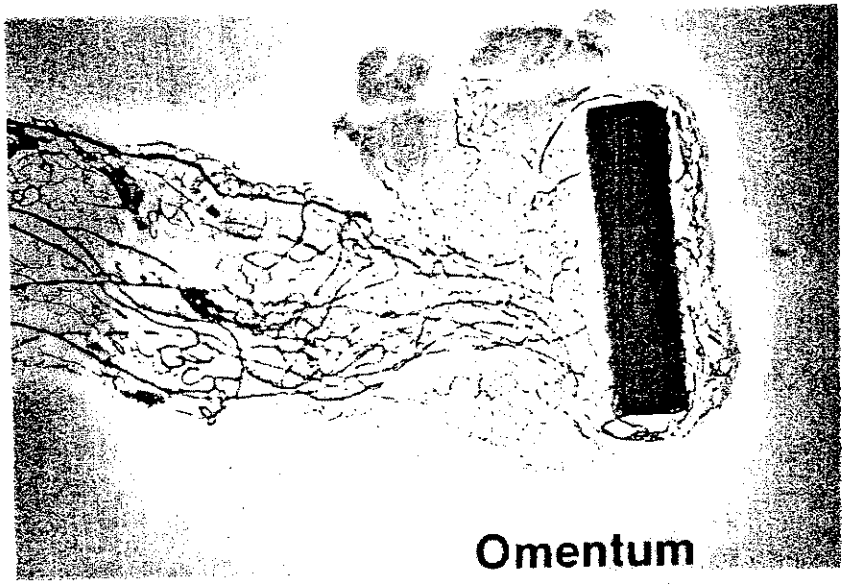
Tetracycline Labeling

Tetracycline (500 mg) was intravenously administered to all animals 4 days prior to sacrifice.

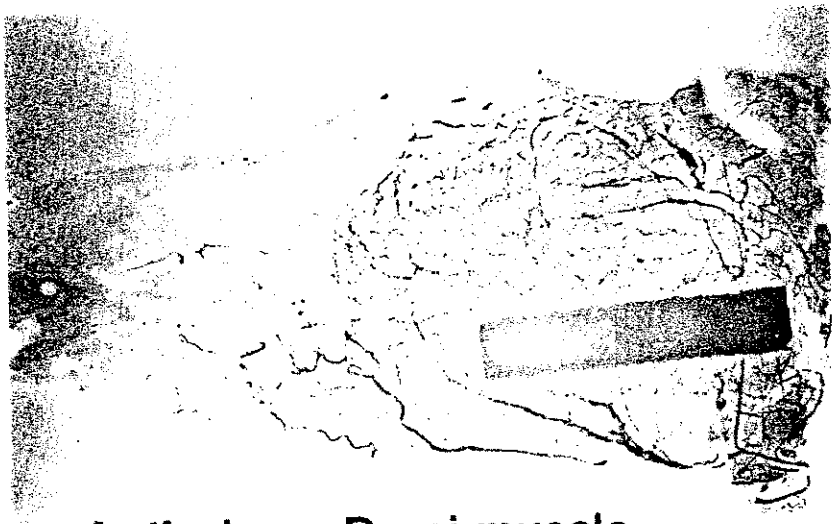
Histology

Blocks were quartered and cylinders were halved for histologic examinations. Pieces were selected at random for thick section and conventionally processed; 40-μm-thick sections were then cut transversely using a slow-speed bone saw. Thin sections were prepared by first partially decalcifying the specimens and then preparing 5-μm thin sections in the usual fashion. Unstained slides were viewed by fluorescent microscopy to detect tetracycline labeling. Hema-

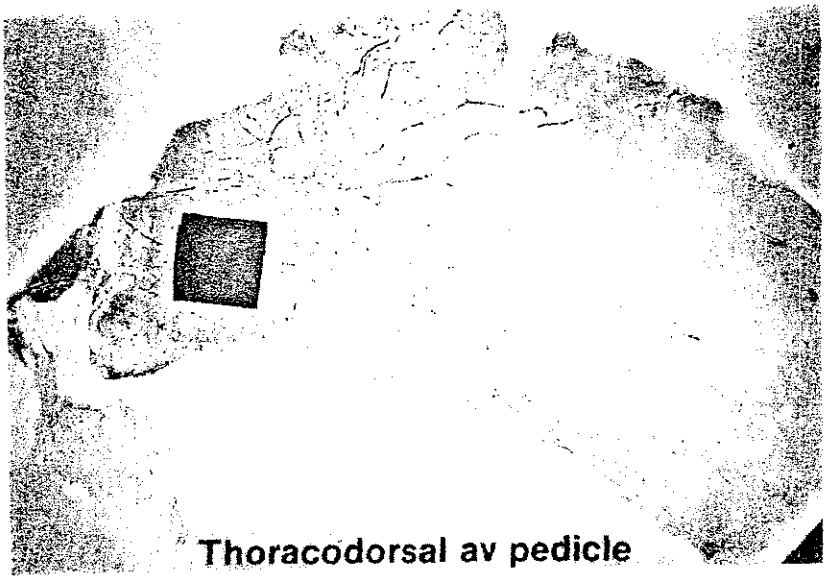
Figure 2. (top) Microfil injection of the omentum. Vessels surrounding the entire implant. (middle) Microfil injection of the thoracodorsal artery in the muscle wrap group shows rich vascularity surrounding the implant. (bottom) A typical xeroradiograph of the av pedicle groups.



Omentum



Latissimus Dorsi muscle



Thoracodorsal av pedicle

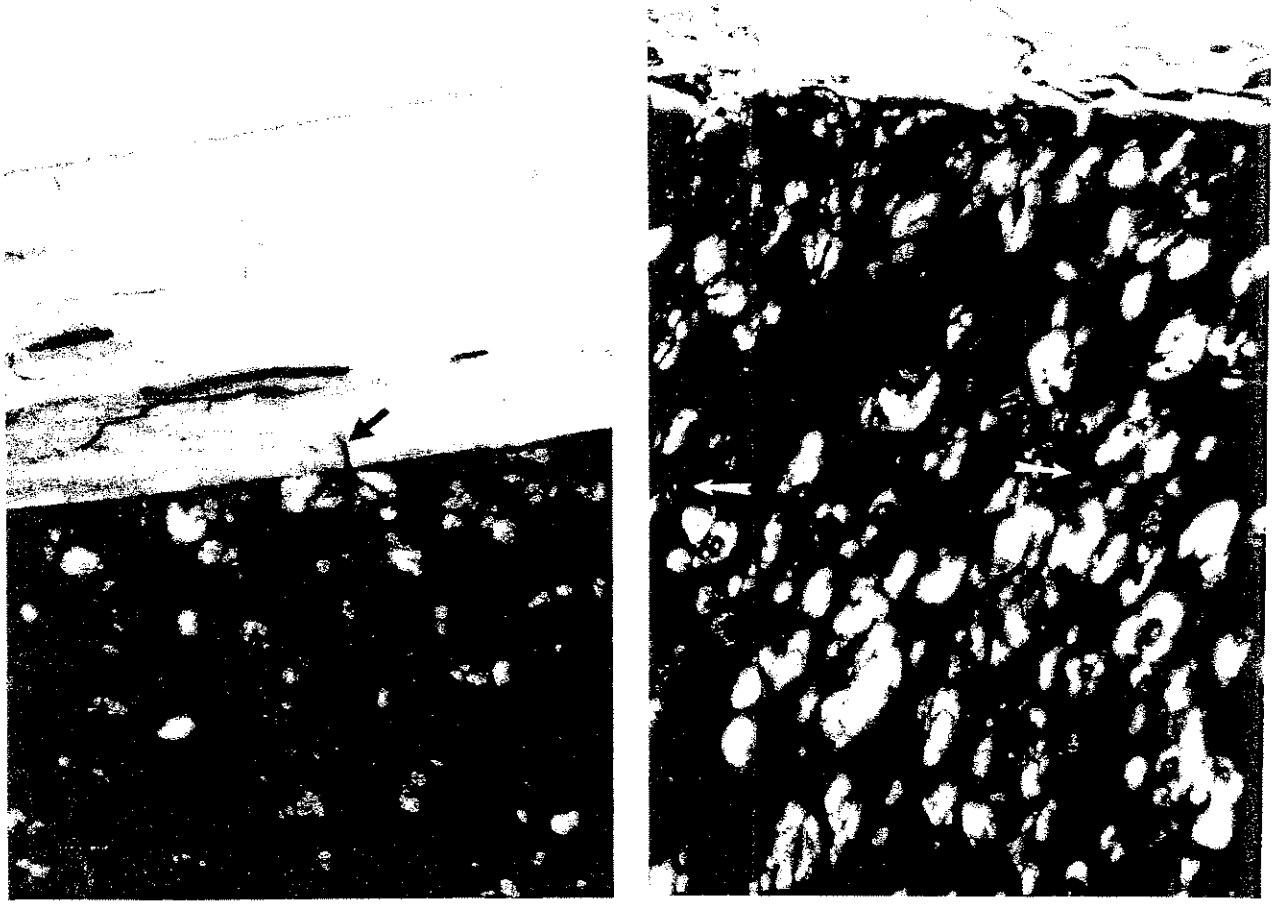


Figure 3. (left) Omental wrap at 3 weeks on the thick section (40 μm) after microfil injection. Only one vessel is seen penetrating into the implant (arrow). Implant is the darkened area on the lower half of the photograph (× 10). (right) Latissimus dorsi wrap at 3 weeks on thick section (40 μm). As compared to the omentum, there are many more vessels which also penetrate much further. Arrows show extent of penetration (× 10).

toxylin eosin-stained slides were viewed by conventional light microscopy.

Penetration of 50–100-μm-size vessels was assessed in a blind fashion on thick section using an eyepiece micrometer on 10× power viewing five fields per specimen. The number of vessels in each field was also noted.

Computerized Axial Tomography

All remaining specimens and several specimens never implanted (0 time controls) were placed in individual containers and imaged by a General Electric 9800 CT scanner (120 kV, 3 sec, 140 mA) making 5-mm-thick sections (two/specimen). Density determinations in Hounsfield units were made to determine TCP resorption.

Analysis of Data

The mean (percent ± SEM) was computed for each test group. The unpaired Student's t-test was employed to evaluate the differences between the groups. Values of $p < 0.05$ were considered significant.

RESULTS

Implants for the most part were well tolerated by the dogs. Two saphenous implants placed early in the study eroded through the skin within 3 weeks. Designing the skin incision away from the subcutaneous implant eliminated this problem.

The patency rate of the av pedicles assessed by xerography was 83.3% (6/7 thoracodorsal and 4/5 saphenous). Both nonpatent implants were from the same dog harvested at 3 weeks.

Xeroradiographs of in situ specimens showed similar vascularity adjacent to the implants in all groups (Fig. 2). However, due to high density of the implants, one could not comment on vessel penetration. Cross-sectional radiographs added no additional information and were discontinued.

Table 1. The Assessment of Vascular Ingrowth Viewing 40-μm-thick Sections Using an Eyepiece Micrometer at 10 × Magnification[a]

	Depth and density of vascular penetration		
	3 Weeks	6 Weeks	9 Weeks
Control	n = 2 0 mm 0 Vessels/field	n = 2 0 mm 0 Vessels/field	— — —
Omentum	n = 3 0.23 ± .03 mm 0.67 Vessels/field	n = 2 0.26 ± 0.05 mm 1.5 Vessels/field	n = 1 0.96 ± 0.11 1.25 Vessels/field
Latissimus dorsi muscle	n = 4 0.95 ± 0.03 mm 3.8 Vessels/field	n = 2 1.33 ± 0.10 mm 2.3 Vessels/field	n = 1 2.94 ± 0.13 4 Vessels/field
Thoracodorsal av pedicle	n = 3 0.95 ± 0.02 4.8 Vessels/field	n = 2 1.60 ± 0.13 2 Vessels/field	n = 1 Throughout TCP 5 Vessels/field
Saphenous av pedicle	n = 2 1.08 ± 0.03 4.5 Vessels/field	n = 1 1.59 ± 0.13 2 Vessels/field	n = 1 Throughout TCP 4 Vessels/field

[a]The number of vessels per field was also recorded.

Tetracycline labeling was negative for all the implants. Representative thick sections viewed under low power are presented in Figure 3.

Table 1 shows penetration of vessels 50–100 μm in size for the test groups assessed by low-power light microscopy. At 3 weeks, omental implants had significantly more ingrowth than the subcutaneously placed controls ($p < 0.001$), although both had significantly less penetration than the muscle wrap ($p < 0.001$) and both av pedicles ($p < 0.001$). There was no difference between the muscle wrap and pedicles at that time (NS).

Although eliminated from the statistical analysis, the two 3-week implants with obstructed av pedicles had vascular ingrowth on the outer surface from the surrounding muscular tissue.

At 6 weeks, the differences between the omentum and latissimus dorsi muscle widened ($p < .001$) as did the gap between the omentum and the av pedicles ($p < .001$). At that time, one noted a small difference in vessel penetration between the av pedicles and the muscle wrap ($p < 0.05$), although the vessel density appeared the same.

The differences already noted continued to widen at 9 weeks. The av pedicle implants had a rich network of vascularity throughout. Because of the intertwining nature of the vessels and the observation that some vascularization can occur from the outer surfaces inward, no calculation of vessel length was made; however, av pedicle vascularity was significantly better than that of muscle.

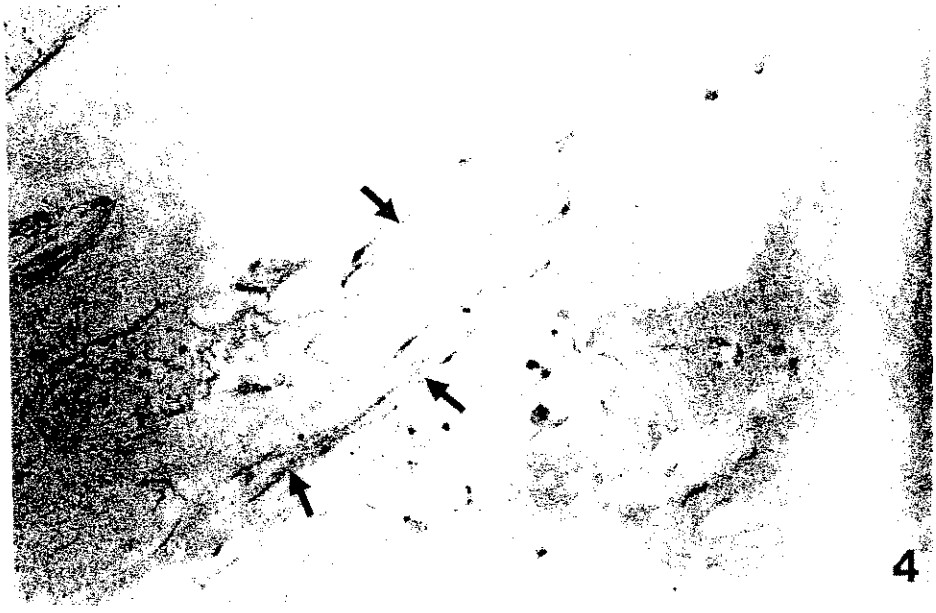
Qualitatively, the nature of the organic material varied with the degree of vascularity. In the omental implants, we noted their relatively sparse vascularity and only a few cells among much fibrous tissue (Fig. 4). Cellularity was increased with less fibrous tissue amid many microfil-injected vessels in both the latissimus dorsi and pedicle groups (Fig. 5). Density measurements by CT scan were inconclusive.

DISCUSSION

The history of bone substitutes has its start in the 1920s, with Nystrom's [21] use of plaster of Paris. Since then, several substitutes have been developed.[15,22,23] Tricalcium phosphate $Ca_3(PO_4)_2$, a ceramic when placed in a bone defect, exhibits two opposing processes simultaneously—implant resorption and new bone formation by osteoconduction. Implant resorption is determined by many factors, those related directly to the implant (size, porosity, etc) and those related to the microenvironment in which the implant is placed (physiochemical factors, extent of vascularization, etc). The remaining implant serves as a scaffold to which new bone formation occurs, presumably by osteoblasts supported by vascular ingrowth.[23,24]

There has been extensive study concerning the biophysiological properties of TCP.[12–20] These implants are well tolerated both in this study and in others.[14,25] Calcium phosphate ions once absorbed are handled by the organism without either an increase in serum chemistries or ectopic calcification.[13–15]

Bone formation is slow; Levin et al[12] noted that 22 months elapsed before 4-×-3 mm periodontal defects were totally replaced by bone. Ferraro[15] created 2-cm bone defects in dogs and observed that at 1 year the defect was bridged by newly formed bone; however, pockets of remaining ceramic of unspecified size were also noted. Other studies have shown similar results.[24] At the time of implantation, the strength of TCP is comparable to cancellous bone.[23] During the months that bone formation is occurring, however, implant resorption causes structural weakening.



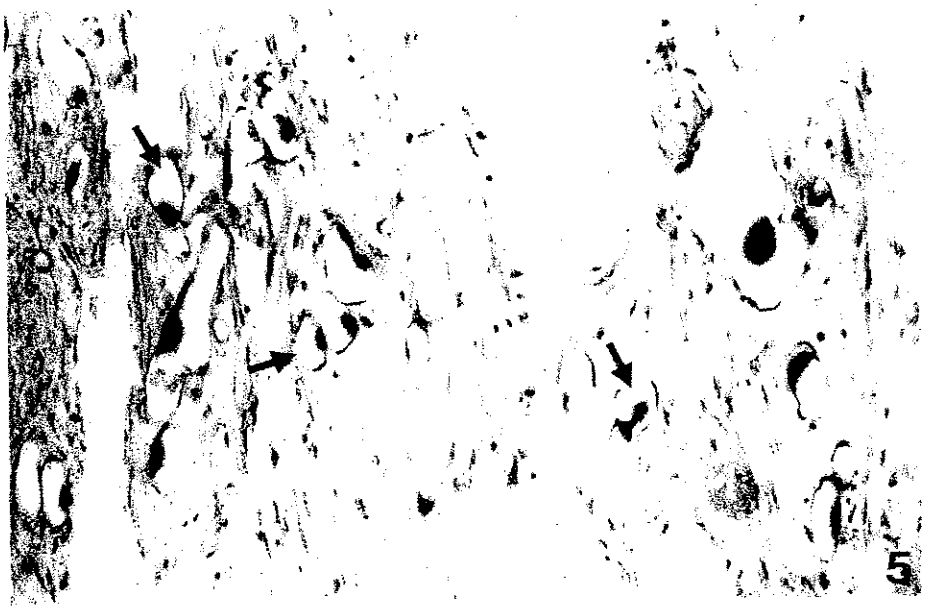


Figure 4. Omental implant at 6 weeks; one notes a few cells with fibrous tissue (arrows). (Hematoxylin-eosin ×200.)

Figure 5. Latissimus dorsi muscle wrap implant at 6 weeks; in contrast to the previous slide one sees greatly increased cellularity. Arrows point to vascularity; the dark objects in the vessels are contracted microfil. (Hematoxylin eosin ×200.)

Implant fracture may occur, which at present is the major drawback in its use.

We undertook this study to vascularize TCP with the ultimate hope of increasing the rate of bone formation within the implant. From this study it has been demonstrated that an artificial bone substitute can be vascularized. The av pedicle group in this study provided the most effective means of affecting microvascular ingrowth. Omentum was clearly inferior to both the av pedicles and the latissimus dorsi muscle wrap. We can only speculate as to the reasons for these differences which consistently occurred and accrued with time. The inferiority of omentum may be due to decreased vessel density, although radiographically there appeared to be similar vascularity surrounding omental and muscle implants.

Nonvascularized TCP does not have osteoinductive properties, ie, the ability to form bone.[23] Vascularizing the implant does not affect this; negative tetracycline labeling showed that no active bone formation was occurring in any of the implants.

To study the problem of implant resorption, we chose CT imaging as a measure of bone density.[26–29] We expected to observe decreasing density as calcium was replaced by lower-density organic material; however, these density measurements were inconclusive. There are several possible explanations for these findings: 1) the time studied (3–9 weeks) was too short for large enough differences in resorption to be detected by the CT; 2) the structure of TCP, a lattice with random interconnecting multisized pores may make such measurements prone to error; 3) the degree of vascularization has no effect on implant resorption. This area will require further study.

CONCLUSIONS

From the current study of implanting TCP in dogs several conclusions can be made.

1) Av pedicles maintain patency documented by latex injection.

2) TCP can be vascularized.

3) Av pedicle threaded through the implant was the most effective means of vascularization; wrapping omentum around the implant was the least.

4) Vascularization does not bestow osteoinductive properties on ectopically placed implants.

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The Classic

Ceramic–Plastic Material as a Bone Substitute

LYMAN SMITH, M.D.

Lyman W. Smith (1912–1991, Fig. 1) was born in Cleveland, Ohio. He graduated from Northwestern University Medical School in 1938 and interned in St. Luke's Hospital in Chicago. He had postgraduate training at the Boston City Hospital and the Children's Memorial Hospital in Chicago. During World War II, Lieutenant Commander Smith served as a U.S. Navy Surgeon attached to the Marines throughout the campaigns in the Pacific. At the end of the war, Smith returned to the Chicago area where he practiced in Elgin, Illinois, for the remainder of his career. During this time, he became an associate clinical professor of orthopedics at Northwestern University Medical School, his alma mater. Lyman W. Smith was a man of many interests and many ideas. They were all associated with clinical problems that he observed in his patients. Although best known for his work with chymopapain and the treatment of disk disease (an effort which consumed his interest and energy during the last 25 years of his life), he was also one of the first orthopedic surgeons to show an interest in the use of ceramic implants. It is for this reason that the following article has been selected as The Classic.

LEONARD F. PELTIER, M.D., PH.D.

The era in which we live has been described by engineers as The Materials Age. It is marked by a bewildering variety of materials developed since the turn of the century at an exponential rate. As surgeons, we are familiar with the metallurgical advances which have given us corrosion resistant alloys, as well as the many developments in the chemistry of plastics, which in some instances have been found to be useful in surgery. Another field of materials—ceramics—has also had tremendous growth in the last 20 years. Ceramic materials are now produced which have considerable strength and impact resistance, as well as great chemical resistivity. The latter characteristic is of prime interest to the surgeon, as the most important property of any surgical material is in its inertness in the environment of human tissue. Although strong, these new ceramic materials have the disadvantage of being extremely rigid. Attempts to produce a ductile ceramic material could follow either of two approaches—one being to alter the microstructures; the other being the formation of a combination or alloy of a ceramic with a more ductile substance. The latter approach has been accomplished by producing a ceramic which has a true interconnecting porosity. This ceramic body has then been impregnated with a close-bonding epoxy resin, thus producing a material which retains the hardness and corrosion resistance of ceramics, but also demonstrates resilience and adequate strength.

From Smith, L.: Ceramic-plastic material as a bone substitute. AMA Arch. Surg. 87:653, 1963.



FIG. 1. Lyman W. Smith, M.D.

METHOD OF PRODUCTION

A mixture was made consisting of alumina (Al_2O_3), silica (SiO_2), calcium carbonate ($CaCO_3$), and magnesium carbonate ($MgCO_3$). A so-called green body was then formed by a method commonly used in ceramic production, known as slip casting. This green body was placed in a furnace, and the temperature slowly raised to about 2,000 F for some hours. During this period, the magnesium carbonate decomposed to magnesium oxide and carbon dioxide gas and the calcium carbonate decomposed into calcium oxide and carbon dioxide gas. Since the individual particles of calcium carbonate and magnesium carbonate were small and thoroughly dispersed throughout the green body, the carbon dioxide gas produced by the decomposition thereof upon heating was also thoroughly dispersed and formed small individual cells that were uniformly distributed and of substantially uniform size. As the carbon dioxide gas formed was further heated, it passed from cell to cell and eventually to the surface of the body. Since about one third of the starting materials, on a dry basis, were carbonates, the green body had a high porosity of about 65% thereof by volume. This so-called prefired body was then finally fired at a temperature of about 2,700 F. The final porosity was controlled by controlling the firing temperature—the lower the firing temperature the higher the porosity and the higher the firing temperature the lower the porosity. In other words, with the higher temperatures, the ceramic body shrank more and thus produced the lower porosity. Porosities ranging from 6% to about 65% by volume of the fired ceramic member were achieved.

Four-inch ceramic bars of varying porosity were impregnated with a liquid aromatic epoxy resin of the diepoxide 0 type mixed with a hydroxy-aliphatic amine hardener. A bar was placed in a casting chamber from which air was evacuated by a water inspirator. The liquid resin and hardener were mixed at 50 C and run into the evacuated chamber. After the mixture had flooded the ceramic piece, positive pressure was applied and the part cooled. To insure complete curing of the resin, the bar was finally baked at 120 C for three hours. The method was successful in completely impregnating the ceramic bar as could be calculated by weight changes and by direct observation following destructive tests.

Cured epoxy resins are particularly inert to most chemicals and solvents as compared with other organic plastic materials. Methylene chloride, a halogenated hydrocarbon, is one solvent that slowly attacks the surface of epoxy formulated parts. Before the final temperature cure at 120 C for three hours is applied to the impregnated ceramic, there is a period just after impregnation when the resin is most susceptible to this solvent. It can be applied in various degrees of time and agita-

tion to effect a complete surface removal of the impregnant. Once the resin has been completely cured, contact with the solvent would be necessary for some days. A specimen is dipped for three to five minutes in methylene chloride solvent after impregnation and before curing. It demonstrates a leaching away of the surface resin to a depth of 50 to 70 mils.

EXAMINATIONS OF THE MATERIAL

Flexural Strength and Modulus of Elasticity. —Bars of the impregnated ceramic were prepared measuring 4 × ½ × ¼ inch. The bars varied in porosity from 6% to 65% by volume. The bar to be tested was supported at each end and a load applied from above at the center on a table model "Instron" machine. The crosshead was lowered at the rate of 0.2 inch per minute, and an automatic recording of the deflection produced in the test bar was made. From the readings obtained, flexural strength in pounds per square inch (psi) was calculated as well as the modulus of elasticity (resistance to bending) for each sample. Both figures varied with the degree of porosity of the sample. A bar of 46% porosity was chosen as ideal because its modulus of elasticity was approximately the same as bone (3.0×10^6 psi) and its flexural strength was 12,000 psi, as compared to an average wet bone sample of 11,000 psi.

Resistance to Aging. —Test bars measuring 4½ × ½ × ¼ inch were placed in isotonic saline solution in glass tubes, and the tubes were sealed with the volume of air therein equal to the volume of the saline solution. The bars were then aged at elevated temperatures for varying periods of time. Three series of tests were run at 124 C, 149 C, and 190 C. The tubes were opened and a maximum bending stress for each bar expressed in psi was determined, by utilizing the test method described above. The value of flexural strength obtained on each test bar was graphed, and then, by extrapolation, the length of time it would take to reduce the flexural strength of the material to 8,000 psi at body temperature of 37 C (98.6 F) could be calculated. This age life was determined to be about 2×10^8 hours, or 23,000 years.

Abrasion Resistance. —A machine was used that provided a fresh abradent surface with each cycle of movement of a pressure head. A water-proof Carborundum silicone carbide paper was moved at a rate of five inches per minute under a one-fourth-inch diameter abradent head at a pressure of 100 pounds per square inch. The change in thickness due to abrasion was recorded as the movement of an electric displacement sensing device attached to the head of the abrader. The impregnated ceramic was abraded for 10,000 cycles as was a polished piece of Vitallium. The results show that the impregnated ceramic wore less than the Vitallium for the first 3,000 cycles and was almost equal in continued cycles. As a further test, the abradent paper was removed and a piece of human bone with a hyaline cartilage face cut to one-fourth-inch diameter was mounted for movement against a piece of the impregnated ceramic. The cartilage was wetted every 1,000 cycles with two drops of synovial fluid. After 24,000 cycles, the impregnated ceramic had no change in its surface, while the cartilage sample lost 0.012 inch, most of which was removed during the first 10,000 cycles.

Hardness. —The hardness of an impregnated porous ceramic structure is difficult to define. Considered as a continuous surface structure rather than as each of two components, it was thought best to test the hardness by methods ordinarily used on metal. A Wilson-Rockwell instrument was used to test the material using a one-eighth-inch and a one-sixteenth-inch ball penetrator. The superficial hardness was found to vary inversely in accordance with the degree of porosity. The ceramic alone retained a hardness of 94 to 97 up to 28% porosity, as compared to a finding of 99 on Vitallium sample. The impregnated ceramic in the 50% porosity range showed a value of 83.

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Pore Size. —Microscopic studies have shown the pores in a 46% porosity body to average 18 μ in diameter with some up to 25 μ.

Fatigue. —Fatigue studies are being made on the material. The early results are good within the range of failure of the material. It is known that Vitallium will fatigue at about 40% of its failure strength; stainless steels fatigue at 45% to 50% of their failure strength. On the basis of preliminary data, it appears that the impregnated ceramic fatigues at 50% to 55% of its failure strength, although it should be realized that the failure strength of this material is well below that of metal.

Compression. —An Eicher type stainless steel hip prosthesis was duplicated out of this material. The stainless steel prosthesis weighed 1 lb 2 oz; the ceramic-plastic prosthesis weighed 11 oz. Each prosthesis was placed under compression in a universal tensile-testing machine. The stainless steel prosthesis failed by plastic deformation at approximately 550 lb; the impregnated ceramic failed by fracture at 608 lb.

Resistance to Chemicals. —The impregnated ceramic has been tested by immersing a piece in aqua regia for 24 hours at room temperature. No weight loss was recorded, and the same lack of reaction was found when the material was placed in 50% sodium hydroxide at body temperature for 48 hours.

ANIMAL STUDIES

Methods. —Forty-two White Satin rabbits weighing an average of nine pounds have been used. At irregular intervals, implants of the epoxy resin, the porous ceramic, and the impregnated ceramic have been placed in subcutaneous tissues, skeletal muscle, and knee joints. Operations were done under pentobarbital sodium (Nembutal) anesthesia plus 1% procaine locally.

A ceramic-plastic prosthesis was shaped for insertion into the knee joint replacing the anterior portion of the femoral condyles in articulation with the patella. At operation, the knee joint was approached from the lateral aspect, and the patella and its tendinous attachments were dislocated medially. The anterior portion of the femoral condyles was removed by an oscillating saw to a point just short of the weight-bearing area and the prosthesis loosely laid into the cavity, the stem being pushed proximally up the medullary canal. The patella was then reduced into apposition with the prosthesis, and the wound was closed in layers after irrigation with saline solution. Some of the prostheses were surface leached of the plastic before insertion; others were not. The rabbits were kept out of doors in narrow cages 20 feet long with food and water at alternate ends to encourage activity. They were sacrificed at irregular intervals.

Results. —Three anesthetic deaths were encountered. Three postoperative deaths occurred at various times due to pneumonia, and three knee joints were grossly infected. Six fractured femurs into and proximal to the prosthesis were seen.

In a transverse section taken through a prosthesis and femur three weeks after operation, The prosthesis was tight in its bed, held so by cancellous bone and fibrous tissue grown in firm apposition to it. It was removed from the femur by chiseling. This firm apposition of bone to prosthesis has been a constant feature of all knees examined. There was adherence of bone and fibrous tissue to a 40-day implant. The bone was allowed to dry and shrink away from the prosthesis, but close adherence is demonstrated even though in this prosthesis the epoxy had not been leached from its surface.

To date, six months have been the longest a leached prosthesis has been in place before autopsy. The knee of that rabbit showed no limitation of motion. On opening the joint, there was no increase in synovial fluid, the capsule was not bound down, and there were no intra-articular adhesions. The articular cartilage was everywhere shiny and glisten-

ing. The prosthesis was firmly held in its bed by new bone and could not be removed until the femur was decalcified. A section through a corner of the bed showed dense, relatively acellular fibrous tissue merging with osteoid and orderly trabeculae of lamellar bone. A section through the articular cartilage of the patella showed no surface reaction to wear against the prosthesis. In the x-ray of the knee at the time of insertion of the prosthesis and the same knee six months later, there is considerable endosteal calcification in the medullary canal about the peg of the prosthesis, and the bone trabeculae of the host appear to be interwomen with the substance of the prosthesis.

In a section from tissue immediately adjacent to a seven-week subcutaneous implant of epoxy resin, the implant was approximately the size of a shirt button and was freely movable. The section shows a thin layer of mesothelial cells overlying a loose areolar tissue. There are no giant cells or collection of polymorphonuclear leukocytes indicating an inflammatory reaction.

The pieces of the porous ceramic and the impregnated ceramic after leaching, which had been embedded in skeletal muscle, were examined after three to nine weeks. They were found to be tightly bound in place by fibrous tissue and normally colored muscle fibers in contrast to the synovial-like sheath found around similarly embedded inert metal alloys. In these instances, and in the case of the closely bound knee prosthesis, it has been assumed that fibrous tissue and perhaps bone had invaded the open pore structure. Such ingrowth has been demonstrated with polyvinyl sponge implants.[4] The ceramic is too hard to cut with the microtome, so thin sections have been prepared by grinding on sandpaper. Examination of these sections has been disappointing in that no fibrous tissue or bone has been seen. However, it is possible that soft tissues have been pulled out of the pores in the grinding process. Other methods of preparation are being attempted.

COMMENT

This material has been developed in the belief that it may act as a better substitute for bone than the metal alloys in common use. These alloys are almost ten times as strong and approximately ten times as stiff as the bone they are called upon to replace or to immobilize. On bending, there is a relative movement between the flexible bone and the rigid alloy which sets up high localized stresses on certain areas, and at these points bone is absorbed. The impregnated ceramic of 46% porosity has the same modulus of elasticity as bone and will bend symmetrically with it, thus avoiding such stresses.

The prime reason the 18-8 stainless steel and the cobalt-chromium molybdenum alloys have been used in surgery is their relative resistance to corrosion. Macrocorrosion is common with stainless steels,[1] and microcorrosion is seen with all types of metal alloys, including Vitallium.[2] This latter type consists in the deposition of metallic elements in the tissues around implants, but its significance is not known. Galvanic corrosion of alloys in the body, an electrochemical phenomena, is not seen in ceramic and plastic materials, which is the reason for their common use in industry for insulation. Some alloys and metals protect themselves from chemical corrosion by the formation of a thin layer of oxides on their surfaces; ceramic materials are commonly oxides, and could be loosely stated to have "already corroded." The epoxy resin used to impregnate the porous ceramic is also chemically inert. The structure of this class of polymers suggests that ether linkages are the only bonds other than the carbon to carbon. Ether linkages are among the most stable known to organic chemists so it follows that these resins are highly resistant to attack by various solvents, acids, and alkalis.

Epoxy shares its chemical inertness with other types of plastics, but was chosen over them because of its unique ability to bond tightly to the ceramic. Most plastics would

only act as fillers in the void cavities of the ceramic, contributing little to the flexural strength of the material. The resistance-to-aging test showed that this tight bond between the epoxy and the ceramic would not materially deteriorate with time and temperature.

Some chemically inert plastics have been found to be toxic in tissues, due to remnants of catalysts or to unreacted molecules of the components of the plastics themselves. The completely cured epoxies have been found nondeleterious to health by medical investigators of the major resin manufacturers. Regardless of the type of curing agent used, the cross-linked epoxy apparently does no harm when powdered and fed to rats in massive doses over long periods.[3] However, dermatitis has been reported in workers handling the liquid amine hardeners used in preparation of the plastic.

The impregnated ceramic is far weaker than the metal alloys but equal with the strength of bone. Its strength should be adequate as a substitute for bone if used in sufficient mass and properly engineered. It is hoped that this material will be re-enforced by the growth of soft tissue and bone into the surfaces which have been leached of epoxy.

SUMMARY

A material developed for use as a bone substitute is described. It is a porous ceramic composed of the high-temperature reaction products of alumina, silica, and the oxides of magnesium and calcium. The honeycomb structure of the ceramic is impregnated with a close-bonding epoxy resin. The resultant material is as strong as bone and has the same modulus of elasticity, is light in weight, inert in rabbit tissues, resilient, hard, difficult to abrade, and is highly resistant to acids and alkalis.

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