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Pathology of Alloplastic Interpositional Implants in the Temporomandibular Joint

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Prior to arthroscopy, the surgical management of internal derangement of the temporomandibular joint (TMJ) involved disk repair or disk removal either without replacement or with replacement by either alloplastic implants or autogenous tissue. The insertion of biologically acceptable alloplastic material into the TMJ has had the objectives of promoting resurfacing and preventing adhesions between the condyle and fossa, articular degeneration, crepitus, and pain. Two of the most widely used materials are Silastic sheeting and a laminate of Proplast with nonporous Teflon. Proplast is used permanently, whereas silicone rubber has been used both permanently and temporarily. Initial reports of Silastic and Proplast implants in joints experimentally and clinically indicated that these materials were successful, but numerous articles since then have demonstrated the destructive effects of both materials in the form of reactive synovitis, destructive arthritis, lymphadenopathy, and foreign-body granulomatous reactions. These TMJ reactions can cause severe loss of bony structure and open bite deformity.

Despite the discouraging results of implantation of these materials in the TMJ, reports of clinically successful cases appeared periodically in the literature.[13, 41, 45] The purposes of this presentation are: (1) to give additional evidence of the destructive potential of these implants; (2) to show that the damage is not short term but lasts far beyond the removal of the rejected implants; (3) to illustrate the destructive effects of these implants on subsequent tissue grafts; and (4) to give practitioners insight into the removal of symptomatic implants even though they appear intact at the time of surgery.

LITERATURE REVIEW

Silicone elastomers have been extensively studied and utilized clinically as implants for a wide range of purposes in various anatomic locations.[21, 41, 53, 64] Swanson in 1969 introduced silicone rubber to replace finger joints.[64] The use of silicone to restore function and to relieve pain in joints damaged by disease or trauma expanded greatly in the 1970s,[65] and the material has been used for reconstruction or repair of wrist, elbow, shoulder, and metatarsal joints and for lower-extremity amputation stumps as well as for reconstruction of the TMJ meniscus.[25, 67]

Initially, experimental evaluation by many investigators showed that Silastic implants in block, sheet, or tubular form become surrounded by a fibrous capsule. This encapsulation process occurs without evidence of significant inflammatory or foreign-body reaction except for the occasional finding of intracellular particles of silicone elastomer in macrophages.[36, 37, 52, 57] It was thought that solid silicone fulfilled many of the requirements of an ideal implant material.[16]

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Silicone implants are also common in the practice of oral and maxillofacial surgery. In 1981, after presentation of a paper by Sanders,[61] silicone rubber replacement after TMJ diskectomy became popular.[5, 32, 58] However, recent reports demonstrate severe reactive synovitis and a foreign-body giant-cell reaction around silicone elastomer particles, occasionally resulting in destructive arthritis.[1, 9, 10, 11, 18, 23, 60, 63, 66]

In an attempt to duplicate the clinical phenomenon of a foreign-body synovitis from particulate silicone elastomer, Worsing and associates[71] introduced finely ground particulate silicone elastomer into the knee joints of adult New Zealand white rabbits. Histologic evidence of inflammatory changes developed in the synovial tissue similar to those seen in patients. Timmis and coworkers[68] used alloplastic materials for TMJ disk replacement in rabbits and found that 21.4 per cent of the Silastic implants were torn. The fragmentation of the implant uniformly observed in the rabbits may have stimulated the marked foreign-body giant-cell reaction.

Eriksson and Westesson[17] used Dacron-reinforced silicone material as temporary disk-replacement implants in 27 patients who underwent diskectomy. They found at the time of removal of the implant (1 to 19 months postoperatively) that all but one of the implants showed wear facets and 15 implants were cracked or perforated. Dolwick and Aufdemorte[18] studied eight patients who had silicone implants, finding that all tissue specimens revealed granulomatous inflammation and multinucleated giant cells associated with fragmented silicone material. Six of the twenty patients in the series of Westesson and associates[70] who had received temporary silicone implants had destructive lesions of the mandibular condyles. A complication of lymphadenopathy resulting from a silicone elastomer finger joint prosthesis has been reported.[9, 22, 46] Silicone-related lymphadenopathy in the parotid gland resulting from TMJ silicone prostheses was reported by Dolwick and Aufdemorte.[18] In 1972, Swanson[65] estimated that approximately 1 per cent of prostheses ultimately fracture. However, accumulating experience indicates that as many as 25 per cent of these implants will develop fractures, with potential release of silicone particles and resultant foreign-body reactions.[22]

Conflicting results were recently reported by Kalamch and coworkers.[41] They studied 68 patients who had intra-articular TMJ arthroplasty with Silastic implants. The longest follow-up period was 14 years, 7 months. Sixty-three of the patients had satisfactory results.

More recently, Proplast has been introduced as an implant for correcting various tissue defects. A laminate of Proplast (Vitek, Inc., Dallas, Texas) is a porous form of polytetrafluoroethylene (PTFE) with an admixture of fibers of either vitreous carbon (PTFE C or Proplast I) or aluminum oxide (PTFE-Al_2O_3 or Proplast II) and Teflon (E. I. Dupont Co., Wilmington, Delaware), a dense smooth form of PTFE. It has a high melting point (above 250°C) and unusual toughness; is insoluble in all common solvents, resistant to chemical attack, and antifrictional; and has a modulus of elasticity resembling that of bone or fibrous tissue.[26, 33, 69] A number of investigators consider that porous PTFE offers more stability than nonporous silicone polymers and hence is more useful clinically.[2, 24, 27, 28] The desirable qualities of Proplast include freedom from adverse reactions,[10, 57] toxicologic safety,[36, 57] rapid tissue ingrowth,[2, 39, 44, 57] and biocompatibility.[15, 19, 38, 44, 57]

Proplast has been studied in a number of animal trials. Proplast coating on stems of replacements for canine femoral heads achieved good results of stabilization without an inflammatory response.[29, 30] Halstead and associates,[33] who studied the reaction of human tissue to Proplast-coated femoral stems of Thompson prostheses by electron microscopic examination and electron probe microanalysis, found neither round-cell or polymorphonuclear leukocytic infiltration nor tissue necrosis, although macrophages and giant cells were present.

A 1983 presentation reported a very large series of Proplast implants as having outstanding clinical and tissue acceptance[6] (TA Kiersch, as quoted by SL Bronstein, Eighth International Conference on Oral Surgery). A survey of 47 oral surgeons with expertise in TMJ surgery conducted by Merrill in 1985 revealed that 17 favored the Proplast-Teflon implants after diskectomy whereas five favored permanent silicone rubber implants.[54] A repetition of this survey in 1987 revealed one using Proplast and four silicone.

As early as 1963, Charnley[8] warned that PTFE used as a joint replacement is subject to abrasion, which produces particles that incite an intense foreign-body giant-cell reaction with resultant osseous necrosis or granuloma formation. In corroboration, Leidholt and Gorman[51] found a foreign-body giant-cell granuloma associated with PTFE fragments between the

implant and bone interface, resulting in implant fracture. Jones and Jones[40] likewise noted intense foreign-body giant-cell reactions at the PTFE-bone interface, causing necrosis of bone and loosening of the prosthesis. Virtually every tissue into which this material has been implanted has shown some type of foreign-body inflammatory reaction. The implantation of PTFE-C in animal subcutaneous tissue resulted in seroma formation, flap necrosis, fragmentation of the material, and numerous foreign-body giant cells. Granulomatous reaction occurred after periurethral injection of Teflon,[52] Teflon implantation into the orbit,[3] Proplast vascular grafts, and ossicular and laryngeal implants.[39] A case of lymphadenopathy following TMJ arthroplasty with Proplast has been reported.[50] Significant pathologic changes, such as a destructive foreign-body granulation reaction resulting in avascular necrosis of the mandibular condyle and condylar neck, have occurred in the TMJ in association with Teflon-Proplast.[6, 24, 34, 42, 43, 49, 50, 62, 68, 70] However, a survey conducted by Vitek, Inc. in 1986, to which 322 surgeons responded, revealed that of a total of 6182 Proplast implants placed during the previous 3 years, 5644 (91 per cent) were considered satisfactory, although criteria for success were not specified (quoted by SL Bronstein, May and October 1986).

Kent and coworkers[45] designed a three-layer Proplast glenoid fossa in which the superior layer was Proplast I, the middle layer Teflon-FEP polymer, and the inferior layer Teflon-PTFE polymer reinforced with graphite fiber. The prostheses were placed in 192 joints (127 patients) for TMJ reconstruction. The cumulative success rate at 36 to 48 months was 96.11 per cent.

MATERIAL AND METHODS

Sixteen Silastic implants used as temporary disk replacements were removed at planned intervals (two implants after 1 month, seven after 3 months, six after 4 or more months, and one after 6 months). Adjacent tissues were taken for histologic evaluation. Another 30 Silastic implants had replaced TMJ disks for periods ranging from 8 months to 5 years. These implants were removed because of symptomatic joints, and the adjacent tissues were obtained for histologic study. Two dermal grafts, four dura mater grafts, and six pedicled temporalis myofascial flaps had replaced the implants. These joints were reoperated on after 1 year because the patients became symptomatic. Nearby tissue also was removed for investigation.

Twenty-two Proplast implants had been used for TMJ disk replacement. All implants were removed because of symptomatic joints (six after 1 year, eight after 2 years, seven after 3 years, and one after 5 years). Two dermal grafts, three dura mater grafts, and two pedicled temporalis myofascial flaps had replaced the implants. After 1 or more years, these joints were reoperated on because patients became symptomatic, and tissue was removed for histologic study.

RESULTS

Silastic Implants

Short-duration Implants

Grossly, the Silastic implants were intact and were usually surrounded by fibrous tissue. Microscopically, fragmentation of silicone with chronic inflammation, foreign-body giant-cell reaction, and various degrees of fibrosis were present in the synovium, capsule, and surrounding tissue.

Long-duration Implants

Grossly, the integrity of the implants ranged from a roughening of the articular surface to tears and frank perforation. The surrounding tissue exhibited fibrosis to form fibrous ankylosis. The articular surface of both the condyle and the glenoid fossa displayed irregularity or erosion. Microscopically, Silastic particles were dispersed throughout the hyalinized fibrous tissue with chronic inflammation and foreign-body reaction (Fig. 1). Cartilaginous or osseous transformations or both often were present. In two cases, the Silastic granules were found within the macrophages and giant cells in the preauricular lymph nodes.

Implants Followed by Dermal Craft Placement

Grossly, the dermal grafts blended with fibrous tissue. An irregularity of the articular surface of the condyle and glenoid fossa was evident. Occasionally, fibrous ankylosis occurred. Microscopically, patchy Silastic foreign-body reactions with chronic inflammation were present. The dermal grafts appeared degenerate, hyalinized, and fibrosed.

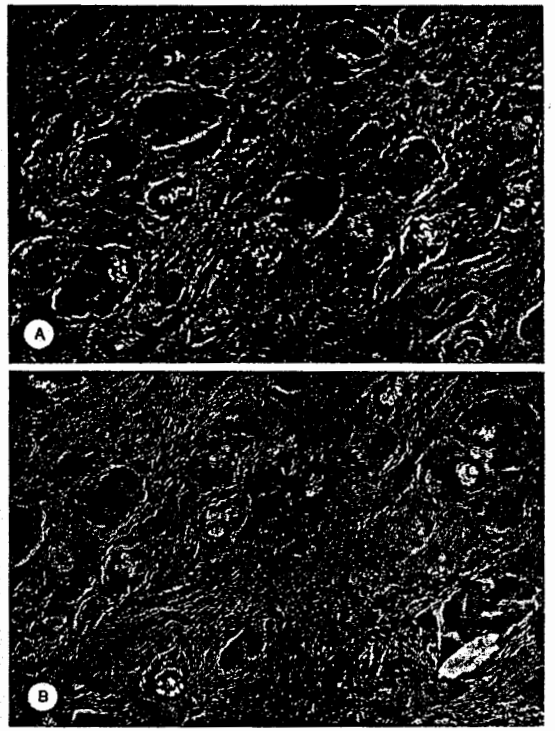

Figure 1. Response to long-term presence of Silastic. *A*, Silastic particles with foreign-body giant cells. *B*, Polarized Silastic crystalline particles in foreign-body giant cells. (Hematoxylin and eosin stain; original magnification ×400)

Implants Followed by Dura Mater Grafts

Grossly, significant fibrosis and granulation tissue were evident. The dura grafts usually could not be recognized. The articular surfaces of both the glenoid fossa and the condyle appeared irregular with occasional fibrous or osseous ankylosis. Microscopically, Silastic foreign-body granulomas were dispersed throughout the tissue. The dura appeared degenerate, fragmented, or fibrosed, and there was cartilaginous or osseous transformation or both.

Implants Followed by Pedicled Temporalis Myofascial Flaps

Grossly, mild to moderate fibrosis of the muscle flap was present. Microscopically, foci of Silastic foreign-body granulomas and adjacent muscle fiber degeneration were observed.

Proplast Implants

Grossly, the integrity of the implants ranged from a rough surface to destruction. The implants were often dislocated. Tissue reaction to the implant ranged from significant fibrosis to granulomatous masses. The articular surfaces of the condyle and fossa usually appeared irregular or eroded. Fibrous or osseous ankylosis often occurred. Microscopically, the tissue showed scattered Proplast particles with significant giant-cell reaction, chronic inflammatory infiltrate, and fibrosis (Fig. 2). Cartilaginous or osseous transformations or both were often ev-

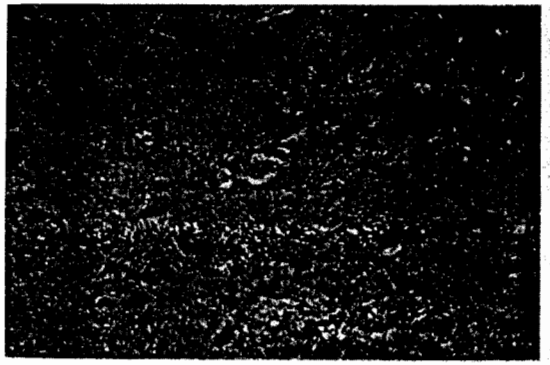

Figure 2. Proplast foreign-body reaction with chronic inflammation. (Hematoxylin and eosin stain; original magnification ×250)

ident. In one case, Proplast granules were found in the macrophages and giant cells in the preauricular lymph nodes.

Implants Followed by Dermal Graft Placement

Grossly, dermal grafts blended with fibrous and granulation tissues. An irregularity of the condylar articular surface and glenoid fossa was seen. Occasional fibrous ankylosis occurred. Microscopically, marked Proplast foreign-body reaction with chronic inflammation was present. The dermal grafts showed hyalinization, degeneration, and fragmentation. In addition, cartilaginous or osseous transformation often occurred.

Implants Followed by Dura Mater Grafts

Grossly, significant fibrosis and granulomatous masses resulted in fibrous and bony ankylosis. The dura tissue blended with the fibrous tissue. An irregularity of the condylar articular surface and the glenoid fossa was often present. Microscopically, a marked Proplast foreign-body reaction with chronic inflammation resulted in necrosis or fragmentation of dura tissue. In one case, an area of casseous-like necrosis was surrounded by Langerhans' giant cells (Fig. 3).

Implants Followed by Pedicled Temporalis Myofascial Flaps

Grossly, granulation tissue and fibrosis were present. Microscopically, foci of Proplast foreign-body granulomas and adjacent muscle fiber degeneration were observed.

DISCUSSION

Early studies with alloplastic implants indicated that they were biocompatible, and reports showed high clinical success rates in the TMJ.[14, 25, 46, 61] Although some degenerative changes in the joints were observed radiographically, it was thought that these were an expected and common result of joint surgery. Histologically, giant-cell reactions were considered an indication of movement of the prostheses rather than a biologic reaction and it was thought that this "micromotion" between bone and "coating" would occur continuously.[6]

The growing concern is that the changes found in the TMJ in conjunction with the insertion of an intra-articular alloplastic substitution after diskectomy are more severe than those described in previous reports. Surgical re-exploration of TMJs with implant prostheses has been necessary because of recurrent joint pain, swelling, or severe occlusal changes and has shown a physical breakdown of the alloplastic material associated with a foreign-body granulation response. Although the exact cause of the foreign-body reaction is not clear, fragmentation of the implant seems to be significant. The production of polymeric wear particles is an inevitable consequence of the gliding movement in artificial joints with plastic components.[4, 20] Biologically inert block-form materials induce macrophage migration and a foreign-

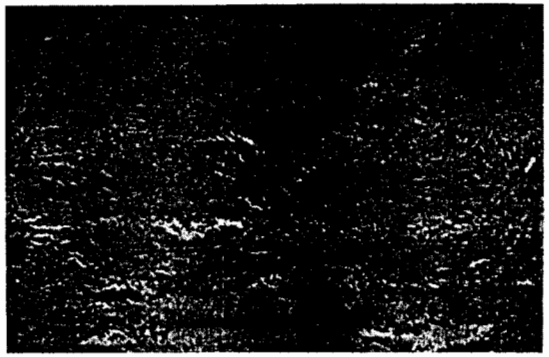

Figure 3. Caseous necrosis with Proplast foreign-body reaction in a dura mater graft. (Hematoxylin and eosin stain; original magnification ×250)

body giant-cell reaction when transformed into small particles as a result of biomechanical wear.[17, 71] If the size or amount of particles exceeds the capacity of the lymphatic system to remove them, foreign-body granulation tissue will form around the joint cavity. Localized tissue destruction then occurs as a result of macrophage secretion of neutral proteinases, acid hydrolases, and other enzymes.[20, 70] Destructive arthritis is possible. The extent of implant damage is variable. All but one of the removed implants in Eriksson's study showed wear facets, and nearly half were perforated or cracked.[17] Twenty-one per cent of the silicone implants and 46 per cent of the Proplast implants were torn in the rabbit study by Timmis and associates.[68] More than half the implants were cracked or perforated at the time of planned removal in our study.

The hypothesis of destructive reaction resulting from excessive functional overloading of the implant cannot explain the fact that a foreign-body giant-cell reaction has been found in the unloading area after an alloplastic material was inserted such as a chin or facial implant. It is possible that foreign-body reactions to alloplastic implants result from an inherent property of the implants, which may be unable to maintain their biomechanical integrity, shedding particles into the tissue the implant contacts.

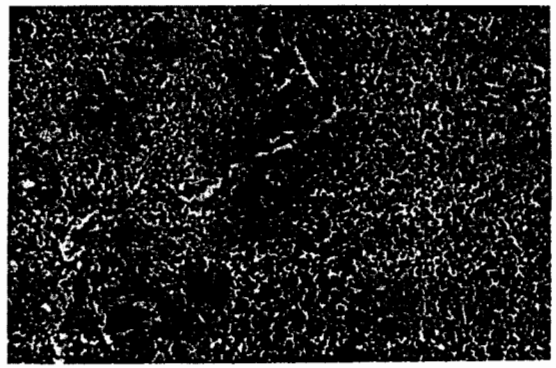

Figure 4. Giant cells containing both Silastic and Proplast particles in a lymph node. (Hematoxylin and eosin stain; original magnification ×250)

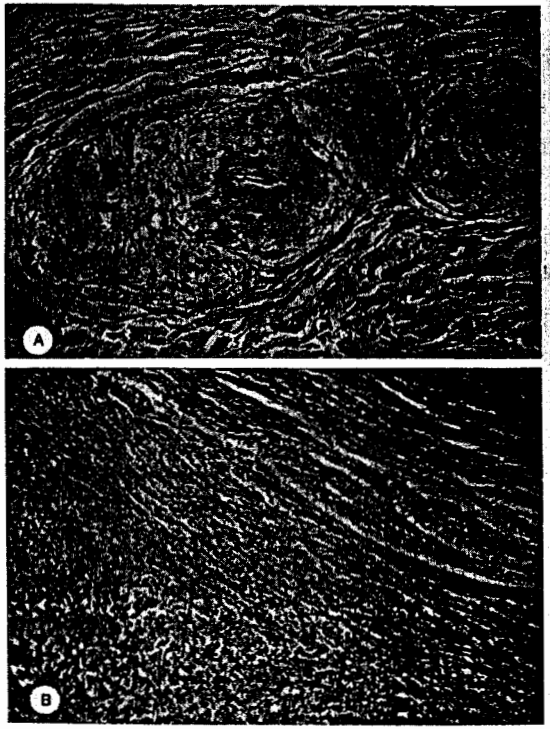

Figure 5. Responses of dura grafts. *A*, Survival of dura graft with Silastic foreign-body reaction. (Hematoxylin and eosin stain; original magnification ×400). *B*, Extensive degeneration of same graft (*upper right*) with Silastic foreign-body reaction (*lower left*). (Hematoxylin and eosin stain; original magnification ×250)

Neel[58] studied the tissue response to three types of synthetic implant material—Gore-Tex (polytetrafluoroethylene), Proplast (Teflon-laminated polytetrafluoroethylene carbon), and porous polyethylene—in New Zealand white rabbits. Recipient sites for the implants were the perichondral space of the pinna, the subcutaneous tissue of the face, and the paraspinal region. Gore-Tex seemed to be better than Proplast. Gore-Tex is biocompatible in that histiocytes and foreign-body giant-cell reaction in the surrounding tissues were minimal, whereas a profusion of these cells was seen around the Proplast. Moreover, Gore-Tex retained its structure integrity. This study demonstrated that under the same experimental condition, the biomechanical or biochemical characters of implants will greatly influence host tissue reactions.

Excessive functional overloading probably is an important cofactor that will enhance particulate formation by implants. An implant must be completely encapsulated by connective tissue if it is to be successful, probably because encapsulated implants will be isolated from the rest of the host tissue, restricting the destructive reaction to that area.

Dolwick and colleagues[18] have described cell-mediated immunity to the inciting agent present in a foreign-body reaction. Granulomatous inflammation with foreign-body giant cells usually originates as an immune reaction to an offending agent that is nondegradable or difficult to process and destroy. Timmis and colleagues[88] have also considered that silicone microparticles may act as a hapten-like substance, adsorbing tissue or plasma proteins to form an antigen complex. Granulomatous in-

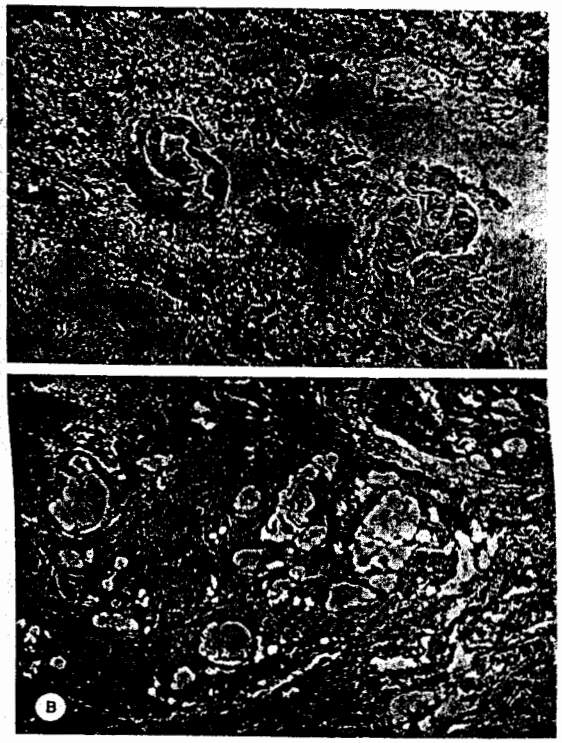

Figure 6. Responses of dermal grafts. *A*, Survival of dermal graft containing sweat gland and its duct. *B*, Silastic foreign-body reaction with chronic inflammation in same graft, which shows extensive hyalinization. (Hematoxylin and eosin stain; original magnification ×250)

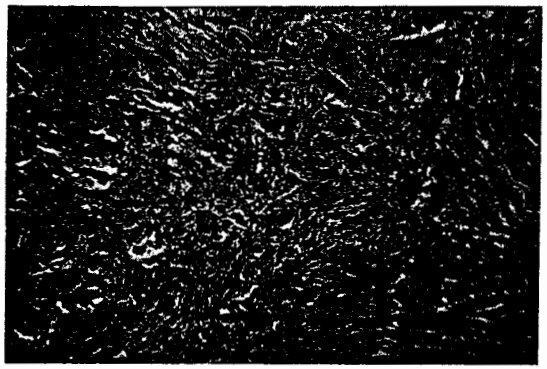

Figure 7. Proplast foreign-body reaction in a dermal graft. (Hematoxylin and eosin stain; original magnification ×250)

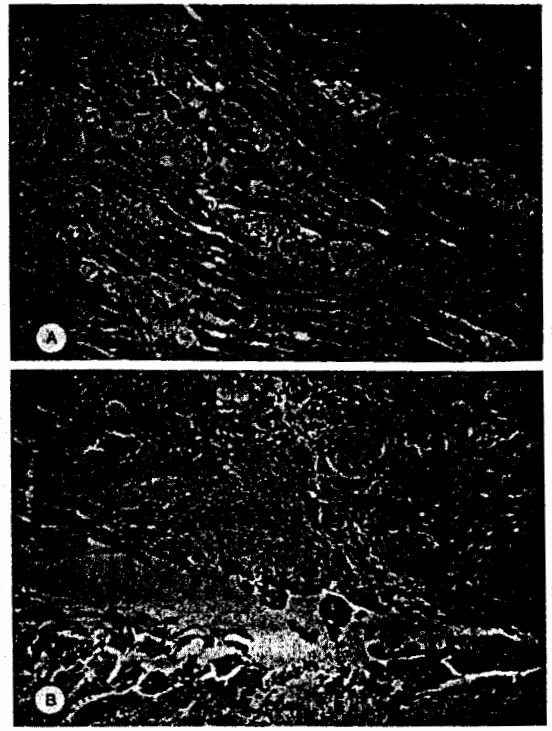

Figure 8. Responses of temporalis muscle flaps. *A*, Survival of temporalis flap consisting of skeletal muscle bundles with interstitial nerve fibers and adipose tissue. *B*, Same flap showing extensive degeneration with Proplast foreign-body reaction and chronic inflammation. (Hematoxylin and eosin stain; original magnification ×250)

flammation will thus be decreased when the fibrous connective tissue grows into the implant. However, in a long-term implant, the histologic constitution of the foreign-body reaction is mainly macrophages and multinucleated giant cells around the particles of implant in the fibrotic stroma. The lack of lymphocytes with the same inciting agent is difficult to reconcile with a specific cell-mediated immunity.

Silicone cytotoxicity may have contributed to the exuberant response seen in the peri-implant tissue.[22] Testing using cell cultures has documented the cytotoxic effects of these materials.[7] A predominant phenomenon is the inevitable fibrosis in the surrounding tissue. This process is possibly related to the cytotoxicity of the implant.[36, 37] This reaction has been used by practitioners with temporary Silastic implants to keep joint recesses open and to stimulate a covering of articular bone. Timmis[46] and Eriksson[17] and their coworkers have shown that particles of implant are present in the surrounding tissue as early as 1 month postoperatively with an accompanying giant-cell reaction. The peak of the foreign-body reaction to implant particles seems to be around 3 to 4 months. The tissue response will persist for years as the implant continues to shed particles.

The giant-cell response has been reported to extend into bone, muscle, adipose tissue, and even lymph nodes.[31] Lymph node involvement by implant particles is seen not only adjacent to the joint but also at a distance.[9, 23, 46, 50] In our series, two cases of preauricular lymph-node involvement were seen. One followed a

Silastic implant in the ipsilateral TMJ. The other showed both Proplast and silicone particles in macrophages in the lymph nodes following both implants in the ipsilateral TMJ (Fig. 4). These widely dispersed microscopic and macroscopic granulomatous responses are very difficult to remove totally from the joint and adjacent tissue and may be part of the reason for the many repeat failures after surgical removal of the implant. Numerous articles have emphasized the destructive nature of foreign-body reactions to interpositional implants, but no comments have been made about the influence of residual implant material after the implant has been removed. This study has presented cases in which residual material has persisted and contributed to the demise of subsequent biologic grafts as long as 5 years after the removal of the original alloplastic implant.

We abandoned alloplastic interpositional implants in 1985 and have used several autografts and allografts to repair the damage caused by the alloplastic foreign-body reaction. Dermis had been used in 1985 and afterward. Lyophilized dura mater was used for a short time in 1986 then abandoned because of findings of foreign-body reaction and arthrofibrosis and the possibility of disease transmission. Pedicled temporalis muscle flaps have also been employed. Both dermis and dura mater showed partial or complete degeneration, necrosis, and persistent residual foreign-body reaction (Figs. 5 through 7). Only the pedicled temporalis muscle fascial flap has shown resistance to foreign-body reaction. However, even this graft has exhibited progressive muscle degeneration (Fig. 8).

Cartilage and bone formation were relatively common findings in addition to the ingrowth of fibrous tissue. Diminishing vascularity associated with tissue fibrosis will decrease local oxygen tension. The fibrous tissue will transform into chondroid or osseous tissue or both.[39] Chronic inflammation and foreign-body reaction in addition to surgical trauma in the joint with an implant promote the process of fibrosis. That reaction may be responsible for subsequent fibrous or osseous ankylosis of the joint.

The foreign-body reaction associated with PTFE in the TMJ caused more severe osseous erosions of both the mandibular condyle and the glenoid fossa than that of Silastic implants.[43] In two cases reported by Schellhas and associates,[42] granulation tissue had eroded through the temporal bone to the dura of the middle cranial fossa. Five of our PTFE implant cases presented a similar severity of complications.

It is now becoming increasingly obvious that a diagnosis of destructive foreign-body reaction should be made as early as possible in order to minimize morbidity. The results of this and other studies have demonstrated that both silicone rubber and Teflon-Proplast are not biologically acceptable implant materials in the functional TMJ.

REFERENCES

1. Aptekar RG, Davie JM, Cattell HS: Foreign body reaction to silicone rubber: Complication of a finger joint implant. Clin Orthop 98:231, 1974
2. Arem AJ, Rasmussen D, Maddren JW: Soft tissue response to Proplast: Quantitation of scar ingrowth. Plast Reconstr Surg 61:214, 1978
3. Aronowitz JA, Bormely SF, Suma M: Long term stability of Teflon orbital implants. Plast Reconstr Surg 79:166, 1986
4. Buchhorn GH, Willert HG: Effects of plastic wear particles on tissue. *In* Williams DF (ed): Biocompatibility of Orthopedic Implants. Boca Raton, Florida, CRC Press, 1982, pp 225–257
5. Bessette RW, Katzberg R, Natiella JR, et al: Diagnosis and reconstruction of the human temporomandibular joint after trauma or internal derangement. Plast Reconstr Surg 75:192, 1985
6. Bronstein SL: Retained alloplastic temporomandibular joint disc implants: A retrospective study. Oral Surg Oral Med Oral Pathol 64:135, 1987
7. Chawla AS: Toxicity evaluation of a novel filler free silicone rubber biomaterial by cell culture techniques. J Biomed Mater Res 16:501, 1962
8. Charnley J: Tissue reactions to polytetrafluoroethylene. Lancet 2:1379, 1963
9. Christie AJ, Weinberger KA, Dietrich M: Silicone lymphadenopathy and synovitis: Complications of silicone elastomer finger joint prostheses. JAMA 237:1463, 1977
10. Christie AJ, Weinberger KA, Dietrich M: Complications of silicone elastomer prostheses [letter]. JAMA 238:939, 1977
11. Davis PKB, Jones SM: The complications of Silastic implant experience with 137 consecutive cases. Br J Plast Surg 24:405, 1971
12. Dolwick MF, Aufdemorte TB: Silicone induced foreign body reaction and lymphadenopathy after temporomandibular joint arthroplasty. Oral Surg Oral Med Oral Pathol 59:449, 1985
13. Dechamplain RW, Gallagher CS, Marshall ET: Autopolymerizing Silastic for interpositional arthroplasty. J Oral Maxillofac Surg 46:522, 1988
14. Estabrooks LN, Murnane TW, Doku HC: The role of condylotomy with interpositional silicone rubber in temporomandibular joint ankylosis. Oral Surg Oral Med Oral Pathol 34:2, 1972
15. Epstein LI: Clinical experiences with Proplast as an implant. Plast Reconstr Surg 63:219, 1979
16. Eiken O, Lindstrom C, Jonsson K: Silicone carpal implants: Risk or benefit? Scand J Plast Reconstr Surg 19:295, 1985
17. Eriksson L, Westesson P-L: Deterioration of temporary

silicone implant in the temporomandibular joint: A clinical and arthroscopic follow-up study. Oral Surg Oral Med Oral Pathol 62:2, 1986
18. Ferlic DC, Clayton ML, Holloway M: Complications of silicone implant surgery in the metacarpophalangeal joint. J Bone Joint Surg 57[A]:991, 1975
19. Freeman BC: Proplast: A porous implant for contour restoration. Br J Plast Surg 29:158, 1976
20. Florine BL, Gatto DJ, Wade ML, et al: Tomographic evaluation of temporomandibular joints following discoplasty or placement of polytetrafluoroethylene implants. J Oral Maxillofac Surg 48:183, 1988
21. Gayou R, Rudolph R: Capsular contraction around silicone mammary prosthesis. Ann Plast Surg 2:62, 1979
22. Groff GD, Schned AR, Tayer TH: Silicone induced adenopathy eight years after metacarpophalangeal arthroplasty. Arthritis Rheum 24:1578, 1981
23. Gordon M, Bullough PG: Synovial and osseous inflammation in failed silicone rubber prostheses: A report of six cases. J Bone Joint Surg 64[A]:574, 1982
24. Gallagher DM, Wolford LM: Comparison of Silastic and Proplast implants in the temporomandibular joint after condylectomy for osteoarthritis. J Oral Maxillofac Surg 40:627, 1982
25. Hansen WC, Deshaza BW: Silastic reconstruction of temporomandibular joint meniscus. Plast Reconstr Surg 43:388, 1969
26. Habbi I, Murnane TW, Doku HC: Silastic and Supramid in arthroplasty of the temporomandibular joint in the rabbit. J Oral Surg 28:267, 1970
27. Homsy CA: Biocompatibility in selection of materials for implantation. J Biomed Mater Res 4:341, 1970
28. Homsy CA: Implant stabilization: Chemical and biochemical considerations. Orthop Clin North Am 4:295, 1973
29. Homsy CA, Kent JN, Hinds EC: Materials for oral implantation: Biological and functional criteria. J Am Dent Assoc 86:817, 1973
30. Homsy CA, Cain TE, Kessler FB, et al: Porous implant systems for prosthesis stabilization. Clin Orthop 89:220, 1972
31. Hausner RJ, Schoen FJ, Pierson KK: Foreign body reaction to silicone gel in axillary lymph nodes after an augmentation mammoplasty. Plast Reconstr Surg 62:381, 1978
32. Hall HD: Meniscectomy for damaged discs of the temporomandibular joint. South Med J 78:569, 1985
33. Halstead A, Jones CW, Rawlings RD: A study of the reaction of human tissue to Proplast. J Biomed Mater Res 13:121, 1979
34. Heffez L, Mafee MF, Rosenberg H, et al: CT evaluation of TMJ disc replacement with a Proplast-Teflon laminate. J Oral Maxilofac Surg 45:657, 1987
35. Hall BK: Cartilage. Biomedical Aspects, vol 3. New York, Academic Press, 1988, pp 322–323
36. Imber C, Schwager RC, Guthrie RH, et al: Fibrous capsule formation after subcutaneous implantation of synthetic materials in experimental animals. Plast Reconstr Surg 54:183, 1974
37. Irving IM, Castilla P, Hall EG, et al: Tissue reaction to pure and impregnated Silastic. J Pediatr Surg 6:724, 1971
38. Jancke JB, Komorn RM, Cohn AM: Proplast in cavity obliteration and soft tissue augmentation. Arch Otolaryngol 100:24, 1974
39. Jancke JB, Shea JJ: Self-stabilizing Proplast total osseocular replacement prostheses in tympanoplasty. Laryngoscope 65:1550, 1975
40. Jones W, Jones D: The tissue response to Proplast coated Thompson prosthesis and the development of a femoral stem design for use with porous coatings. Proc R Coll Surg 61:381, 1979
41. Kalanich S, Walker RV: Silastic implant as a part of temporomandibular joint arthroplasty: Evaluation of its efficacy. Br J Oral Maxillofac Surg 25:222, 1987
42. Kaplan PA, Ruskin JD, Tu HK, et al: Erosive arthritis of the temporomandibular joint caused by Teflon-Proplast implants: Plain film features. AJR 151:337, 1988
43. Katzberg RW, Laskin DM: Radiographic and clinical significance of temporomandibular joint alloplastic disc implants. AJR 151:736, 1988
44. Kent JN, Homsy CA, Hinds EC: Proplast in dental facial reconstruction. Oral Surg Oral Med Oral Pathol 38:512, 1974
45. Kent JN, Block MS, Homsy CA, et al: Experience with a polymer glenoid fossa prosthesis for partial or total temporomandibular joint reconstruction. J Oral Maxillofac Surg 48:520, 1986
46. Kent JN, Misiek DJ, Akin RK, et al: Temporomandibular condylar prostheses: A ten year report. J Oral Maxillofac Surg 41:245, 1983
47. Kessler FB, Homsy CA, Berkeley ME, et al: Obliteration of traumatically induced articular surface defects using a porous implant. J Hand Surg 5:328, 1980
48. Kirch T: Silicone lymphadenopathy. Hum Pathol 11:240, 1980
49. Knelland JB, Ryan DE, Carrera G, et al: Failed temporomandibular joint prosthesis: MR imaging. Radiology 165:179, 1987
50. Lagrotteria L, Scapino R, Granston AS, et al: Patient with lymphadenopathy following temporomandibular joint arthroplasty with Proplast. J Craniomandib Prac 4:172, 1986
51. Leidholt JD, Gorman HA: Teflon hip prosthesis in dogs. J Bone Joint Surg 47[A]:1414, 1965
52. Malizia AA, Reiman HM, Myers RP, et al: Migration and granulomatous reaction after periurethral injection of polytef (Teflon). JAMA 251:3277, 1984
53. Marzoni FA, Upchurch SE, Lambert CJ: An experimental study of silicone as a soft tissue substitute. Plast Reconstr Surg 24:600, 1959
54. Merrill RG: A survey of preferred implant after TMJ discectomy. Presented at Western Society of Oral and Maxillofacial Surgeons Annual Meeting, Lake Tahoe, June 1986
55. Neal HB: Implants of Gore-Tex: Comparisons of Teflon-coated polytetrafluoroethylene carbon and porous polyethylene implants. Arch Otolaryngol 19:427, 1983
56. Parkes ML, Kamee FM, Merrin ML: Proplast chin augmentation. Laryngoscope 86:1829, 1976
57. Rhinelander FW, Stewart CL, Wilson JW, et al: Growth of tissue into a porous low modulus coating on intra-medullary nails. Clin Orthop Apr 1982, 293
58. Rippert ET, Flanigan TJ, Middlebrooks ML: New design for Silastic implants in temporomandibular joint surgery. J Oral Maxillofac Surg 44:163, 1986
59. Rooney TP, Haug RH, Toor AH, et al: Rapid condylar degeneration after glenoid fossa prosthesis insertion: Report of three cases. J Oral Maxillofac Surg 46:240, 1988
60. Rosenthal DI, Rosenberg AE, Schiller AL, et al: Destructive arthritis due to silicone: A foreign body reaction. Radiology 149:69, 1983
61. Sanders B, Brady FA, Adams D: Silastic cap temporomandibular joint prostheses. J Oral Surg 35:933, 1977
62. Schellhas KP, Wilkes CH, El-Deeb M, et al: Permanent Proplast temporomandibular joint implants: MR imaging of destructive complication. AJR 151:731, 1988
63. Smith RJ, Atkinson RE, Jupiter JB: Silicone synovitis of the wrist. J Hand Surg 10A:47, 1985
64. Swanson AB: Finger joint replacement by silicone rubber implants and its concept of implant fixation by encapsulation. Ann Rheum Dis 28(suppl):47, 1969
65. Swanson AB: Flexible implant arthroplasty for arthritic finger joints. J Bone Joint Surg 54[A]:435, 1972
66. Swanson AB: Complications of silicone elastomer prostheses [letter]. JAMA 238:939, 1977
67. Swanson AB, Meester WD, Swanson G, et al: Durability of silicone implants: An in vivo study. Orthop Clin North Am 4:1097, 1973
68. Timmis DP, Aragon SB, Van Sickels J, et al: Comparative study of alloplastic materials for temporomandibular joint disc replacement in rabbits. J Oral Maxillofac Surg 44:541, 1986
69. Vistnes LM, Ksander GA, Kosek J: Study of encapsulation of silicone rubber implants in animals: A foreign body reaction. Plast Reconstr Surg 62:580, 1978
70. Westesson P-L, Eriksson L, Lindstrom C: Destructive lesions of the mandibular condyle following discectomy with temporary silicone implant. Oral Surg Oral Med Oral Pathol 63:143, 1987
71. Worsing RA, Engber WD, Lange TA: Reactive synovitis from particulate Silastic. J Bone Joint Surg 4:581, 1982

Department of Oral and Maxillofacial Surgery
Oregon Health Sciences University
611 Southwest Campus Drive
Portland, Oregon 97201-3097

APPENDIX 3.—FDA WARNING LETTERS TO MANUFACTURERS OF JAW IMPLANTS AND FDA SAFETY ALERT TO DENTISTS

JUN 12 1992

WARNING LETTER

CERTIFIED MAIL-
RETURN RECEIPT REQUESTED

Dr. Andrew Tose
President
CeraMed Corporation
12860 West Cedar Drive
Lakewood, Colorado 80228

Re: PermaRidge Alveolar Ridge
Hydroxylapatite Matrix

OsteoGraf/AR Alveolar Ridge
Hydroxylapatite

Dear Dr. Tose:

It has come to our attention that CeraMed Corporation has been promoting and commercially distributing PermaRidge and OsteoGraf/AR Alveolar Ridge Hydroxylapatite implants. These products are devices as that term is defined in Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

Your firm has not submitted a premarket notification for the above products, as required by Section 510(k) of the Act. Failure to submit a premarket notification at least 90 days prior to the intent to market a device in interstate commerce is a prohibited act under Section 301(p) of the Act, and results in the device being misbranded within the meaning of Section 502(o) of the Act.

Should your Alveolar Ridge Hydroxylapatite implant devices be found to be not substantially equivalent to existing class I or class II devices, then they are classified by statute in class III, requiring an application for premarket approval (PMA) to support the safety and efficacy of the devices. Failure to submit a PMA application prior to marketing a class III device adulterates the devices under Section 501(f)(1)(B) of the Act.

Continued distribution of these devices may result in the misbranding and/or adulteration of the devices, which may result in regulatory actions without further notice. These actions include, but are not limited to seizure, injunction, or civil penalties.

You should notify this office in writing within fifteen (15) working days of your receipt of this letter of the specific steps you have taken to correct these violations, including an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be completed within fifteen (15) working days, state the reason for the delay and the time within which the correction will be completed. A copy of this letter has been provided to the Denver District Office. We request that the action being taken to remove the products from the market also be reported to them.

Your response to this letter should be sent to FDA, Center for Devices and Radiological Health, Regulatory Guidance Branch (HFZ-323), 1390 Piccard Drive, Rockville, Maryland 20850, to the attention of Mr. Eric Latish.

Sincerely yours,

Ronald M. Johnson
Director
Office of Compliance
and Surveillance
Center for Devices and
Radiological Health

MAY 29 1992

WARNING LETTER

CERTIFIED MAIL-
RETURN RECEIPT REQUESTED

Douglas Morgan, D.D.S.
President
TMJ Research Foundation
3043 Foothill, Suite #8
La Cresenta, California 91214

Re: TMJ Implants for Partial or
Total Joint Prostheses

Dear Dr. Morgan:

It has come to our attention that you have been promoting and commercially distributing temporomandibular joint (TMJ) implants intended as partial or total joint prostheses. These products are medical devices as that term is defined by Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

Your firm has not submitted a premarket notification for the above products, as required by Section 510(k) of the Act. Failure to submit a premarket notification at least 90 days prior to the intent to market a device in interstate commerce is a prohibited act under Section 301(p) of the Act, and results in the device being misbranded within the meaning of Section 502(o) of the Act. Additionally, your firm has not submitted an establishment registration nor listed any devices with the FDA, as required by 21 CFR Part 807. Failure to do this also misbrands your device within the meaning of Section 502(o).

Should your TMJ devices be found to be not substantially equivalent to existing class I or class II devices, then they are classified by statute in class III, requiring an application for premarket approval (PMA) to support the safety and efficacy of the device. Failure to submit a PMA application prior to marketing a class III device, adulterates your device under Section 501(f)(1)(B) of the Act.

Continued distribution of these devices may result in the misbranding and/or adulteration of the devices, which may result in regulatory actions without further notice. These actions include, but are not limited to, seizure, injunction, or civil penalties.

You should notify this office in writing within fifteen (15) working days of your receipt of this letter of the specific steps you have

Dr. Morgan - Page 2

taken to correct these violations, including an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be completed within fifteen (15) working days state the reason for the delay and the time within which the correction will be completed. A copy of this letter has been provided to the Los Angeles District Office. We request that action being taken to remove the products from the market also be reported to them.

Your response to this letter should be sent to FDA, Center for Devices and Radiological Health, Regulatory Guidance Branch, (HFZ-323), 1390 Piccard Drive, Rockville, Maryland 20850, to the attention of Mr. Eric Latish.

Sincerely yours,

Ronald M. Johnson
Director
Office of Compliance
and Surveillance
Center for Devices and
Radiological Health

MAY 29 1992

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. Richard A. Buss
President
Osteomed Corporation
6062 San Fernando Road
Glendale, California 91202

Re: TMJ Implants for Partial or
Total Joint Prostheses

Dear Mr. Buss:

It has come to our attention that Osteomed Corporation has been promoting and commercially distributing temporomandibular joint (TMJ) implants intended as partial or total joint prostheses. These products are medical devices as that term is defined in Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

Your firm has not submitted a premarket notification for the above products, as required by Section 510(k) of the Act. Failure to submit a premarket notification at least 90 days prior to the intent to market a device in interstate commerce is a prohibited act under Section 301(p) of the Act, and results in the device being misbranded within the meaning of Section 502(o) of the Act.

Should your TMJ devices be found to be not substantially equivalent to existing class I or class II devices, then they are classified by statute in class III, requiring an application for premarket approval (PMA) to support the safety and efficacy of the device. Failure to submit a PMA application prior to marketing a class III device, adulterates your device under Section 501(f)(1)(B) of the Act.

Continued distribution of these devices may result in the misbranding and/or adulteration of the devices, which may result in regulatory actions without further notice. These actions include, but are not limited to, seizure, injunction, or civil penalties.

You should notify this office in writing within fifteen (15) working days of your receipt of this letter of the specific steps you have taken to correct these violations, including an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be completed within fifteen (15) working days state the reason for the delay and the time within which the correction will be completed. A copy of this letter has been provided to the Los Angeles District Office. We request that action being taken to remove the products from the market also be reported to them.

Page 2 - Mr. Buss

Your response to this letter should be sent to FDA, Center for Devices and Radiological Health, Regulatory Guidance Branch, (HFZ-323), 1390 Piccard Drive, Rockville, Maryland 20850, to the attention of Mr. Eric Latish.

Sincerely yours,

Ronald M. Johnson
Director
Office of Compliance
and Surveillance
Center for Devices and
Radiological Health

MAY 29 1992

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. Roger Ammann
President
Techmedica, Inc.
1380 Flynn Road
Camarillo, California 93012

Re: TMJ Implants for Partial or
Total Joint Prostheses

Dear Mr. Ammann:

It has come to our attention that Techmedica, Incorporated has been promoting and commercially distributing temporomandibular joint (TMJ) implants intended as partial or total joint prostheses. These products are medical devices as that term is defined in Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

Your firm has not submitted a premarket notification for the above products, as required by Section 510(k) of the Act. Failure to submit a premarket notification at least 90 days prior to the intent to market a device in interstate commerce is a prohibited act under Section 301(p) of the Act, and results in the device being misbranded within the meaning of Section 502(o) of the Act.

Should your TMJ devices be found to be not substantially equivalent to existing class I or class II devices, then they are classified by statute in class III, requiring an application for premarket approval (PMA) to support the safety and efficacy of the device. Failure to submit a PMA application prior to marketing a class III device, adulterates your device under Section 501(f)(1)(B) of the Act.

Continued distribution of these devices may result in the misbranding and/or adulteration of the devices, which may result in regulatory actions without further notice. These actions include, but are not limited to, seizure, injunction, or civil penalties.

You should notify this office in writing within fifteen (15) working days of your receipt of this letter of the specific steps you have taken to correct these violations, including an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be completed within fifteen (15) working days state the reason for the delay and the time within which the correction will be completed. A copy of this letter has been provided to the Los Angeles District Office. We request that the action being taken to remove the products from the market also be reported to them.

Your response to this letter should be sent to FDA, Center for Devices and Radiological Health, Regulatory Guidance Branch, (HFZ-323), 1390 Piccard Drive, Rockville, Maryland 20850, to the attention of Mr. Eric Latish.

Sincerely yours,

Ronald M. Johnson
Director
Office of Compliance
and Surveillance
Center for Devices and
Radiological Health

WARNING LETTER

MAY 29 1992

CERTIFIED MAIL-
RETURN RECEIPT REQUESTED

Ms. Mary P. Morgan
President
TiMesh, Inc.
76 Spectrum Road
Las Vegas, Nevada 89101

Re: TMJ Implants for Partial or
Total Joint Prostheses

Dear Ms. Morgan:

It has come to our attention that TiMesh, Incorporated has been promoting and commercially distributing temporomandibular joint (TMJ) implants intended as partial or total joint prostheses. These products are medical devices as that term is defined in Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

Your firm has not submitted a premarket notification for the above products, as required by Section 510(k) of the Act. Failure to submit a premarket notification at least 90 days prior to the intent to market a device in interstate commerce is a prohibited act under Section 301(p) of the Act, and results in the device being misbranded within the meaning of Section 502(o) of the Act.

Should your TMJ devices be found to be not substantially equivalent to existing class I or class II devices, then they are classified by statute in class III, requiring an application for premarket approval (PMA) to support the safety and efficacy of the device. Failure to submit a PMA application prior to marketing a class III device, adulterates your device under Section 501(f)(1)(B) of the Act.

Continued distribution of these devices may result in the misbranding and/or adulteration of the devices, which may result in regulatory actions without further notice. These actions include, but are not limited to, seizure, injunction, or civil penalties.

You should notify this office in writing within fifteen (15) working days of your receipt of this letter of the specific steps you have taken to correct these violations, including an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be completed within fifteen (15) working days

state the reason for the delay and the time within which the correction will be completed. A copy of this letter has been provided to the San Francisco District Office. We request that the action being taken to remove the products from the market also be reported to them.

Your response to this letter should be sent to FDA, Center for Devices and Radiological Health, Regulatory Guidance Branch, (HFZ-323), 1390 Piccard Drive, Rockville, Maryland 20850, to the attention of Mr. Eric Latish.

Sincerely yours,

Ronald M. Johnson
Director
Office of Compliance
and Surveillance
Center for Devices and
Radiological Health

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Bldg. 20, Denver Federal Center
Post Office Box 25087
Denver, Colorado 80225-0087
303-236-3000 (FTS: 776-3000)

January 27, 1992

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Robert W. Christensen, President
TMJ Implants, Inc.
17301 West Colfax Avenue, Suite 275
Golden, Colorado 80401

WARNING LETTER

Dear Mr. Christensen:

During an inspection of your firm TMJ Implants, Inc., located at 17301 West Colfax Avenue, Suite 275, Golden, Colorado, between December 16, 1991 and January 7, 1992, Investigator Jose R. Hernandez determined that your establishment had failed to provide pre-market notification submissions (Section 510(k) of the Federal Food, Drug, and Cosmetic Act) for certain implantable devices. Our inspection revealed that the manufacturing process was significantly altered by TMJ Implants, Inc. for the purpose of rendering the devices sterile. You were informed by Investigator Hernandez at the time of the inspection that a pre-market submission is required for such a change in the device manufacturing process.

In your January 10, 1992 letter to Mr. Richard Aleman, Director of Investigations, Denver District, you cite page 329 of the HHS Publication, "Sterile Medical Devices: A GMP Workshop Manual" as justification for not having to submit a 510(k) pre-market notification. However, per that document, a manufacturer must have "... provided adequate assurance through change control procedures, ... process validation, personnel training, and development of routine sterilization procedures that those changes could not affect the safety and effectiveness of the device...". Our inspection of your firm revealed that you did not properly validate this change in order to assure that radiation sterilization has not in fact affected the safety and effectiveness of your devices.

The continued marketing of medical devices without complying with the pre-market notification requirements of Section 510(k) causes the articles to be misbranded under Section 502(o) of the Act. The continued marketing of these devices may result in regulatory action without further notice. These actions include seizure and/or injunction.

Several deviations from the Good Manufacturing Practice Regulations (Title 21, Code of Federal Regulations, part 820) were noted during this inspection. Those deviations include:

1. Inadequate quality assurance and audit procedures (21 CFR 820.20(a) & (b));
2. Incomplete device master records (21 CFR 820.181);
3. Inadequate finished device inspection procedures (21 CFR 820.160), and
4. Failure to perform adequate complaint investigations (21 CFR 820.198(b)).

The above identification of violations is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure adherence with each of the regulations. Until these violations are corrected, Federal agencies will be informed that FDA recommends against the award of contracts for the affected products.

You should notify this office in writing, within 15 working days of receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to prevent the recurrance of similar violations. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the correction will be completed.

Your reply should be sent to the Food and Drug Administration, Denver District Office, Attention: Regina A. Barrell, Compliance Officer at the above address.

Sincerely,

John H. Scharmann
District Director

Enclosure:
FDA 483

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Bldg. 20, Denver Federal Center
Post Office Box 25087
Denver, Colorado 80225-0087
303-236-3000; FTS: 776-3000

May 27, 1992

Dr. Robert W. Christensen
President
TMJ Implants, Inc.
17301 West Colfax Avenue, Suite 275
Golden, Colorado 80401

Dear Dr. Christensen:

This letter is in response to your correspondence dated March 16, 1992 and April 17, 1992, and as a follow-up to our meeting of March 10, 1992. As you will recall during our March 10 meeting, we discussed the need for your firm to have validated the sterilization procedures used on the Fossa and Condylar Prosthesis. We informed you that without such validation data, a premarket notification application (510(k)) was required to be submitted.

The documentation you submitted indicates that you have utilized a bioburden of 4.2 cfu's per device as the challenge for the AAMI B1 dose setting determinations. Examination of the bioburden data shows that some of the individual devices tested, greatly exceeded (five times the average of 4.2) this contamination level. The utilization of 4.2 cfu's and a verification dose of .4 Mrads may not be valid as it appears that your firm has not reliably determined the true bioburden levels present on your devices. In order to support your use of these levels, the results of several lots for which bioburden levels were determined would need to be studied.

The package integrity testing performed by your firm is not adequate in validating the sealing operations. Your firm has not documented the sealing equipment operational settings, in order to demonstrate the process, are under control and that the settings are traceable to the satisfactory package integrity results submitted. Further, you have failed to submit standard operating procedures that reflect the operational settings for the packaging equipment.

The adequacy of these and other responses made to the FDA 483 list of observations regarding sterilization and/or GMP issues will be determined at the next inspection of your facility. However, we

have determined that the changes made to your devices are indeed significant ones which do, in fact, require the submission of a premarket notification application.

Aside from the issue of sterilization, it has come to our attention that at a symposium held in Morristown, New Jersey, March 1992, TMJ Implants advertised that they have made "great improvements" to these implants. These improvements include a change in the articulating surface of the implants, as well a change in the condylar stem geometry in order to increase the size in response to reports of stem fractures. We consider these changes in the devices to be significant, as stated above, and, therefore, require a 510(k) filing, per 21 Code of Federal Regulations, part 807.81 (a)(3)(i). Per the warning letter dated January 27, 1992, the continued marketing of medical devices without complying with the pre-market notification requirements of Section 510(k), causes the articles to be misbranded under Section 502(o) of the Act. Failure to comply with the above requirements may result in such regulatory action as seizure of the devices or injunction without further notice.

Sincerely,

Regina A. Barrell
Compliance Officer

bcc:
HFA 224
HFC 230
HFF 310
HFZ 323
DIB f/u 6-30-92
EI
RF
[redacted]
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DEPARTMENT OF HEALTH & HUMAN SERVICES — Public Health Service

Food and Drug Administration
1390 Piccard Drive
Rockville MD 20850

MAY 29 1992

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Charles A. Homsy, Sc.D.
President and Chairman of the Board,
Novamed, Inc.
Chairman of the Board,
Oral Surgery Marketing Inc.
3142 Telge Street
Houston, Texas 77054

Dear Dr. Homsy:

After review by our Office of Device Evaluation of your labeling, catalogues and other material obtained during inspections of your companies, we have concluded that Proplast devices (including those made in whole or in part of Proplast I, Proplast II, or Proplast HA) are in violation of the Federal Food, Drug, and Cosmetic Act (the Act). These devices include, but are not limited to:

Product Identification

Otoplasty
Glenoid Fossa VK
Mandibular Condyle VK
Ocular Globe (Proplast II)
Trochanter Pad (Proplast HA)
Staple Cushion Pad (Proplast HA)
Tissue Cusion Pad (Proplast HA)
Other Reconstruction Block & Sheeting material
Preformed Implants
Other Implants, i.e., mandible, forehead, maxilla, pectus and orbital areas

These devices are misbranded under Section 502(o) in that you have either failed to file a premarket notification submission as required by Section 510(k) of the Act or these devices have undergone significant changes in labeling or material composition, which warrant the submission of a new premarket notification [510(k)].

Furthermore, we note that labeling for your Proplast products contain claims which have not been included in any previous 510(k)'s. These claims include references which describe the properties of the Proplast material, such as "chemically inert; its porosity promotes stabilization enabling as much as 80% of implant volume to become tissue without encapsulation, sagging or migration." Labeling also describes Proplast II and HA as being "inert, biocompatable, free from observable systemic or cytotoxic effects, and aids in the migration of cells, and Proplast HA as osteoconductive."

We are not aware of preclinical or clinical evidence to support these claims. Therefore, if you have any information supported by preclinical or clincal evicence from scientifically valid studies that you wish us to consider you must provide the information in new 510(k) submissions filed in accordance with 21 CFR 807.81, as outlined in the described format in 21 CFR 807.90.

Continued distribution of these devices may result in the misbranding and/or adulteration of the devices, which may result in regulatory action without further notice. These actions include, but are not limited to, seizure, injunction, civil penalties, and/or automatic detention and refusal to permit entry of products offered for entry into the United States.

You should notify this office in writing within fifteen (15) working days of your receipt of this letter of the specific steps you have taken to correct these violations, including an explanation of each step being taken to prevent the recurrence of similar violations. A copy of this letter has been provided to the Dallas District Office. We request that the action being taken to remove these violative products from the market be reported to them.

Your response to this letter should be sent to:

Mr. Donald Watchko
Case Management Branch, HFZ-322
Center for Devices and Radiological Health
Food and Drug Administration
1390 Piccard Drive
Rockville, Maryland 20850

Sincerely yours,

William H. Damaska

William H. Damaska
Director
Division of Compliance Operations
Office of Compliance and Surveillance
Center for Devices and
Radiological Health

cc:

Linda Marshall, Esq.
Alexander & McEvily
5 Post Oak Park
24th Floor
Houston, Texas 77027

Dr. Charles A. Homsy
11526 Raintree Circle
Houston, Texas 77024

DEPARTMENT OF HEALTH & HUMAN SERVICES — Public Health Service

Food and Drug Administration
Rockville MD 20857

FDA SAFETY ALERT

SERIOUS PROBLEMS WITH PROPLAST®-COATED TMJ IMPLANT

To Oral and Maxillofacial Surgeons: December 28, 1990

This is to urge you to re-examine all of your patients who have received temporomandibular joint (TMJ) interpositional implants which were manufactured or marketed by either Vitek Inc. or Oral Surgery Marketing, Inc. (both of Houston, Texas). These implants were distributed between February 1983 and June 1988 and were the subject of Vitek's March 23, 1990 safety alert. The patent for this medical device is currently held by Hadaco, Ltd. (British Virgin Islands). Any remaining implants should not be used and should be returned to:

Bonham, Carrington, and Fox
Bankruptcy Trustee for Vitek, Inc.
400 One Shell Plaza
Houston, Texas 77002
Attention: Mr. Bea Floyd

PROBLEM:
These implants, all of which are made of Proplast® (Teflon®-carbon or Teflon®-aluminum oxide fiber composite), have been associated with implant perforation, fragmentation and/or a foreign body response which may result in progressive bone degeneration of the mandibular condyle and/or the glenoid fossa (1-3). If bone degeneration continues unchecked, patients may experience intense pain and severely limited joint function. One study found that all patients with Proplast®-coated TMJ interpositional implants who experienced complications demonstrated progressive bone degeneration in as little as one to two years (1). In a second study, implant failure and bone degeneration occurred in both symptomatic and asymptomatic patients (2).

RECOMMENDATIONS:
Because asymptomatic patients may experience bone degeneration, FDA recommends that all patients with these implants who have not had a radiograph taken in the past six months undergo immediate and appropriate radiographic examination. The examination will assist in determining if loss of implant integrity has occurred or if progressive bone degeneration is occurring.

- If loss of implant integrity or progressive bone degeneration is not occurring, regular radiographic examinations of the implant should be performed every six months for as long as it remains in the jaw.

- If either loss of implant integrity or progressive bone degeneration is found, explantation may be appropriate. If explantation is chosen, patients should be evaluated to determine what alternative procedures might be appropriate, e.g., a non-Proplast® coated implant, an autologous bone graft, or no replacement (symptomatic management).

APPENDIX 4.—DOCUMENTS PROVIDED BY MANUFACTURERS ABOUT SAFETY OF THEIR JAW IMPLANTS

DOW CORNING

[redacted]

June 2, 1992

The Honorable Ted Weiss
Chairman, Subcommittee on Human Resources
and Intergovernmental Relations
U. S. Government Operations Committee
B-372 Rayburn House Office Building
Washington, D.C. 20515-5148

Dear Chairman Weiss:

Thank you for your letter of May 28th offering Dow Corning the opportunity to provide information for your June 4 subcommittee hearing.

As indicated in the attached product brochure and package insert, Dow Corning developed a temporary implant specifically designed for treating internal derangements in the temporomandibular joint or TMJ. Available since 1985, the Silastic® Temporomandibular Joint Implant HP (Wilkes Design) differs from other TMJ implants in the following ways:

- It is a temporary implant which should be removed one to two months after surgery. This modality was specifically selected to minimize the potential problems occasionally noted with long-term TMJ implants.

- This device is a disk used as a temporary spacer rather than a permanent total joint replacement implant. This approach was selected because it was known in the medical community that a permanent device could have complications in load bearing joints. For additional information, please reference the enclosed paper from the American Association of Oral and Maxillofacial Surgeons.

- The device is fully fabricated from silicone elastomer rather than other materials like carbon fiber or teflon.

Dow Corning's TMJ implant became commercially available in 1985 after receiving FDA 510K approval in 1984. This special purpose implant was specifically designed solely for the treatment of TMJ dysfunctions in accordance with the package insert and is our preferred product for those specific situations.

Dow Corning also provides general purpose silicone sheeting which is sold to distributors for a variety of applications. This material is sometimes used to prevent soft tissue fibrosis or bony ankylosis following surgical corrections of trismus, a condition in which a patient has problems opening his or her jaw, or related TMJ dysfunctions . The attached product data sheet for Silastic Medical Sheeting makes reference to this application, as well as the many others. It has been known in the medical community that this sheeting is not to be used as a permanent interface in load bearing joints. The attached product data sheet for Silastic® HP sheeting clearly recommends that this material not be used as a permanent interface. This additional recommendation was included to ensure physicians would not infer that they could use this newer, more durable form of sheeting as a permanent interface.

In addition to product literature, I am also including the following:

- A summary of our safety research which we developed as a specific response to your request of May 28th.
- 1984 Criteria for TMJ Meniscus Surgery. This paper was developed by the Ad Hoc Study Group on TMJ Meniscus Surgery, under the auspices of the American Association of Oral and Maxillofacial Surgeons.

In addition to sending this letter and information via facsimile, I am arranging to have original copies of our product literature delivered to Dr. Diana Zuckerman of your staff on Tuesday, June 2. An original copy of this letter and the attachments will follow.

If I can be of any more assistance to you, please do not hesitate to contact me.

Very truly yours,

Robert T. Rylee II
Chairman
Health Care Business

cc: Diana Zuckerman, Ph.D.

SYNOPSIS

NON-CLINICAL BIOCOMPATIBILITY STUDIES OF SILICONE ELASTOMERS USED IN TEMPOROMANDIBULAR JOINT APPLICATIONS

This summary of non-clinical safety studies of silicone elastomers is directed to dimethylsiloxane elastomers, peroxide and platinum-catalyzed, that are relevant to materials used in temporomandibular joint (TMJ) applications. Safety studies of closely related dimethyl elastomers are also included in the non-clinical review.

ACUTE TOXICITY - These silicone elastomers are not toxic with regard to cytotoxicity, U.S.P. Class V, pyrogenicity, skin sensitization, hemolysis or thrombogenicity.

TERATOLOGY/REPRODUCTION - Silicone elastomers are without teratogenic activity nor do they alter normal reproduction.

GENOTOXICITY - Silicone elastomers and elastomer extracts are genetically inactive in the Ames bacterial reverse mutation assay.

IMMUNOLOGY - Platinum system elastomer does not have immunoenhancement or immunosuppression activity in validated animal models.

SUBCHRONIC/CHRONIC TOXICITY - Peroxide and platinum system silicone elastomers all associated with a foreign body reaction characteristic of a broad range of persistent alloplastic materials. That is, an early acute inflammatory response is superseded by a chronic inflammatory phase (i.e., an infiltrate of predominantly macrophages) that transitions to fibroblastic activity and fibrous connective tissue encapsulation of the foreign body. A sparse dispersal of macrophages and giant cells may persist long-term although this is not characteristic of all implantation sites in all animals. This response pattern is the same for both intramuscular and subcutaneous implantation sites.

The results of elastomer implantation studies ranging in duration from a few days to 2 years demonstrate that reinforced silicone elastomers induce no consistent systemic adverse effects on any organ system.

Elastomer samples measuring 0.1x1 cm (0.245 cm^2) and total surface areas up to 2 cm_2 per rat do not induce implantation site tumors (solid-state tumorigenesis) nor an excess of tumors remote

from the implantation site.

ADME -The fumed amorphous silica used as a reinforcing silica maintains a stable distribution within silicone elastomers. In addition, the surface morphology of the elastomer is not influenced by up to 6 month subcutaneous implantation.

SILICONE ELASTOMERS USED IN TMJ APPLICATIONS

SUMMARY OF BIOCOMPATIBILITY TESTING

Silicone sheeting is known to have been used as an intra-articular spacing material to correct TMJ defects. In addition a fabricated spacer known as the Wilkes design is manufactured by Dow Corning Corporation and distributed by Dow Corning Wright. Sheeting catalog numbers 500, 501 and 502 are polydimethylsiloxane elastomers that are peroxide catalyzed using 2,4-dichlorobenzoyl peroxide. The basic materials in this category include MDF-372 (also known as MDX4-4515) and MDF-373 (also known as MDX4-4516). These peroxide-catalyzed elastomers are compositionally closely related. Safety studies supporting these materials are summarized below. Another elastomer sheeting and the Wilkes design TMJ device are both of the platinum-catalyzed high performance (H.P.) type. Safety data supporting these materials is summarized following the peroxide systems.

PEROXIDE-CATALYZED ELASTOMERS -

These peroxide-catalyzed elastomers encompass a small number of products by material number including MDF-372 (also known as MDX4-4515) and MDF-373 (also known as MDX4-4516).

ACUTE TOXICITY:

Acute toxicity testing of peroxide elastomers includes cytotoxicity, U.S.P. Class V, pyrogenicity, sensitization and hemolysis/thrombogenicity testing.

1. IN VITRO CYTOTOXICITY -

   Tissue cell culture biocompatibility testing usually employed WI-38 human embryonic lung cells. The tabulated results indicate that peroxide system elastomers are not cytopathic in culture.

TISSUE CELL CULTURE BIOCOMPATIBILITY

MATERIAL	DIRECT CONTACT	MATERIAL EXTRACTS
MDX4-4515	NCE	NCE
MDX4-4516	NCE	NCE

* NCE = No Cytopathic effect.

2. U.S.P. CLASS V -

U.S.P. Class V tests have been done for both of the peroxide elastomers. Each elastomer was tested for systemic toxicity in the mouse and intradermal toxicity in the rabbit using U.S.P. protocols. No adverse effects were seen.

3. PYROGENICITY -

Both peroxide elastomers pass U.S.P. pyrogenicity testing.

4. SENSITIZATION -

Both peroxide elastomers have been tested for skin sensitization in the guinea pig using topical contact and intradermal FCA injected between the insult and challenge applications of silicone gel. There was no evidence of sensitization for any of the silicone gel formulations.

5. HEMOLYSIS AND THROMBOGENICITY -

MDX4-4515 has been tested directly and as saline extracts for hemolytic activity using rabbit blood. This elastomer is not hemolytic.

MDX4-4515 has been assayed for thrombogenicity in a closed cell kinetic blood coagulation test using dog blood. This elastomer was found to not be more thrombogenic than a reference elastomer.

SUBCHRONIC TOXICITY:

SUBCHRONIC ELASTOMER IMPLANTATION

GEL	SPECIES	DOSE	DURATION	RESULT
MDX4-4515	Rabbit	4: 0.1x1 cm I.M.	3,30,90 Days	FBR
		2: 0.1x1 cm S.Q.	3,30,90 Days	FBR
MDX4-4515	Rabbit	4: 0.1x1 cm I.M.	30,60,90 Days	FBR
		2: 0.1x1 cm S.Q.	30,60,90 Days	FBR
MDX4-4515	Rabbit	4: 0.1x1 cm I.M.	7,28,91 Days	FBR
		2: 0.1x1 cm S.Q.	7,28,91 Days	FBR
MDX4-4515	Rabbit	4: 0.1x1 cm I.M.	7,28,91 Days	FBR
		2: 0.1x1 cm S.Q.	7,28,91 Days	FBR
MDX4-4515	Rabbit	4: 0.1x1 cm I.M.	7,28,91 Days	FBR
		2: 0.1x1 cm S.Q.	7,28,91 Days	FBR
MDX4-4516	Rabbit	4: 0.1x1 cm I.M.	10,30,90 Days	FBR
		2: 0.1x1 cm S.Q.	10,30,90 Days	FBR

* 4 rods I.M. and 2 rods S.Q. per animal.
# FBR = Foreign Body Reaction.

These subchronic studies indicate that peroxide system silicone elastomers are associated with a foreign body reaction characteristic of a broad range of persistent alloplastic materials such as the U.S.P. polyethylene employed as the control material in these studies. That is, an early acute inflammatory response is superseded by a chronic inflammatory phase (i.e., an infiltrate of predominantly macrophages) that transitions to fibroblastic activity and fibrous connective tissue encapsulation of the foreign body. A sparse dispersal of macrophages and giant cells may persist long-term although this is not characteristic of all implantation sites in all animals. This response pattern is the same for both intramuscular and subcutaneous implantation sites.

CHRONIC TOXICITY:

Three chronic peroxide-catalyzed elastomer studies are available as summarized in the following table.

CHRONIC ELASTOMER IMPLANTATION

MATERIAL	SPECIES	DOSE	DURATION	RESULT
MDX4-4515	Dog	5 dogs, Wafers, I.M. & S.Q. Perforated and not Perforated	3 Year	FBR #
MDX4-4515	Rat	0.1x1 cm Rod S.Q.	2 Year	NAE **
MDX4-4515	Dog	2 Dogs Amputation Stumps	10 Year	FBR with Particle Generation

\# FBR = Foreign Body Reaction.
** NAE = No Adverse Effect.

PLATINUM-CATALYZED ELASTOMERS -

These dimethyl elastomers are of the tear resistant high performance type and are classified as system D elastomers; i.e., platinum catalyzed. Safety studies are also available for several other elastomer products that contribute to an understanding of the safety of system D elastomers. The product designations are Q7-2423, Q7-2222, Q7-2383, Q7-2412, Q7-2424, Q7-2566, Q7-2722, Q7-2743, Q7-2744 and MDF-0077 and MDF-0081. All of these elastomers are closely related using the same elastomer base, amorphous silica filler, silicone plasticizer, catalyst, cross-linker and inhibitor in varying ratios to achieve the desired physical properties. In addition, some of these products contain additives such as water and barium sulfate to impart radiopacity.

ACUTE TOXICITY:

Acute toxicity testing of system D elastomers includes eye/skin/oral, cytotoxicity, U.S.P. Class V, pyrogenicity, sensitization and hemolysis/thrombogenicity testing.

1. IN VITRO CYTOTOXICITY -

   Tissue cell culture biocompatibility testing usually employed WI-38 human embryonic lung cells. The tabulated results indicate that system D elastomers are not cytopathic in culture.

TISSUE CELL CULTURE BIOCOMPATIBILITY

MATERIAL	DIRECT CONTACT	MATERIAL EXTRACTS
Q7-2222	NCE	NCE
Q7-2352	NCE	NCE
Q7-2412	NCE	NCE
Q7-2423	NCE	NCE
Q7-2424	NCE	NCE
Q7-2566	NCE	NCE
Q7-2643	NCE	NCE

TISSUE CELL CULTURE BIOCOMPATIBILITY (cONT)

MATERIAL	DIRECT CONTACT	MATERIAL EXTRACTS
Q7-2722	NCE	NCE
Q7-2743	NCE	NCE
Q7-2744	NCE	NCE
MDF-0077	NCE	--
MDF-0081	NCE	NCE

* NCE = No Cytopathic effect.

2. U.S.P. CLASS V -

U.S.P. Class V tests have been done for 11 of the 12 elastomers listed in the preceding table. Each elastomer was tested for systemic toxicity in the mouse and intradermal toxicity in the rabbit using U.S.P. protocols. No adverse effects were seen.

3. PYROGENICITY -

Ten of the 12 system D elastomers have passed U.S.P. pyrogenicity testing.

4. SENSITIZATION -

Ten of the 12 system D elastomers have been tested for skin sensitization in the guinea pig using topical contact and intradermal FCA injected between the insult and challenge applications of silicone gel. There was no evidence of sensitization for any of the silicone gel formulations.

5. HEMOLYSIS AND THROMBOGENICITY -

Q7-2566, Q7-2643 and Q7-2743 have been tested directly and as saline extracts for hemolytic activity using rabbit blood. Neither elastomer was found to induce hemolysis.

Q7-2383, Q7-2424,Q7-2566 and Q7-2643 have been assayed for thrombogenicity in a closed cell kinetic blood coagulation test using dog blood. These elastomers were found to not be

more thrombogenic than a reference elastomer.

TERATOLOGY/REPRODUCTION:

Elastomer Q7-2423/Q7-2551 was tested for teratogenic potential in the rabbit. U.S.P. polyethylene and a viscous solution of carboxymethylcellulose served as the control materials. All materials were implanted subcutaneously 6 weeks prior to insemination in groups of 25 rabbits. There were no significant treatment-related effects on adult female appearance, behavior, body weight change or necropsy findings for the silicone elastomer group. No developmental effects including teratogenicity were observed in the litters in the treatment group implanted with Q7-2423/Q7-2551.

Elastomer Q7-2159A/Q7-2551 has been the subject of study regarding reproductive effects and teratogenicity in a one-generation rat reproduction study. No adverse effects were reported.

GENOTOXICITY:

MDF-0077 has been evaluated for mutagenic activity in the Ames bacterial reverse mutation assay using Salmonella typhimurium. There was no evidence of genetic activity for DMSO, ethanol or saline extracts of MDF-0077.

IMMUNOLOGY:

1. NONSPECIFIC IMMUNE SYSTEM EFFECTS -

An imbalance in the regulatory network of the immune system may result in immune enhancement; e.g., hypersensitivity, or suppression; e.g., decreased resistance to infection. Silicone elastomer Q7-2423 was tested in mice for a nonspecific (constitutive) modulation of the immune system using a Listeria host resistance assay which primarily assesses competency of T lymphocytes and macrophages. This assay has been validated by the National Toxicology program. Female mice received cured 0.1 cm x 1 cm rods of elastomer subcutaneously at 1 rod per mouse (surface area = 0.245 cm^2). This is equivalent to 863 cm^2 elastomer surface area normalized to a 50 kg human. The surface area of one Dow Corning teardrop mammary implant is 401 cm^2. Immunosuppression was demonstrated using cyclophosphamide and immunoenhancement using Corynebacterium parvum. Resistance to Listeria infection was evaluated in terms of life-span and

mortality 10, 45 and 90 days after elastomer implantation.

No treatment-related effects were found whether the data were evaluated separately or collapsed over the 3 exposure periods. Therefore, it was concluded that elastomer Q7-2423 under the conditions of the assay has no effect on immune competence.

2. SPECIFIC IMMUNE SYSTEM EFFECTS -

Silicone elastomer Q7-2423 was tested for immunologic sensitization potential in a granuloma model utilizing immune deficient nude mice (nu/nu) and their immunologically normal heterozygous littermates (nu/+). In this model the challenge granulomatous reaction at the site of material implantation in mice previously exposed to the same material can be distinguished as being immune regulated or a classic foreign body reaction that is not immune dependent. While a granulomatous reaction that is a simple foreign body reaction is not distinguishable from an immunologically regulated granuloma on morphologic grounds alone, the latter exhibits memory. That is, the granulomatous response in a sensitized host is accelerated and/or amplified.

Q7-2423 was implanted subcutaneously as described above in nu/+ and nu/nu mice followed with a challenge implantation of Q7-2423 at the same dose at 28 days. At 2, 6 and 13 weeks thereafter the challenge implantation sites were evaluated with regard to capsule thickness, cellular composition, capsule cellularity and capsule connective tissue maturity. Comparisons of the sensitized (Q7-2423 + FCA) versus the non-sensitized (sham + FCA) mice were made for each mouse strain and exposure period using a series of statistical approaches, that is, chi-square, Mantel-Haenszel and Fisher's exact test). No PDMS treatment-related effects were observed for any of the 4 histological parameters measured.

Based on these findings it was concluded that the granulomatous response to Q7-2423 is of the classic foreign body reaction type and not an immunologically active inflammatory response.

These studies of effects on the immune system demonstrate that silicone elastomer Q7-2423 is not inherently an immune adjuvant nor does Q7-2423 at a relatively large subcutaneous dose cause immunoenhancement or immunosuppression in appropriate animal models.

SUBCHRONIC TOXICITY:

SUBCHRONIC ELASTOMER IMPLANTATION

GEL	SPECIES	DOSE	DURATION	RESULT
Q7-2222	Rabbit	4: 0.1x1 cm I.M.	3,10,30,90 Days	FBR #
		2: 0.1x1 cm S.Q.	3,10,30,90 Days	FBR
Q7-2352	Rabbit	4: 0.1x1 cm I.M.	10,30,90 Days	FBR
		2: 0.1x1 cm S.Q.	10,30,90 Days	FBR
Q7-2412	Rabbit	4: 0.1x1 cm I.M.	7,28,91 Days	FBR
		2: 0.1x1 cm S.Q.	7,28,91 Days	FBR
Q7-2423	Rabbit	4: 0.1x1 cm I.M.	10,29,90 Days	FBR
		2: 0.1x1 cm S.Q.	10,29,90 Days	FBR
Q7-2566	Rabbit	4: 0.1x1 cm I.M.	3,10,30,90 Days	FBR
		2: 0.1x1 cm S.Q.	3,10,30,90 Days	FBR
Q7-2743	Rabbit	4: 0.1x1 cm I.M.	10,30,90 Days	FBR
		2: 0.1x1 cm S.Q.	10,30,90 Days	FBR

SUBCHRONIC ELASTOMER IMPLANTATION (Cont)

GEL	SPECIES	DOSE	DURATION	RESULT
Q7-2744	Rabbit	4: 0.1x1 cm I.M.	10,30,90 Days	FBR
		2: 0.1x1 cm S.Q.	10,30,90 Days	FBR
MDF-0081	Rabbit	4: 0.1x1.5 cm I.M.	7,28,91 Days	FBR
		2: 0.1x1.5 cm S.Q.	7,28,91 Days	FBR

* 4 rods I.M. and 2 rods S.Q. per animal.
# FBR = Foreign Body Reaction.

These subchronic studies reviewed here indicate that silicone system D elastomers are all associated with a foreign body reaction characteristic of a broad range of persistent alloplastic materials such as the U.S.P. polyethylene employed as the control material in these studies. That is, an early acute inflammatory response is superseded by a chronic inflammatory phase (i.e., an infiltrate of predominantly macrophages) that transitions to fibroblastic activity and fibrous connective tissue encapsulation of the foreign body. A sparse dispersal of macrophages and giant cells may persist long-term although this is not characteristic of all implantation sites in all animals. This response pattern is the same for both intramuscular and subcutaneous implantation sites.

Another subchronic study in rabbits was designed to compare the local tissue response of the smooth silicone elastomer with the micro-pillared silicone elastomer.

Groups of 4 rabbits were implanted subcutaneously with one cm disks of elastomers as well as disks of material from competitive products; i.e., Biocell and the Meme polyurethane coated shell. Groups were sacrificed at 7, 28, 56 and 91 days after implantation for histopathologic evaluation of the local tissue response.

There was a continuum of local foreign body response with the Meme polyurethane eliciting the greatest degree of acute and chronic inflammation, capsule formation, nonaligned fibroblast organization, disruption of capsule collagen geometry and incidence of implant material particulates. The smooth silicone elastomer elicited the least response for all measured

parameters. Biocell was intermediate in the degree of response and generally to a greater extent than observed for micropillared silicone elastomer.

CHRONIC TOXICITY:

Several chronic elastomer studies are available as summarized in the following table.

CHRONIC ELASTOMER IMPLANTATION

MATERIAL	SPECIES	DOSE	DURATION	RESULT
Q7-2566	Rabbit	25 mg/Animal Knee Joint	1 Year	FBR #
		25 mg/Animal I.M.	1 Year	FBR
Q7-2383	Rabbit	25 mg/Animal Knee Joint	1 Year	FBR
		25 mg/Animal I.M.	1 Year	FBR
MDF-0077	Rat	0.1x1 cm Rod S.Q.	2 Year	NAE**
Q7-4750	Rat	6: 0.1x1 cm Rods S.Q.	2 Year	NAE
Q7-2423	Rat	8: 0.1x1 cm Rods S.Q.	2 Year	In-Process
MDF-0082	Dog	6: Rectangles	2 Year	FBR
MDF-0083	Dog	6: Rectangles	2 Year	FBR
MDF-0084	Dog	6: Rectangles	2 Year	FBR
MDF-0085	Dog	6: Rectangles	2 Year	FBR
MDF-0086	Dog	6: Rectangles	2 Year	FBR

CHRONIC ELASTOMER IMPLANTATION (Cont)

MATERIAL	SPECIES	DOSE	DURATION	RESULT
MDF-0087	Dog	6: Rectangles	2 Year	FBR
MDF-0088	Dog	6: Rectangles	2 Year	FBR
MDF-0089	Dog	6: Rectangles	2 Year	FBR
MDF-0099	Dog	6: Rectangles	2 Year	FBR
Q7-2383	Rabbit	25 mg Particles Joint Injection	1 Year	Granulomas

* Number of elastomer rods/animal.
\# FBR = Foreign Body Reaction.
** NAE = No Adverse Effect.

1. ONE-YEAR RABBIT IMPLANTATION STUDY OF Q7-2566 AND Q7-2383 -

Groups of 15 rabbits were implanted as outlined in the above table using elastomer spallation particles. There was a sham control group. Groups were sacrificed at 2, 4, 12, 24 and 52 weeks after implantation for histopathologic evaluation of the implanted paravertebral muscle and knee synovium and perisynovial connective tissue. Inguinal lymph nodes were also examined. The contralateral knee was examined as well. The reaction at the muscle site was a typical foreign body reaction as described previously. At the synovial and perisynovial sites the reaction varied from essentially none to a relatively mild inflammatory reaction; i.e., a granulomatous reaction. There was no evidence of pathologic change in the contralateral knee suggestive of an absence of a systemic immunologic reaction. There was no pathology observed in the inguinal lymph nodes.

2. TWO-YEAR RAT SUBCUTANEOUS IMPLANTATION STUDY OF MDF-0077 -

Groups of 50 male and 50 female rats were implanted subcutaneously with MDF-0077 in a study contracted to Industrial Bio-Test. The precise dimensions and number of elastomer rods is not clearly stated in the study report but was most probably a single rod per animal measuring 0.1x1 cm. U.S.P. polyethylene served as the control material. No adverse material-related effects were observed with regard to mortality, gross pathology or the types and incidence of tumors. This study does not conform to GLP regulations.

3. TWO-YEAR RAT SUBCUTANEOUS IMPLANTATION STUDY OF Q7-4750 -

Q7-4750 is a system D (that is, platinum catalyzed) elastomer that differs from Q7-2423 only in that Q7-4750 is formulated with hexamethyldisilazane (HMDZ) while Q7-2423 is formulated without this reactive dimer. In final composition these elastomers are virtually identical in that HMDZ does not survive cure conditions.

A 2-year rat implantation study of Q7-4750 was recently completed and conformed to GLP regulations throughout. Groups of 50 rats per sex were implanted with 6 implants measuring 0.1x1 cm. Control groups of 60 rats per sex received an equal number of U.S.P. polyethylene rods as a material control. Two rods were placed I.M., 2 I.P. and 2 S.Q. There were no treatment-related adverse effects in terms of body weights, food consumption, mortality, clinical chemistry, hematology, organ weights, gross pathology or histopathology including tumor types or incidence. The absence of site-associated sarcomas demonstrated that the size and total surface area (1.47 cm^2) of material implants falls below the threshold for solid-state tumorigenesis to be a detectable event.

4. TWO-YEAR RAT SUBCUTANEOUS IMPLANTATION STUDY OF Q7-2423 AND Q7-2551 -

The in-life phase of a 2-year rat implantation study of Q7-2423 and Q7-2551 was completed in January, 1991 and conformed to GLP regulations throughout. Groups of 60 rats per sex were implanted subcutaneously with 8 implants measuring 0.1 x 1 cm. Control groups of 60 rats per sex received an equal number of U.S.P. polyethylene rods as a material control. At the present stage of data analysis there are no known treatment-related adverse effects in terms of body weights, food consumption, mortality, clinical chemistry, hematology or organ weights. Histopathology is in-process.

5. TWO-YEAR IMPLANT STUDIES WITH SILASTIC MATERIALS IN DOGS -

Groups of 3 male and 2 female beagles were implanted S.Q., I.P. and I.M. with various combinations of a series of 9 system D elastomers. The elastomer samples were prepared as rectangles varying in size from 5/8 x 1 1/4 inches to 7/8 x 1 3/8 inches. A control group was not included. One dog of each sex in each group was sacrificed at 6 months after implantation and the remaining animals were sacrificed at 2 years. The implantation sites and selected tissues were examined histologically. No abnormal clinical signs were observed throughout, body weight was not affected and no

changes in organ weights were noted. The reaction at the implantation sites was a typical foreign body reaction with fibrous encapsulation and chronic inflammation. Chronic inflammation was generally more evident at 6 months than at 2 years.

On the basis of these subchronic and chronic studies of closely related dimethyl system D elastomers it is concluded that:

1. Silicone system D elastomers are all associated with a foreign body reaction characteristic of a broad range of persistent alloplastic materials such as the U.S.P. polyethylene employed as the control material in these studies. That is, an early acute inflammatory response is superseded by a chronic inflammatory phase (i.e., an infiltrate of predominantly macrophages) that transitions to fibroblastic activity and fibrous connective tissue encapsulation of the foreign body. A sparse dispersal of macrophages and giant cells may persist long-term although this is not characteristic of all implantation sites in all animals. This response pattern is the same for both intramuscular and subcutaneous implantation sites.

2. The results of elastomer implantation studies ranging in duration from a few days to 2 years demonstrate that reinforced silicone elastomers induce no detectable systemic adverse effects on any organ system.

3. Elastomer samples measuring 0.1x1 cm (0.245 cm^2) and total surface areas up to 2 cm^2 per rat do not induce implantation site tumors (solid-state tumorigenesis) nor an excess of tumors remote from the implantation site.

ABSORPTION/DISTRIBUTION/METABOLISM/EXCRETION (ADME) -

Silicone elastomers are not subject to possible systemic distribution as might occur with PDMS or silicone gel. However, there has been speculation that the fumed amorphous silica used as a reinforcing filler in silicone elastomers may be available for distribution. This hypothesis has been evaluated by examining elastomer samples implanted subcutaneously in mice for up to 6 months for evidence of filler redistribution within the elastomer and for signs of change in the surface topography of the elastomer.

There was no degradation or surface modification of the elastomer observed using transmission electron microscopy at 1, 3 or 6 months after subcutaneous implantation. No alterations in silica distribution within the body of the elastomer or at the surface were observed at any time point.

Therefore, this study demonstrated that the fumed amorphous silica used as a reinforcing silica maintains a stable distribution within the silicone elastomer. In addition, the surface morphology of the elastomer is not influenced by up to 6 month subcutaneous implantation.

techmedica
A company of SULZERmedica

June 2, 1992

Diana Zuckerman
Congress of the United States
House of Representatives
Human Resources and
Intergovernmental Relations Subcommittee
of the Committee on Government Operations
Rayburn House Office Building, Room B-372
Washington, DC 20516-6148

Dear Ms. Zuckerman:

Techmedica has designed and produced a limited number of patient specific Custom TMJ prostheses over the past 3½ years for patients with severe degenerative TM Joint disease.

These implants employ biomaterials that have a long clinical history of successful use in orthopedics for reconstructing joints such as the hip and knee.

As in orthopedics, the goal of TM Joint replacement is to reduce pain while improving mobility, function, and alignment of the affected limb or part.

It has been Techmedica's perception that the clinical problems associated with previous alloplastic (artificial) TMJ prosthesis were a result of poor implant material selection as well as use outside of the proper clinical utility where a more conservative treatment may have been preferable.

These implants have been available to a limited clinician group so as to facilitate patient follow-up at prescribed intervals. Although Techmedica actively pursues patient follow-ups there are invariably those patients that will become lost to this program. Fortunately data has and is currently being collected for the vast majority of these patients so as to evolve this product in a controlled and scientific way.

1380 Flynn Road • Camarillo, California 93012-8016 • Tel: (805)987-0466 • (800)541-9511 • (800)732-8535 (CA)
Fax: (805)987-4111

Enclosed you will find clinical follow-up information for 95 patients over a two-year period. Also enclosed, are the ASTM specifications for the biomaterials comprising these devices and published articles regarding the use of these materials for implants.

Sincerely,

Dave Samson
Regulatory Affairs Manager

DS/cc
Enclosures

TECHMEDICA CAD/CAM TOTAL TMJ PROSTHESIS

ANALYSIS OF DATA TO DATE, JUNE 1, 1992

LOUIS G. MERCURI, DDS,MS
CHICAGO, ILLINOIS

There are a total of 95 patients in the data set of this closely monitored limited clinical study. The average age of the patients is 42.02 (22 - 64) years. There are 5 males and 90 females with a total of 159 joints treated. These patients have averaged 10.3 (0 - 30) years of TMJ problems and undergone a mean of 5.32 (0 - 22) prior unsuccessful surgeries.

There has been 24 months of pre and post operative data that has been collected to date using a standardized data collection format. Subjective data: pain, function of the mandible, and diet, are collected using a visual analogue scale (VAS) to objectify this data. Objective measures of mandibular range of motion read as interincisal opening and left and right lateral excursions were directly measured from the patient pre and post operatively.

Preliminary analysis of this data reveals a statistically significant decrease in pain ($p<.004$), increase in function ($p<.002$), and increase in diet ($p<.007$). There was improvement in mandibular range of motion recorded as well.

Tissue removed from the articular surfaces of a prosthesis functioning in a patient 2 years post CAD/CAM placement during the revision of scar tissue from around the joint revealed no evidence of a tissue reaction, or the fragments of metal or polyethylene when this tissue was examined histologically.

There have been 9 (5.6%) joints in which complications have been reported. One post operative wound infection requiring removal and replacement of the prosthesis; 3 early prostheses that did not fit properly and had to be remade; 3 prostheses in which the ramal component screw loosened necessitating replacement; and 2 early cases of condylar dislocation from the prosthetic fossa. This problem has been resolved with a design change which added a lip to the anterior of the fossa. There have been no cases of breakage, material or mechanical failure.

Materials and Orthopaedic Surgery

By DANA C. MEARS,
B.M., B.Ch., Ph.D., M.R.C.P., F.R.C.S.(C)

Associate Professor of Orthopaedic Surgery and
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Staff, Presbyterian-University Hospital,
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Consultant, Veteran's Administration Hospital, Pittsburgh, Pennsylvania.

Fellow, American Academy of Orthopaedic Surgeons.

Member, British Standards Committee for Surgical Implants.

American Society for Metals.

Fellow, Nuffield Orthopaedic Research, North American Orthopaedic Travelling,
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Winter and Shirley,[38] described large numbers of orthopaedic implants after removal from human implantation. They reported the incidence of corrosion of metallic combinations of different austenitic stainless steel alloys (*e.g.*, 18% chromium-8% nickel alloy with 18% chromium-8% nickel and 2.5% molybdenum) and of combinations of austenitic stainless steel alloys with a cobalt-chromium-molybdenum alloy. The alloys in combination did not show an increased incidence of corrosion compared to their behavior when used alone. Indeed, for combinations of stainless steel alloys, mutual protection seemed to be conferred by the combination. More recently, Cohen and Wulff[39] have reported observations of the corrosion of a combination of a wrought cobalt-chromium-tungsten-nickel alloy with a cast cobalt-chromium-molybdenum alloy. Crevice attack was observed in the former alloy but not in the latter material. Laboratory tests were undertaken in which Teflon gaskets were applied to specimens of each cobalt-chromium alloy to form crevices between the metal and the polymeric material. The specimens were immersed individually in solutions of sodium chloride. Potential-time studies and metallographic observations showed that the cobalt-chromium-tungsten-nickel alloy underwent crevice attack, while the cobalt-chromium-molybdenum alloy did not undergo similar corrosion. The experiments confirm that the crevice corrosion in passive metals is provoked by the presence of a crevice on a susceptible alloy and *not* by the presence of dissimilar passive alloys.

Recently two types of total hip replacement have utilized combinations of dissimilar metals. The Müller type of total hip replacement,[40] uses a cast cobalt-chromium alloy femoral head prosthesis welded to a wrought cobalt chromium alloy intramedullary stem. More recently, the latter alloy has been replaced with a titanium alloy (Ti-6A1-4V), also welded to the cobalt-chromium femoral head prosthesis. Both combinations have performed satisfactorily. The Russin modified Sivash prosthesis[41] has combined a similar cast cobalt-chromium alloy with titanium. Again, this combination of materials has performed satisfactorily in the clinical situation. Similar observations are required for other potentially useful combinations of dissimilar surgical alloys.

Effects of Galvanic Currents on Tissues and Cells

There has been widespread speculation on the effects of corrosion currents on tissues and cells, although few facts are available. Corrosion ma
alter cells in at least three ways: (a) the metal
dissolution products may affect cell metaboli
and thereby damage extracellular matrix; a
(b) corrosion may be accompanied by chan
in the chemical environment of the cell, such
the production of hydrogen ions or hydroxyl
or the evolution of a gas such as hydro
oxygen or chlorine; and (c) the corrosion
rents may affect cell behavior.

The first two factors are fully reviewed
Chapter 7. For cells exposed to metals sing
in combination, toxicity would be a funct
the rate of the dissolution process of a part
dissolving anode and not of the presen
combinations of metals. At present, the eff
of electric currents on cell behavior are
intense scrutiny. Observations of the eff
applying direct or alternating current to
cultures reveal a variety of potentially ben
as well as potentially harmful actions, in
induction of osteogenesis, alignment
domly oriented collagen fibers, transfor
of red cell precursor cells into fully differe
red cells, and stimulation of neurom
events. While the last mentioned has
the most attention as an adverse side-eff
implanted dissimilar metals, it is most
to be clinically significant for the com
of metals recommended in this chapte
the magnitude of electric power req
neuromuscular stimulation is orders o
tude greater than corrosion currents
the recommended combinations of im
loys. Ultimately the toxicity of corrosion
tials between dissimilar implant alloys
assessed in the clinical situation. In the
studies performed to date, the auth
aware of any deleterious biological re
implantation of combinations of the
ommended here.

Conclusion

Even a cursory glance at present
attempts to replace or repair human o
man made devices will show the eno
vantage of the simultaneous use of
alloys, each selected for its particular
attributes. In many cases, nonmet
stances will also be required. A caref
the electrochemical and biological
combinations of alloys shows that a
of passive alloys may be safely used
vivo. Admittedly, in the absence of ex
edge of the properties of metals a

Supports cobalt couples & UHMWPE

Component wear of total knee prostheses using Ti-6Al-4V, titanium nitride coated Ti-6Al-4V, and cobalt-chromium-molybdenum femoral components

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A knee simulator was used to study the wear of carbon fiber reinforced UHMWPE (Poly Two) (Poly Two is a registered trademark of Zimmer, USA) tibial and patellar components against Ti-6Al-4V, titanium nitride (TiN)-coated Ti-6Al-4V, and cobalt-chromium-molybdenum femoral components. The prostheses tested were regular sized Miller-Galante total knees mounted on 316L stainless steel fixtures using bone cement. An environmental chamber surrounded the knee and maintained bovine serum lubricant at 37°C. The specimens were tested using consecutive blocks of 464 level walking steps, 8 ascending stairs and 8 descending stairs for a total of 100,000 steps. The wear mechanisms found on the tibial components were scratching, carbon-fiber associated damage, surface deformation, pitting, minor abrasion, and delamination. Three forms of carbon fiber associated damage were identified; fibers pulled from the surface, broken fibers, and UHMWPE removed from the surface fibers. The SEM evaluation revealed a pit forming mechanism. No correlation was found between femoral component material and tibial surface damage. Visual examination of the femoral components revealed no signs of wear or scratching on the cobalt-chromium-molybdenum or TiN-coated Ti-6Al-4V components. There were, however, many light surface scratches on the uncoated Ti-6Al-4V components, which were also observed in a supplementary test of an uncoated Ti-6Al-4V component tested with a conventional polyethylene tibial component.

INTRODUCTION

There has been considerable interest in the use of titanium, and especially the Ti-6Al-4V alloy, for orthopedic implants because of its biocompatibility, fatigue strength, and corrosion resistance. However, there has been some question of the wear resistance of Ti-6Al-4V against ultrahigh molecular weight polyethylene (UHMWPE).[1] A number of studies have been conducted which evaluate the wear of Ti-6Al-4V and UHMWPE combinations under clean conditions and with acrylic contaminants.[2] Within these studies a number of wear-resistant surface treatments have been evaluated, including nitriding, ion implantation, and special passivation techniques.[3,4] These

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studies have been run under sliding conditions, either pin-on flat or hip simulator studies.

Studies of the wear of Ti-6Al-4V against UHMWPE have had conflicting results. Rostoker and Galante[1,4] found that Ti-6Al-4V specimens exhibited scratches, black deposits, and abnormal wear in two studies of Ti-6Al-4V wearing against UHMWPE using a disk-on-flat geometry. These reports disagree with the results of Miller et al.[5] and McKellop et al.,[6] who found the wear characteristics of Ti-6Al-4V similar to those of stainless steel. In further tests, McKellop et al.[2] found that Ti-6Al-4V is especially susceptible to abrasive wear from acrylic cement particles.

Several studies have been conducted using hip simulators. McKellop et al.[7] studied the wear of hip prostheses with cobalt-chromium-molybdenum (Co-Cr-Mo) alloy and Ti-6Al-4V alloy femoral components using bovine serum lubrication. The tests were conducted under both clean conditions and with several approximately 2-mm-diameter fragments of PMMA cement placed in the acetabular cup. Under the clean conditions the Co-Cr-Mo ball had only light scratching and the titanium ball exhibited slightly more scratching. With acrylic chips present, the Co-Cr-Mo ball had only very light surface scratches, whereas the Ti-6Al-4V ball was severely scored and smeared with black residue. Greer,[8] however, found that acrylic contaminants caused no change in the appearance of the Ti-6Al-4V femoral heads or the serum lubricant.

Rostoker and Galante[3] found that special passivation techniques eliminated the abnormal wear of Ti-6Al-4V that they had previously reported.[1,4] McKellop et al.[9] reported that nitrided Ti-6Al-4V was virtually undamaged in a pin-on-flat study that included acrylic contamination. Lucas et al.[10] concluded that the corrosion characteristics of TiN coated and nitrogen ion implanted Ti-6Al-4V were very similar to those exhibited by the Ti-6Al-4V control samples, however there have been no studies published on the wear of these coatings against UHMWPE.

There have been two studies of UHMWPE wear of tibial components using knee simulators.[11,13,14] Treharne et al.[11] used a computer controlled simulator which controls the flexion angle and the joint load. Bovine serum lubrication at 37°C was used and wear was determined as weight loss from the tibial component using the method developed by McKellop et al.[12] Wear debris which consisted of fibrous and, in some cases, granular or globular debris was recovered by Rose et al.[13,14] The prostheses with higher wear rates had regular periodic cracking. No correlation was found with molecular weight, but rather, it was concluded that the wear rate of UHMWPE knee components was dominated by high contact stress.

Rose et al.[15] examined the UHMWPE wear mechanisms of eight failed hip and 16 failed knee prostheses and found large craters in regions where there was no evidence of abrasion. Craters were found forming at the edges of UHMWPE fusion defects. Hood et al.[16] in a retrieval study, found pitting on 90% of recovered tibial components. Much of the pitting appeared to be caused by acrylic debris; however, pits were also found in areas with

abrasion. In a 10-year retrieval study, Landy and Walker[17] described fatigue/delamination as a prominent wear mechanism where cracks and fusion defects eventually coalesced to produce wear fragments. Ainsworth et al.,[18] in the original wear study on carbon fiber reinforced UHMWPE, (Poly Two)* found wear rates 3.8 to 10 times lower than for conventional UHMWPE; however, subsequent studies of carbon-fiber UHMWPE have found wear rates 1.8 times higher,[19] increased contact stresses and much higher fatigue crack propagation rates[20] compared to UHMWPE.

METHODS

The prostheses were tested in a computer-controlled knee test machine[21] programmed to simulate walking and ascending/descending stairs. A schematic of the simulator, which has been used for a number of studies[22,23] is shown in Figure 1. Motion and force plate data recorded from normal subjects† is used as input to the computer. Hydraulic cylinders, operating in closed-loop control, impart the abduction/adduction force, the tibial torque at the "ankle" and the vertical force at the "hip." The quadracep cylinder is

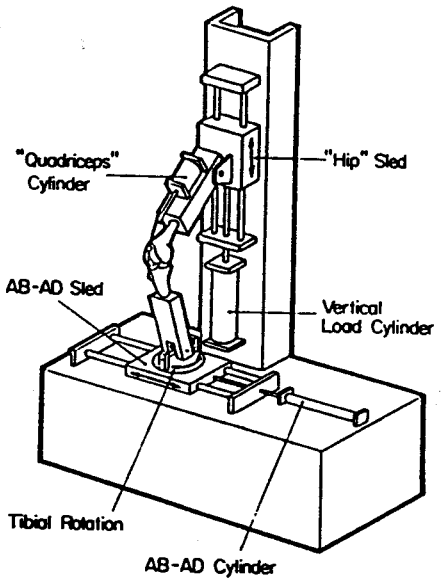


Figure 1. Schematic drawing of knee simulator.[21]

*Poly Two is a registered trademark of Zimmer, USA.
†Data provided by Rush-Presbyterian Hospital, Chicago, Illinois.

connected to a cable which passes over a fixture holding the
thesis and attaches to the "tibia." The simulator is operated a
second which is approximately one-half normal walking spee
theses tested consisted of tibial, femoral, and patellar comp
methylmethacrylate (PMMA) was used to cement the com
stainless-steel fixtures. The knee joint was enclosed in an
chamber containing bovine serum, maintained at 37°C, as

Test protocol

A total of 10 tests were run during this testing program. The
were Miller/Galante total knee prostheses donated by Zim
tibial component consisted of two parts, a metal tibial fixa
carbon fiber reinforced UHMWPE (Poly Two) tibial articular
nent. The patellar buttons were also made of Poly Two. Three
used for the femoral articulating surfaces:

(1) Ti-6Al-4V titanium alloy (regular production—sterilize
(2) Titanium nitride coated Ti-6Al-4V alloy (experimental
(3) Co-Cr-Mo alloy (regular production—sterilized)

Three prostheses of each type of femoral component were

One supplemental test was run using an uncoated Ti-6
component and conventional UHMWPE patella and tibial com
test was run only to make visual comparisons with the femo
being tested. The polyethylene tibial component was not co

Each test consisted of 100,000 cycles (100 K) of simulated
82 kg (180 lb) subject. Each test was divided into 209 block
sisted of 464 level walking steps, 8 steps ascending stairs
scending stairs. This approximates the ratio of level walkin
for normal activity.[24] The third TiN coated prosthesis (TiN
an extended period for a total of 500,000 cycles of only leve
In a previous study[23] seven different prostheses were teste
cycles in the knee simulator using deionized water as
retrieval analysis comparison* the simulator tested prosth
same damage modes, damage location, and severity tha
approximately 2 years of clinical service with the except
was observed in the simulator tested tibial components

Visual, microscopic, and SEM evaluation

After testing, all femoral and tibial components were vis
surface damage. Following visual inspection, the tibial com
an additional inspection using a stereoscopic microscope a
×20 to ×210. Tibial component surface damage was categ

*Performed by Dr. T. M. Wright, Hospital for Special Surgery, N

e seven damage modes used by Hood et al.[16] plus an eighth category, arbon-fiber-associated damage. If distinct presence of a damage mode was bserved, then this mode was recorded as existing for that prosthesis. Those ibial components which clearly illustrated one or more of the damage categories were then examined using a scanning electron microscope (SEM). The umber of components examined with the SEM was limited because the equired carbon coating contaminates subsequent observations.

ontact area measurements

Tibiofemoral static contact areas were measured before and after each test knee flexion angles of 20° and 80° in all of the tests and additionally 40° in e of the tests. The 20° and 80° angles were selected to approximately rrespond to those used by Wright et al.[19] Contact areas were measured by serting Prescale pressure sensitive film (Fuji Photo Film Company) beeen the tibial and femoral components and maintaining a vertical load at e "hip" of 32 Kg for 10 min.

ability test

The 100,000 cycle tests were interrupted at steps 1, 100, 400, 900, 4900, 00, 49,900, and 100,000 to conduct stability tests.[23] The stability test procedure was also conducted at the end of the 500,000-cycle test. In each stability st the machine is moved through five activities which study flexion performance as well as adduction/abduction (ad–ab) and tibial rotation stability. ertical force applied at the "hip" for each assessment is 32 kg (70 lb). This duced loading is used to avoid possible excessive loading during the stability test. The flexion performance routine holds the ad–ab force and tibial rque at zero while the knee is flexed from 10° to 40° and the quadriceps rce is measured. The ad–ab stability routine holds the knee at 10° of flexion d tibial torque at zero, while the ad–ab displacement is measured. The ial rotation stability routine holds the knee at 10° of flexion and ad–ab force zero while the tibial torque is varied and tibial displacement is measured. e ad–ab and tibial rotation tests are repeated at 40° of flexion. Changes in ability are associated with the change in surface conformity. This is a flection of the wear and/or deformation which occurs with cyclic loading. r the rotational stability tests hysteresis loops of the applied torque versus tation is plotted. A least-squares fit is used to determine the rotational ffness (torque per degree of rotation) of the prosthesis assembly under the Kg vertical load applied to the "hip."

ear measurement

Wear of the tibial components was characterized by the weight of material moved. The tibial and patellar components were presoaked in bovine

serum at room temperature for a minimum of 14 days prior to th
of the test in order to minimize fluid absorption during the
presoaking, the parts were cleaned, vacuum desiccated and
a Mettler H20 analytical balance. Following testing, the parts
cleaned, desiccated and weighed. The amount of wear was th
between the weights before and after the test. Fluid absorp
the test was corrected for by using a soak control similar to
by Treharne.[11]

RESULTS

Visual, microscopic, and SEM examination

On an unused Poly Two component, the surface has a gloss
and a layer of carbon fibers can clearly be seen in the surface pla
in Figure 2. After testing in the simulator, the most common su
modes found were scratching and carbon-fiber-associated dam
fiber-associated damage was defined as any surface disrup
associated exclusively with the presence of carbon fibers. The
different types of carbon-fiber-associated damage: fiber rem
UHMWPE matrix, fiber breakage, and UHMWPE removal
Figure 3 shows the three modes of carbon-fiber-associated

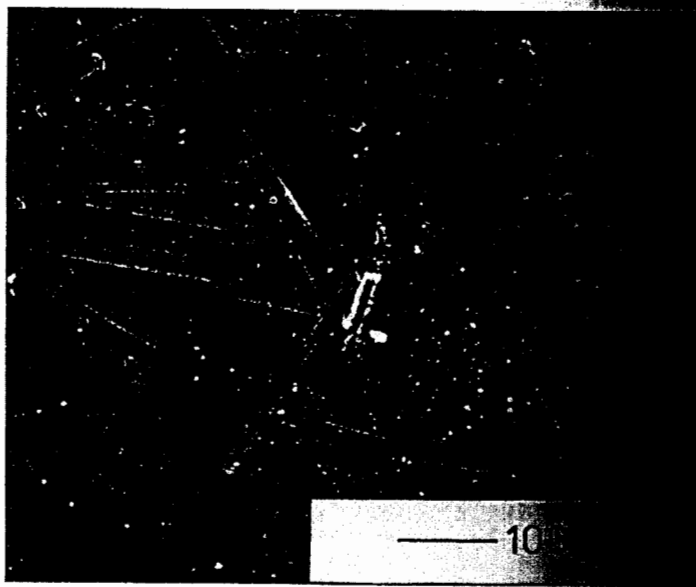
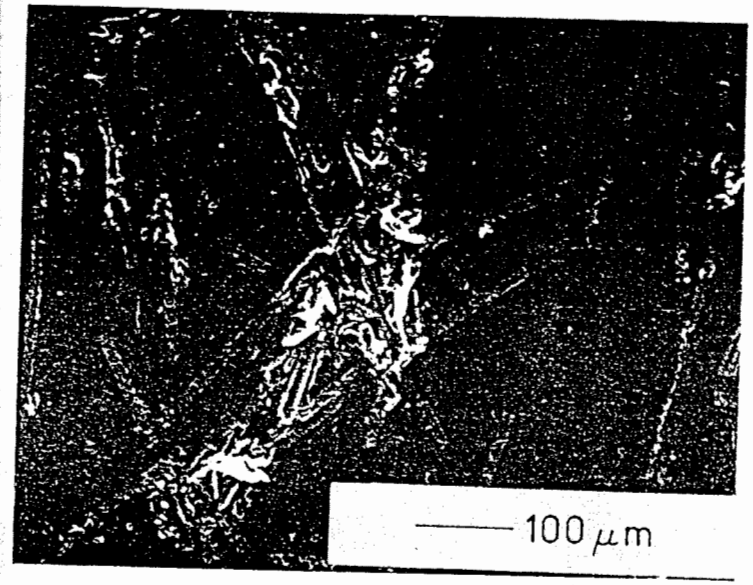
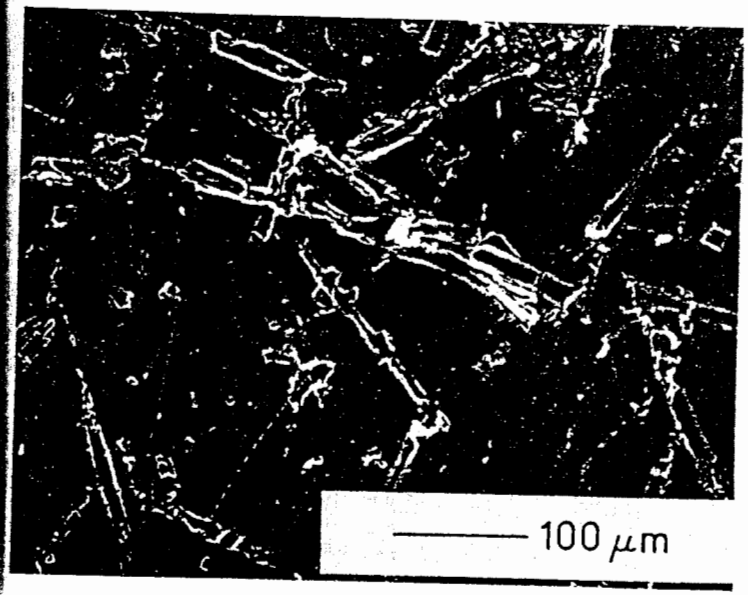


Figure 2. SEM micrograph of unworn carbon fiber rein

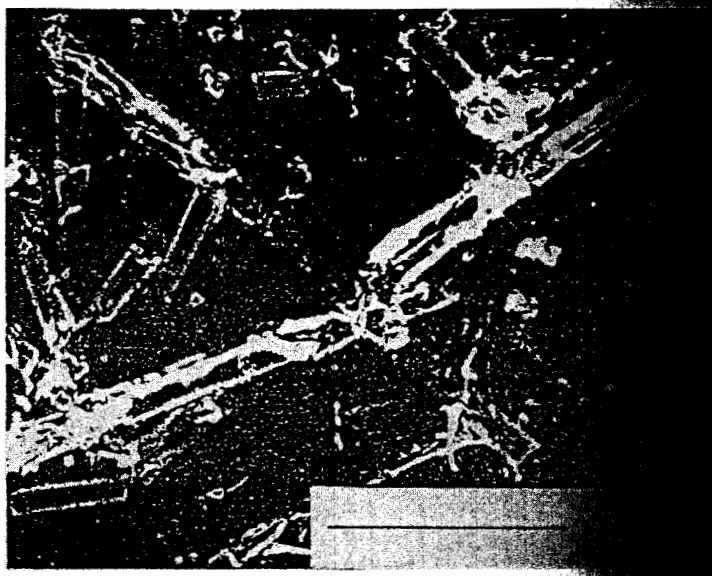


(a)



(b)

Figure 3. SEM micrograph of carbon fiber associated damage: (a) UHMWPE removal from carbon fibers, (b) trough from surface carbon fiber removal, (c) carbon fiber breakage.

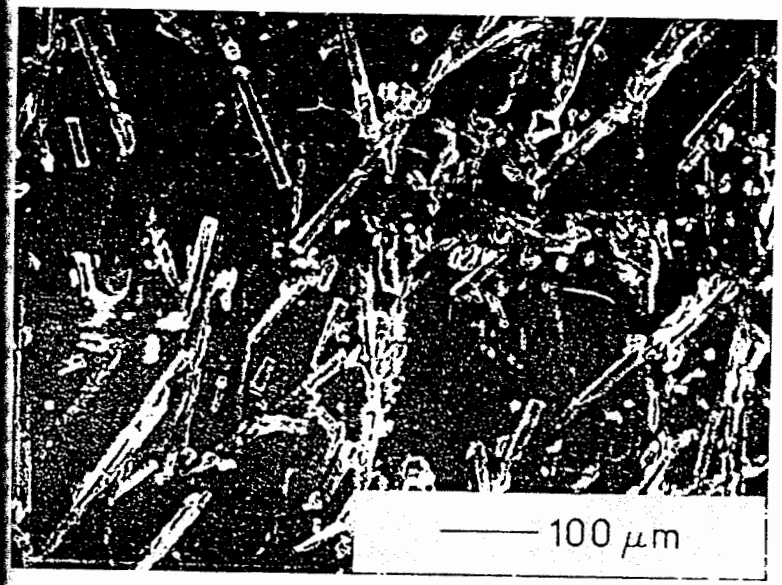


(c)

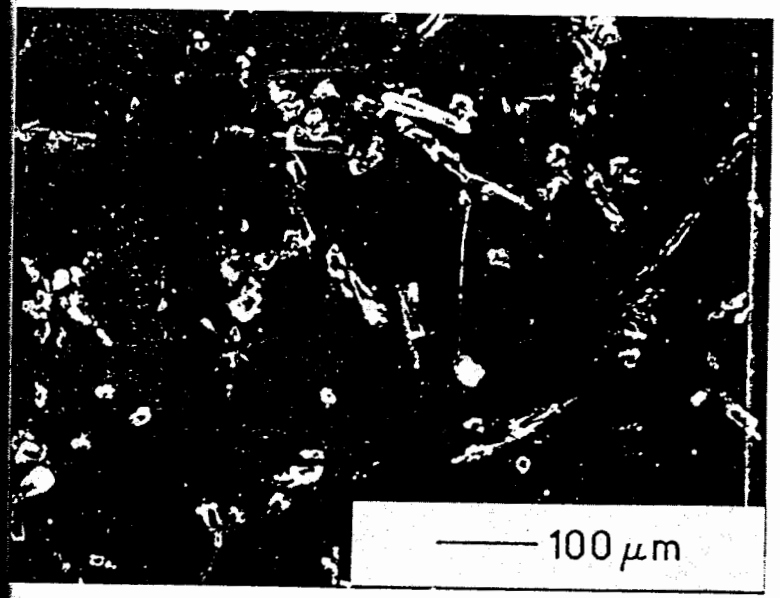
Figure 3. (continued)

areas of carbon-fiber-associated damage also exhibited the
of wear. Scratches, such as those seen in Figures 3(b) and
in the anteroposterior direction and were possibly due to
of the broken fibers or removed particles of UHMWPE
tibial component from the 500,000 cycle test shows
associated wear mode when the surface layer of carbon
Figure 4(a), the UHMWPE removal and carbon fiber
carbon fiber associated damage can be seen along with
scratches. The scratches shown were on the anterior
plateau wear zone. In the center of the wear zone, fre
surface fibers and relatively little UHMWPE damage, but
scratches are still present.

Surface deformation was noted in eight of the nine
tests exhibited excessive surface deformation. The ma
deformation on the tibial components took place in the
areas of each tibial plateau. Also, the areas of wear ex
to the medial edge of the medial plateau in five out
tested. This implies that, during a step, some portion
condyle is not being supported by the tibial plateau. The
tibial component constrains the femoral component
tended. However, the gap between the femoral condyl
allowing enough medial/lateral translation for the medial
be partially unsupported when the knee is flexed.



(a)



(b)

Figure 4. SEM micrograph of 500,000 step test's tibial component: (a) anterior edge of wear area, (b) center of wear area.

Pitting was found on seven tibial components. In several
evident that the process had begun with some abrasive or gou
In the others, however, there was no apparent abrasion,
gouging from which the pit began. Figure 5 shows a portion
was found on the posterior edge of the lateral condylar wear
component. The carbon fibers visible at the bottom of the pi
the surface with no signs of carbon fiber ends, as if the pit wer
UHMWPE pulled away from the carbon fibers that now ma
posed surface. Figure 6 shows a pit that is in the process of
a surface made up of carbon fibers. The material being
rounded by what appears to be a crack.

Two tibial components exhibited minor abrasion. These
what appeared to be wide shallow scratches but under magni
areas where tufts of polyethylene extended away from the

Table I lists the incidence of the tibial surface damage m
and carbon fiber associated damage were found together o
components. Surface deformation was found on eight and p
mechanism on six of the tibial components. Minor abrasio
two of the tibial components. Embedded PMMA and bu
observed on any of the tibial components. From the informa
in Table I, no correlation could be found between the
incidence and the femoral material.

Figure 5. SEM micrograph of a portion of large pit lined w

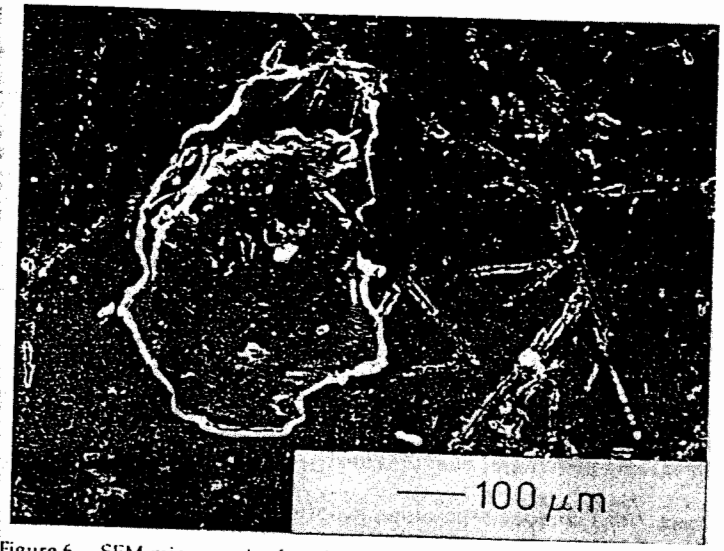


Figure 6. SEM micrograph of pit forming along a boundary of three carbon fibers and a crack.

tact area measurements

he results from the contact area measurements are shown in Table II. ing the course of the study, contact area measurements were made re and after each test for a total of 28 different tests and flexion angle binations. Of these combinations, 16 had an increase in contact area and ad a decrease in contact area. The variation in these results was caused ultiple stable assembly positions for a given flexion angle due to the ively flat, unconstrained tibial component and multi-radius geometry of emoral component.

TABLE I
Observed Damage Modes

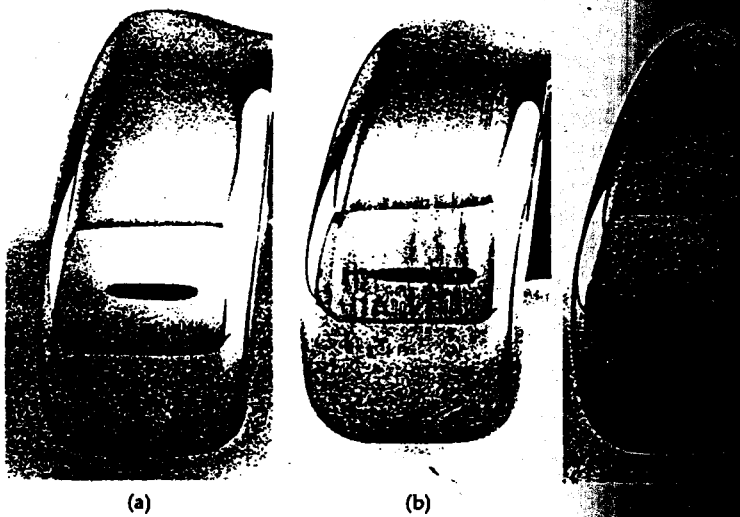
	Prosthesis Material and Test Number									
	Ti-6Al-4V			Ti-Ni			Co-Cr-Mo			
Damage Mode	1	2	3	1	2	3	1	2	3	Totals
rface deformation	×	×	—	×	×	×	×	×	×	8
ting	—	×	×	—	—	×	×	×	×	6
mbedded PMMA	—	—	—	—	—	—	—	—	—	0
ratching	×	×	×	×	×	×	×	×	×	9
rnishing	—	—	—	—	—	—	—	—	—	0
brasion	—	—	—	—	×	×	—	—	—	2
lamination	—	—	—	—	—	—	—	—	—	0
rbon fiber damage	×	×	×	×	×	×	×	×	×	9

TABLE II
Tibial Surface Contact Areas at Beginning and End of 100,000 Cy

	Contact Area (mm^2)					
	Beginning of Test				End of	
Test	10 deg	20 deg	40 deg	80 deg	10 deg	20 deg
Co-Cr-Mo	89	68	80	89	84	54
Co-Cr-Mo	83	87	93	60	80	74
Co-Cr-Mo	92	81	80	63	80	88
Ti-6Al-4V 1	93	69	122	101	86	71
Ti-6Al-4V 2	—	64	—	79	—	79
Ti-6Al-4V 3	—	82	—	79	—	87
Titanium nitride 1	—	45	—	69	—	86
Titanium nitride 2	—	56	—	94	—	70
Titanium nitride 3	80	103	93	98	82	83

Observations of femoral components

Figure 7 is a composite photograph of the lateral condyl
Ti-6Al-4V, and TiN-coated Ti-6Al-4V components after 100,00
bined level walking and ascending/descending stairs activiti
component photographs have marks oriented in the media
and lines forming an "H" shape. These marks and lines ar
the camera opening and photographer's enclosure, respec
ble scratching or other damage was found on the co



(a) (b)

Figure 7. Lateral condyles of (a) Co-Cr-Mo, (b) Ti-6Al-4V
6Al-4V femoral components.

lybdenum femoral components. The titanium nitride coated Ti-6Al-4V
oral components, like cobalt-chromium-molybdenum, showed no
atches and retained a polished surface. The uncoated Ti-6Al-4V femoral
nponents, however, exhibited a large number of shallow scratches ori-
ed in the anteroposterior direction. These shallow surface scratches were
observed in the supplementary test of an uncoated Ti-6Al-4V femoral
nponent run with a conventional UHMWPE tibial component which indi-
s the scratches were not necessarily due to the presence of carbon fibers.

bility tests

he results of the knee stability tests showed that the range of tibial
tion gradually decreased from a range of 7°–10° to a range of 2°–6° as the
oral component created a "seat" on the tibial component. The rotational
ness (torque per degree rotation) showed a significant increase during
100,000 step test as illustrated in Figure 8. In the extended test the
tion increased and the stiffness decreased between 100,000 steps and
000 steps indicating that the "seat" was gradually being removed by
r and/or deformation. No significant correlation was found between the
oral component material and the wear and/or deformation observed with
stability tests.

ght loss measurements

he results of the specimen weight loss study was inconclusive. The speci-
weight loss results were variable due to a residue of denatured serum

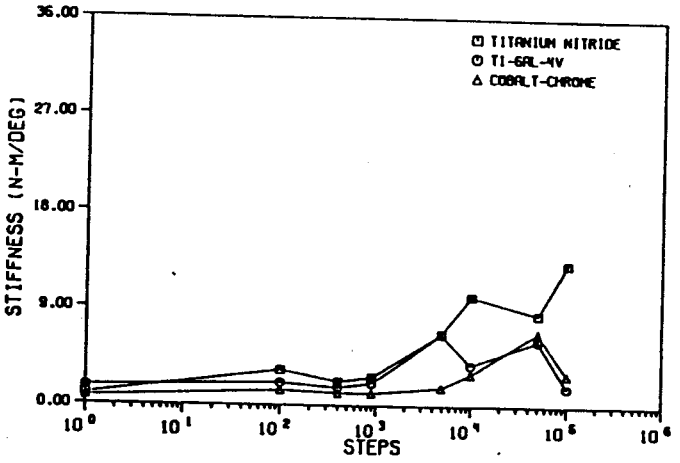


Figure 8. Rotational stiffness over the 100,000 cycle step test as measured
with the rotational stability test.