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Biocompatibility of Materials for Total Joint Replacement

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Summary

The clinical use of total joint prostheses demands absolute biocompatibility of the materials employed.

The purpose of this experiment was the bioassay of some materials considered as possible candidates for use in total joint prostheses as load-bearing members or as wear-resistant surfaces.

Some materials already in use were also tested. 316L stainless steel was used as a control. The materials were implanted as a standardized rod and in particulate form.

An average of 12 samples per material were implanted in soft tissue for six months and a total of 145 rabbits were used in this study. Twenty-five materials including metals, polymers, and ceramics were tested in solid and powdered form.

A semiquantitative evaluation of local tissue reaction and a study of organs was performed.

Polymers and metallic materials showed in general a mild tissue reaction. Ceramics, which some authors describe as the best tolerated materials, elicited variable tissue responses. Some of these (glass–ceramics) presented very poor tissue tolerance. The least reactive, titanium oxide, titanium aluminate, and aluminum oxide, presented a degree of tissue reaction comparable to that of corrosion resistant metals, but not superior to them. Moderate reactivity was the general rule for particulate materials except for the Pyroceram glass–ceramics, polyimides, and Teflon. Ultrahigh molecular weight polyethylene in particulate form elicited a rather cellular tissue response, a fact to be considered when projecting long-term results in total joint arthroplasty.

No pathological changes compatible with systemic toxicity by materials tested were observed in the study of the organs.

INTRODUCTION

Mechanical failure of total hip prostheses is a possible occurrence in long-term follow-up studies.[1] Mechanical limitations of the materials used could account for some of these failures.[2,3] The quality of these materials becomes critical as the service lives of total joint prostheses increase. Awareness of their limitations has accounted for an extensive search for new materials. To avoid the pitfalls which plagued past attempts to promote new materials for clinical use,[4] biological testing became mandatory.

Total joint prostheses differ fundamentally from other types of implants because of the presence of wearing surfaces that lead to the production of small particles. As a result of particle formation, the exposed surfaces of material in contact with tissues are considerably increased. The smaller the particle size the greater the surface per given weight, with faster solubility and greater local exposure.[5,6] In the biological assay of a material which is a candidate for a joint surface, it is important to determine its *in vivo* behavior in particulate form in addition to the standard studies done with solid specimens. The purpose of this study was to evaluate in that manner the tissue response to 26 different materials, all potential candidates for internal prostheses.

LITERATURE REVIEW

Measurement and grading of the fibrous tissue membrane around the implant[7] has proved to be a practical method of quantitating tissue reaction. According to membrane thickness, titanium appears to be superior. Stainless steel and cobalt-chromium alloys were well tolerated.

The comparison of experimental data available from different sources demonstrates the multiple variables influencing the final tissue response: the surface characteristics,[8] the shape and the size of the implants,[9] the type of tissue where the material was tested,[10] etc. The ASTM F-4 Committee[11] has recommended certain standards for testing of metallic materials and has standardized the controls to enable a better correlation among results from different sources.

Recent data obtained by the study of human tissues adjacent to removed metallic prostheses support the conclusions reached by experimental animal implantation. Minimal fibrosis is observed

around titanium implants; increased fibrosis was demonstrated in tissues around cobalt-chromium and stainless steel.[12]

Interest in the local reaction induced by particulated metals was motivated initially by the idea of increasing the reactive surface, and later by the possibility of reproducing the tissue reaction to wear particles. Cohen[5] described in experimental animals a benign tissue response with minimal fibrosis for Co-Cr alloy powder and a greater fibrosis for stainless steel and polymers. Bullough[13] reported similar results in the study of tissue reaction to particulate Co-Cr and stainless steel in humans, concluding that cobalt-chromium was locally less toxic.

The convenience of an *in vitro* bioassay quick screening method stimulated the search for a suitable technique. Pappas[14] demonstrated that many metal powders are more or less toxic in cell cultures with an indirect relationship to particle size. Stainless steel proved to be more toxic than Co-Cr alloys. Hegyeli,[15] using cells cultured on a metal base, demonstrated a high degree of growth inhibition by titanium. The results from culture methods are still scarce and not standardized; results have to be considered and carefully compared with *in vivo* testing methods[16] to determine their mutual relationship and significance.

Ceramics and glasses are generally considered as inert materials in the tissues.[17] The first attempts to use these materials as hard tissue substitutes failed because of their inherent brittleness.[18] Plaster of Paris ($CaSO_4$), although very poor from a mechanical point of view, appeared well tolerated. However, reabsorption of the implant limited its use.[19] Cerosium, a porous aluminate ceramic impregnated with epoxy, was developed in an effort to improve the strength of these materials. Tissue responses were controversial in short-term studies, but long-term follow-up showed increasing local reaction[20] and biodegradation with loss of flexural strength.[21] Solid implants of single phase ceramics, titanium dioxide[22,23] and aluminum oxide,[24,25] induced tissue reactions similar to those of corrosion resistant metals in contact with bone and soft tissue. Nonductile fractures still constitute a major limitation to their use.[26]

The local tissue reaction of calcium zirconate to polyphasic ceramics[27] was also similar to that of corrosion resistant metals, calcium titanate being the best tolerated.[22] Dense magnesium aluminate produced a highly cellular reaction implanted in solid form in bone.[28]

Several glasses have been experimentally tested as solid implants in soft tissue. The results reported indicated no adverse response for soda-lime, alumino-silicate, and borosilicated glasses.[29] In the same study, high sulfur glasses showed severe attack by tissue and abscess formation. Several other glass ceramics in crystallized and uncrystallized form were tested by the same author reporting no adverse effects.

Fused quartz (silica) was apparently well tolerated when implanted as a solid block subcutaneously[29] or in the muscle.[30] However, the local granulomatous reactions produced by silica particles in some tissues are well known in human pathology. Particulate magnesium silicate appeared to induce experimental granulomatosis in animals.[31]

Combination of ceramics with metals to increase flexural strength or to supply special purpose surfaces for skeletal implants have been recently considered. Some bioassay data on these materials are available. Ceramic-coated metals with alumina and phosphorus glass enamels appear to be well tolerated in bone.[32]

High purity carbons in different physical forms have shown very good tissue tolerance in experimental animal models in solid and particulate form[33–35] and in tissue cultures.[4]

Among fluorocarbons, Teflon, used initially in hip prostheses, appeared well tolerated in experimental animal implantation in solid and particulate samples. Later, it proved to be locally and systemically toxic[36] in the human subject.

Tissue reactions to polyethylene of different molecular weights were described by several authors. Reaction around solid implants in soft tissues and bone was moderate;[37–40] local tissue response around blocks of ultrahigh molecular weight polyethylene showed minimal fibrosis.[12] Particulate low molecular weight polyethylene appeared specifically toxic in soft tissues inducing granuloma formation.[41]

Polymer composites show local tissue reactions in accordance with their constituent materials.[35] Quartz and graphite composite polyethylenes induced moderate degrees of fibrosis in surrounding tissues.[35,42]

MATERIALS AND METHODS

Twenty-six materials were used in solid and powder form. All the materials were obtained commercially, except ultrahigh molecular

weight polyethylene graphite composite which was manufactured in the laboratory with commercial RCH-1000 and Airco Speer graphite powder.

The materials and their sources are listed in Table 1.

Preparation of Samples

Implants

The solid implants were rods of 3/16 in. diameter by 0.091 in. long. The surfaces of the implants were finished according to ASTM standards[43] for metallic implants in human subjects. One surface of the implant was highly polished for metallographic study. Different samples were all of the same approximate dimensions and therefore of different weights.

Sterilization was accomplished by dry heat or gas exposure according to ASTM specifications for each type of material.

Powders

In the case of unalloyed titanium, titanium oxide, stainless steel 316L, titanium 6% aluminum 4% vanadium, graphite, and molybdenum disulfide, the powders were directly obtained from the sources described in Table I.

In the case of ceramics including aluminum oxide, aluminum titanate coating, Lucallox, chromium oxide, boron carbide, fused quartz, Pyroceram, and silicon carbide, the powders were obtained by comminution of the corresponding solids in a mortar. In the case of the polymers, because of their particular mechanical characteristics, samples were prepared by filing or machining the commercial product, obtaining, for this reason, larger particles, in general above 50 μ.

Following comminution the powders were separated in homogeneous particle size samples. With metals and ceramics, powders in the range from 8–20 μ were obtained using a water elutriation apparatus. With polymers, because of the large particle size and because of lower than water density, this technique could not be used.*

* Samples of polyethylenes and Teflon consisted of commercial powders supplied with a particle size of 50 to 75 μ for the former and 35 μ average for the latter. Polyimide powders were also commercial samples of particle sizes, averaging 100 to 150 μ.

TABLE I

List of Materials

Material	Supplier	Test sample
316L stainless steel	Joslyn Stainless Steels	Solid
316L stainless steel	Hoegones Corp.	Powder
titanium (unalloyed)	Titanium Metals Corp. of Amer.	Solid
titanium (unalloyed)	Penn. Nuclear Corp.	Powder
Ti 6 Al 4 V	Titanium Metals Corp. of Amer.	Solid
Ti 6 Al 4 V	Penn. Nuclear Corp.	Powder
Zircalloy 2	Wah Chang Albany Corp.	Solid
wrought cobalt chromium	Howmedica Inc.	Solid
graphite (commercial)	Superior Graphite Co.	Powder
graphite (high purity)	Airco Speer Graphite	Powder
fused quartz, 7940	Corning Glass Works	Solid/Powder
high-density 9681 aluminum oxide	Coors Porcelain	Solid/Powder
Lucalox, high-density aluminum oxide	General Electric	Solid/Powder
molybdenum disulfide coating	Norton Co.	Powder
titanium dioxide	Norton Co.	Solid/Powder
chromium oxide high-density K-ramic	Kaman Corp.	Solid/Powder
boron carbide high-density grade	Carborondum Corp.	Solid/Powder
silicon carbide KT grade	Carborondum Corp.	Solid/Powder
titanium aluminate Norton coating	Norton Corp.	Solid/Powder
Pyroceram experimental grade	Corning Glass Works	Solid/Powder
9608, Pyroceram	Corning Glass Works	Solid/Powder
9606, Pyroceram	Corning Glass Works	Solid/Powder
Vespel, SP-1	DuPont	Solid/Powder
Vespel, SP-21	DuPont	Solid/Powder
Vespel, SP-3	DuPont	Solid/Powder
Teflon	Chicago Molded Products	Powder
RCH-1000 graphite composite	Howmedica Inc. Superior Graphite Co. (Manufactured in lab.)	Solid/Powder
RCH-1000 (ultrahigh molecular polyethylene)	Howmedica Inc.	Solid/Powder
high-density polyethylene, 5095	Phillips Petroleum Co.	Solid/Powder

Fig. 1. Water elutria
powder samples. (a) F
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Water flowed to the
0–16 cm³/min and
was calculated that
min yielded a 1 cm

	Test sample
s	Solid
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	Powder
p. of Amer.	Solid
	Powder
Corp.	Solid
	Solid
	Powder
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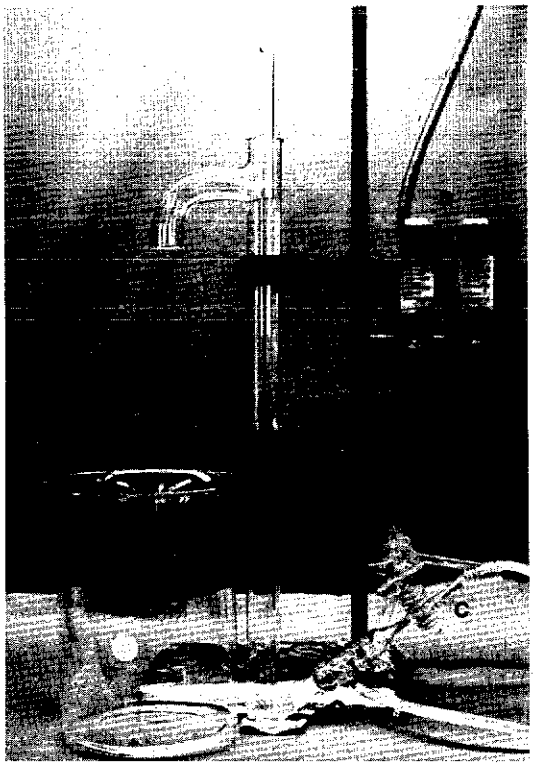

Fig. 1. Water elutriation apparatus used to obtain the metallic and ceramic powder samples. (a) Flow regulator meters, (b) fractionating column, (c) air bleeder outlet.

The water elutriation apparatus (Fig. 1) consisted of a constant pressure reservoir, adjustable flow-regulated meters, an air bleeder outlet, and a fractionating tube. Tap water filled the reservoir to capacity, the overflow being discarded from the constant pressure reservoir and the rest of the system operated under constant pressure. Water flowed to the two flow regulator meters, one measuring from 0–16 cm^3/min and the other measuring from 0–90 cm^3/min. It was calculated that in this particular fractionating column, 20.3 cm^3/min yielded a 1 cm rising height of the water level. From the flow-

regulating meters the water went to the fractionating column, where the powder lay that was to be separated.

The principle of powder size fractionation by utilizing water elutriation is based on Stoke's Law where the critical particle size is determined by:

$$c = \frac{18\ nv}{(p_p - p_f)\ g}$$

v is the linear velocity of fluid through the chamber, g is the acceleration due to gravity, n is the viscosity of the fluid, p_p is the density of powder particles, p_f is the density of fluid.

By simply adjusting the rate of water rise in the fractionating tube, the powder was separated into different size fractions.

After fractionation the metallic samples were cleaned and passivated following ASTM recommendation.[43] Materials other than metal were cleaned with a detergent, washed, and centrifuged several times. After washing and drying, the powder samples were placed in sealed glass ampoules. The 316L stainless steel control dose consisted of 464 mg powder. The dosage of the other test materials were determined by weighing out the amount of material which would give a volume equal to the control.

Implantation Procedure

One-hundred forty-five Adult New Zealand albino rabbits 5–6 lb in weight, six weeks of age were used as test hosts for implantation. The standard aseptic surgical technique was observed.

After parenteral anesthesia, the solid rods were introduced surgically in the paravertebral muscle using Teflon-coated forceps.

The powders were introduced through a glass funnel directly from the ampoule to a pocket dissected in the paravertebral muscle fibers.

Histology Technique

Six months after surgery, the animals were sacrificed and the implants retrieved en bloc with the surrounding tissues. The liver, lung, kidney, and spleen were also obtained. The specimens were immediately fixed in 10% buffered formalin for a minimum of 48 hr.

The fixed tissue blocks were dissected. Those containing the powders were sectioned across the powder pocket; those containing

the solids were sliced and the implants removed manually with care so as not to damage the encapsulating fibrous membrane. The tissue samples were embedded in paraffin and sectioned in 6 μ slices with a Jung microtome. A minimum of six sections were processed from each sample and stained with Hematoxilin-Eosin and with Mallory II. The organs were sectioned and representative blocks processed for histology study.

Histology and Scoring System—Solids

The tissues around the implant were examined at low and high power optical microscopy.

The thickness of the fibrous membrane encapsulating the implant was measured with a Zeiss measuring eyepiece at four different points, an average value was calculated[7] and the mean value for each material was entered in the table. When measuring the membrane thickness, special care was taken to avoid the areas in direct contact with the angles of the implant where increased thickness and cellularity occurs.[9] The zone of loose, fatty, or connective tissue between the membrane and the muscle was measured using the same procedure and recorded in the same way.

The tissue response peripheral to the fibrous membrane was evaluated according to:

a) cellularity which included an estimate of the number of cells present in that area,
b) cell types with a qualitative evaluation of different cellular types present according to their morphological pattern,
c) the degree of inflammatory reaction according to cellular response was tabulated from +1 to +3 for each material, following the conventional patterns for inflammatory tissue response,[6]
d) the presence of blood vessels in the membrane or adjacent to it was recorded as well as small opaque extracellular debris. These two parameters were graded from 0 to +3 in increasing order of incidence.

Histology and Scoring System—Powders

The tissues around the powder packet and infiltrating between powder clumps were examined as described for the solid implants for

granulomas, abnormal cellular proliferation, and signs of cellular malignancy in these areas. The surrounding muscle was examined for necrosis or degeneration.

An attempt to quantitate the amount of fibrous tissue embedding the powder clumps was done measuring the average thickness and abundance of fibrous strands between these structures. Values from 0 to +3 were given to increasing abundance of fibrous tissue separating the muscle from the implant. Clear spaces between powder and tissue, although in many cases obviously representing sectioning artifacts, were recorded from 0 to +3, the maximum value corresponding to abundant spacing with average width above 100 μ.

Vascularity present among the tissue was tabulated. Macrophages, fibrocytes, giant cells, and eosinophils* were tabulated as in the solid implants. An average value of all tested samples was entered in the table.

EXPERIMENTS AND RESULTS

One-hundred forty-five rabbits were implanted in the paravertebral muscles with the different materials, 22 solids and 25 powders. Six implants were made per animal: three in solid and three in powder form, two control samples, and four test samples. The control samples consisted of 316L stainless steel. As a rule, six animals were used for evaluation of each material.

Six months after implantation, the animals were sacrificed. Local reaction, lung, liver, kidney, and spleen were studied histologically as described above. Pathological findings in the organs were compared with expected spontaneous pathology in laboratory animals.

Solids

The muscle surrounding the implant did not show gross necrosis in any of the materials tested. Few specimens presented changes compatible with hyaline degeneration in isolated muscle fibers, but because of its random distribution and very low incidence, this was not considered to be directly related to the implant toxicity. The cellular reaction depicted by the tissues in close contact with the implants exhibited in general a typical pattern of unspecific chronic

* Includes all eosine staining granulocytes: the equivalent to neutrophils, pseudoeosinophils staining heterophils in some rodents[44] and true eosinophils.

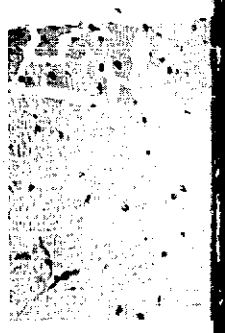

Fig. 2. Microphotog
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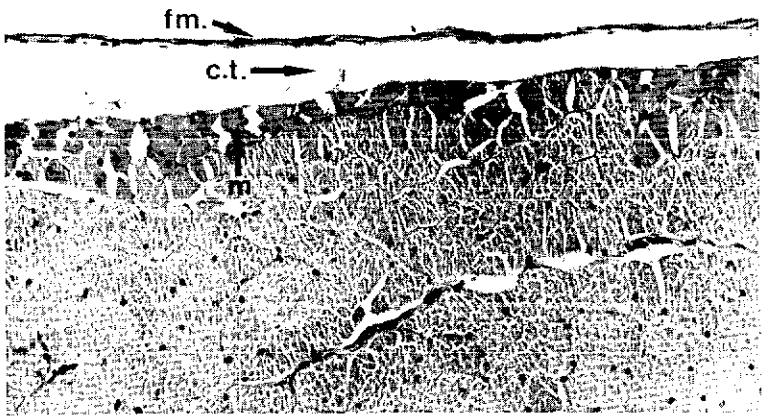

Fig. 2. Microphotograph of the tissues in contact with a solid 316L stainless steel control sample. A very thin fibrous membrane (f.m.) adjacent to the implant is shown, separated from muscle fibers (m) by a very poorly cellular connective tissue layer (c.t.). The fissuring apparent in the muscle is a fixation artifact. × 100.

inflammation. Small typical granulomas were present in some instances (Vespel, Pyroceram) and more frequently small focuses of cellular proliferation occurred. None of those areas showed changes compatible with malignancy.

Vitallium and titanium appeared as the least reactive metals in relation to fibrous membrane thickness; 316L and titanium 6 AL 4V were slightly more reactive (Fig. 2). Zircalloy showed to be a poorly tolerated metal (Fig. 3).

According to fibrous membrane thickness and standard pattern of chronic inflammatory response, titanium oxide, titanium aluminate, and silica appeared as the least reactive of the ceramics. Cellular reaction was minimal and fibrosis scarce. Giant cells were present in rare instances. The glass-ceramics studied (Pyroceram) exhibited marked fibrosis and cellular proliferation (Fig. 4).

Polyimides appeared as particularly toxic and showed some granulomas around a necrotic center. Ultrahigh molecular weight poly-

ethylene elicited a reaction comparable to stainless steel and no obvious difference was observed when graphite was incorporated into the matrix.

The results are summarized in Table II. The materials are listed according to increasing thickness of their fibrous membrane.

TABLE II

Histological Evaluation of the Solid Implants

Solid materials[a]	Average membrane thickness, μ	Cellularity surrounding tissues	Cellular type of inflammatory reaction	Dark extracell bodies	Average loose connective tissue thickness, μ
titanium dioxide	10	0	+1	+2	150
titanium aluminate	11	+1	+1	+2	46
Vitallium	14	0	+1	0	207
fused quartz	14	+1	+1	+1	15
chromium oxide	14	+1	+2	+3	312
boron carbide	14	+1	+1	+1	260
titanium	15	0	+1	+1	450
RCH. 1000 + graphite	15	+1	+1	+2	300
Lucalox	15	+1	+1	+1	180
Ti 6 Al 4 VA	17	+1	+1	+1	260
316L stainless steel	18	+1	+1	+1	200
silicon carbide	19	0	+1	+3	600
high density polyethylene	20	+1	+1	0	280
RCH. 1000	20	+1	+1	+1	126
Pyroceram, experimental grade	25	+1	+2	+3	190
9608 Pyroceram	25	+2	+2	+1	60
Vespel SP-21	26	+3	+2	+3	120
aluminum oxide	29	+1	+2	+1	140
Vespel SP-3	30	+2	+3	+3	220
Vespel SP-1	36	+2	+3	+1	70
9606 Pyroceram	46	+3	+3	+2	40
Zircalloy	51	+2	+2	+2	29

[a] Assuming an error in measurement of ± 5 μ, materials whose difference in membrane thickness appear within this range can be considered to belong to the same group.

Fig. 3. Microphotogr
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lar of m- ory ion	Dark extra- cell bodies	Average loose con- nective tissue thick- ness, μ
l	+2	150
l	+2	46
l	0	207
l	+1	15
2	+3	312
l	+1	260
l	+1	450
l	+2	300
l	+1	180
l	+1	260
l	+1	200
l	+3	600
l	0	280
l	+1	126
2	+3	190
2	+1	60
2	+3	120
2	+1	140
3	+3	220
3	+1	70
3	+2	40
2	+2	29

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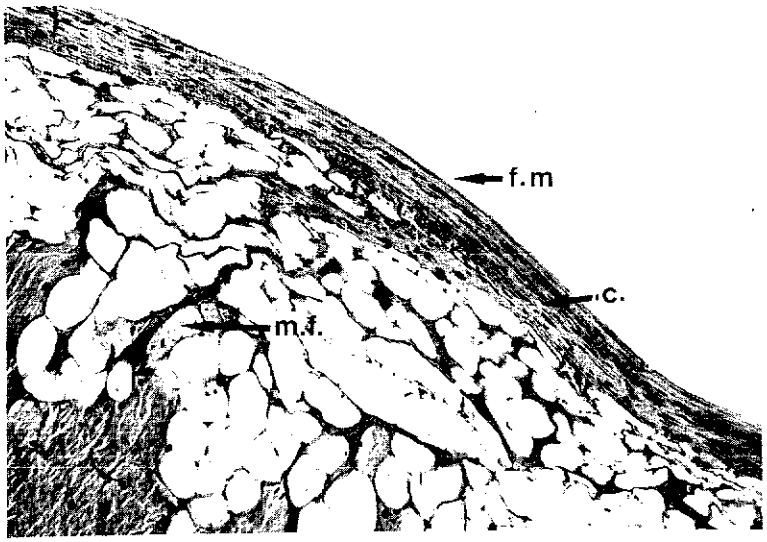

Fig. 3. Microphotograph of the fibrous membrane (tim) and adjacent tissues in a solid sample of Zircalloy. The membrane appears extremely thick and moderate cellularity is present in its basal layers. Muscle fibers (m.f.) show centrally located nuclei. × 100.

If we assume that a single cell layer is approximately 10 μ thick, an error in measurement of ± 5 μ can be easily incurred. A statistical analysis of membrane thickness data was not done because of the nature of the data, but it is felt that differences up to the thickness of one cell layer (10 μ) are probably not significant.

Powders

The histological findings in the particulate materials are listed in Table III following the same criteria used in the solids. The last four materials listed were tested only in particulate form.

The muscle around the implants did not present signs of necrosis. Areas of cellular proliferation were seen far from the powder only in a few instances among those more reactive materials, Pyrocerams, polyimides, and Teflon. Granulomas and abundant cellular infiltrates were seen with the polyimides, Pyroceram, and RCH-1000 (Fig. 5). No malignant cellular growth was observed.

TABLE III

Histological Evaluation of the Particulate Materials

Particulate materials[a]	Cell proliferation	Fibrous strands	Clear spaces	Blood vessels	Interface	Fibrocytes	Macrophages	Giant cells	Eosinophils[b]
titanium dioxide	0	0	0	+3	+3	2	+2	0	0
titanium aluminate	+1	0–1	0–1	+1	+2	2–3	+1	+2	+1
Vitallium	0	0–1	2	+1	+1	2	+2	0	0
fused quartz	+1	1–2	1	+2	+1	2	+2	+3	+1
chromium oxide	+1	1	1	+1	+1	2	+2	+3	+1
boron carbide	+2	1	1–2	+3	+0–1	2	+2	+2	+1
titanium	0	0	1–2	+1	+2	2	+2	0	0
RCH-1000 + graphite	+2	1	1–2	+1	+2	2	+2	+3	0
Lucalox	+2	0	1	+1	+2	2	+2	+2	0
Ti 6 Al 4 VA	+1	1	1	+1	+1	2	+2	+2	0
316L stainless steel	+1	1	1	+1	+1	2	+2	+1	+1
silicon carbide	+1	1	2	0	0	2	+2	+2	0
RCH-1000	+2	1	0	+3	+1	2	+2	+3	0
high-density polyethylene	+3	1	0–1	+3	+1	2	+2	+3	0
Pyroceram, experimental grade	+1	1–2	0	+2	+2	2	+2	+3	+1
9608 Pyroceram	+2	1–2	1	+2	+1	2	+2	+2	+1
Vespel SP-21	+3	2	1	+1	+2	1	+3	+3	0
aluminum oxide	+1	0–1	0–1	+1	+2–3	2–3	+1	+2	+1
Vespel SP-3	+3	3	2	+1	+2	1	+3	+3	0
Vespel SP-1	+2	1	1	+2	+2	2	+2	+2	0
9606 Pyroceram	+2	1	1	+3	+1	2	+2	+3	0
high purity graphite	0	1	0–1	0	+2	2	+2	+2	0
low purity graphite	+1	0	1	+1	+1	2	+2	+2	0
molybdenum disulfide	+1	0–1	0–1	+2	+1	2	+2	+3	0
Teflon	+3	1	0	+2	+1	3	+1	+2	0

[a] Materials are listed in the same order appearing in Table II, except for the last four materials which were tested only as particulate samples.

[b] Includes eosine staining neutrophils and true eosinophils.

Fig. 4. This photomicro
specimen of 9608 Pyroceram
round cells proliferation (e

Fibrous tissue surro
between the particles
Vitallium, Ti6Al4Va,
appeared slightly more
frequently present with
corresponded to a ma
abundant among the
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RCH-1000) (Fig. 7) a
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Fig. 4. This photomicrograph of the fibrous membrane (m) around a solid specimen of 9608 Pyroceram, shows a very abundant underlying fibrous and small round cells proliferation (c) with occasional giant cells (g.c.). × 100.

Fibrous tissue surrounding the powder clumps or infiltrating between the particles was particularly scarce in graphite, titanium, Vitallium, Ti6A14Va, and stainless steel 316L (Fig. 6). Vitallium appeared slightly more reactive than titanium. Blood vessels were frequently present within the fibrous tissue. Fibrocytes in general corresponded to a mature type and macrophages were especially abundant among the polyethylene powder. Giant cells were observed frequently around polymers (high-density polyethylene and RCH-1000) (Fig. 7) and some ceramics (fused quartz, chrominum oxide, Pyroceram, molybdenum). Eosin staining granulocytes constituted an occasional finding. Some ceramic particles appeared to be very well tolerated, especially titanium dioxide. However, Lucalox and Pyroceram samples showed abundant cellular proliferation.

Organs

The macroscopic study of the organs revealed a small number of abnormalities. The surfaces of a few kidneys appeared mottled,

aluminum oxide	+1	0–1	0–1	+1	+2–3	2–3	+1	+2	+1
Vespel SP-3	+3	3	2	+1	+2	1	+3	+3	0
Vespel SP-1	+2	1	1	+2	+2	2	+2	+2	0
9606 Pyroceram	+2	1	1	+3	+1	2	+2	+3	0
high purity graphite	0	1	0–1	0	+2	2	+2	+2	0
low purity graphite	+1	0	1	+1	+1	2	+2	+2	0
molybdenum disulfide	+1	0–1	0–1	+2	+1	2	+2	+3	0
Teflon	+3	1	0	+2	+1	3	+1	+2	0

[a] Materials are listed in the same order appearing in Table II, except for the last four materials which were tested only as particulate samples.

[b] Includes eosine staining neutrophils and true eosinophils.

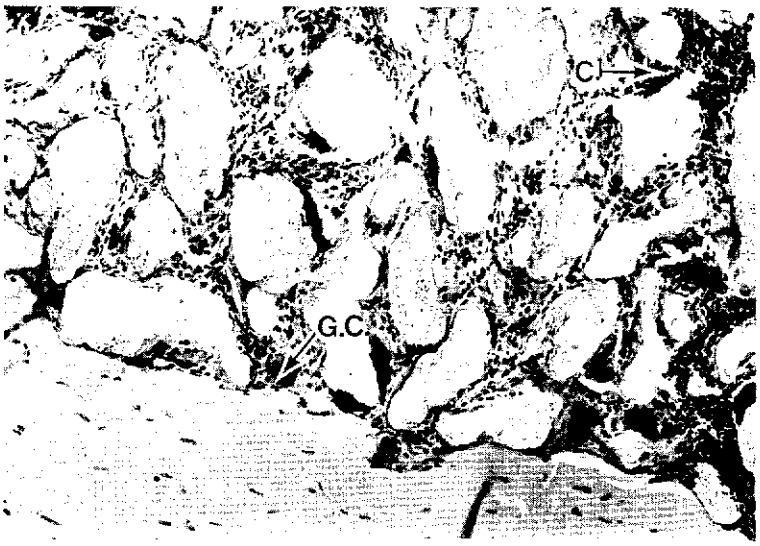

Fig. 5. Clusters of inflammatory small round cells (c) are abundant in the tissue proliferation between particles of Vespel SP-21. Conventional foreign body giant cells (g.c.) are abundant in this microphotograph. × 100.

representing superficial nephritic scars as it was later revealed by microscope examination. The livers appeared grossly normal and some sections showed small periportal infiltrates. Lungs showed a somewhat higher incidence of abnormalities, interstitial inflammatory changes, and lymphocytic hyperplastic peribronchial infiltrates being rather common. No significant abnormalities were detected in the spleens.

DISCUSSION

The study of the fibrous membrane thickness around the solid implant constitutes a reliable source of quantitative data to test a material, provided that mechanical effects are minimized.

Histological data on cellularity and cellular type must be interpreted cautiously. The arbitrary values used in this kind of evaluation make it difficult to accurately quantitate the inflammatory response and do not make statistical analysis recommendable. This model is restricted to a general system lacking very fine discrimin-

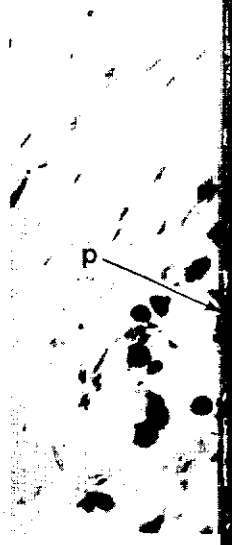

Fig. 6. The 316L sta
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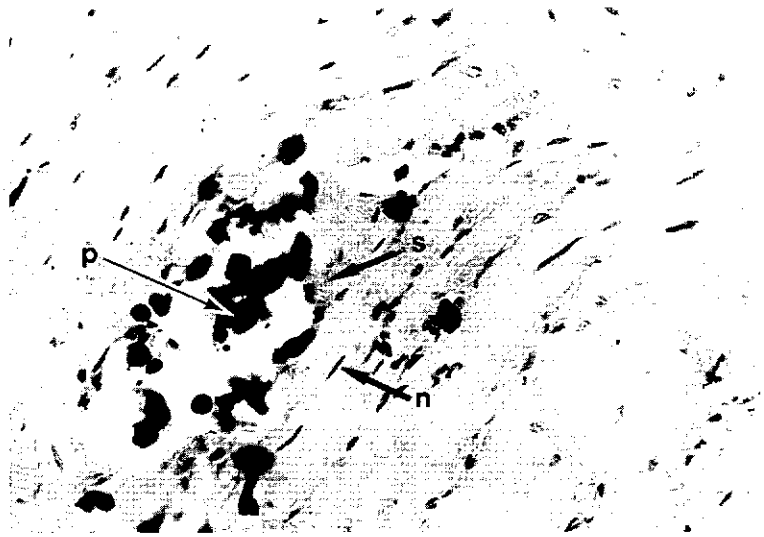

Fig. 6. The 316L stainless steel particles (p) used in this study as the powder control sample appears in this microphotograph eliciting minimal reaction in the muscle tissue. Nuclei (n) of cells in direct contact with the particles are peripherally located and striation of the sarcoplasma (s) is present. No tissue proliferation is present between the particles. × 160.

as later revealed by grossly normal and s. Lungs showed a interstitial inflam- peribronchial infil- abnormalities were

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atory potential, other bioassay techniques providing more accurate quantification of the local tissue response have to be developed. Laing's[7] studies indicated a correlation of fibrous membrane thickness with surrounding tissue in inflammation. Other studies[45] failed to reveal the same correlation; however, implantation times and mechanical characteristics of the materials tested differed considerably.

The significance of the presence of small opaque particles around the implants is difficult to assess as the exact nature of these particles is impossible to identify by means of optical microscopy. The value of the thickness of the zone of loose connective tissue appears to be more related to the local mechanical effect of the implant than to any type of inflammatory response.

Many of those materials presenting a thick fibrous membrane around the solid implant showed abundant cellularity in the surrounding tissues (Table II). Many of those materials showing abundant inflammatory cells when implanted as solid samples

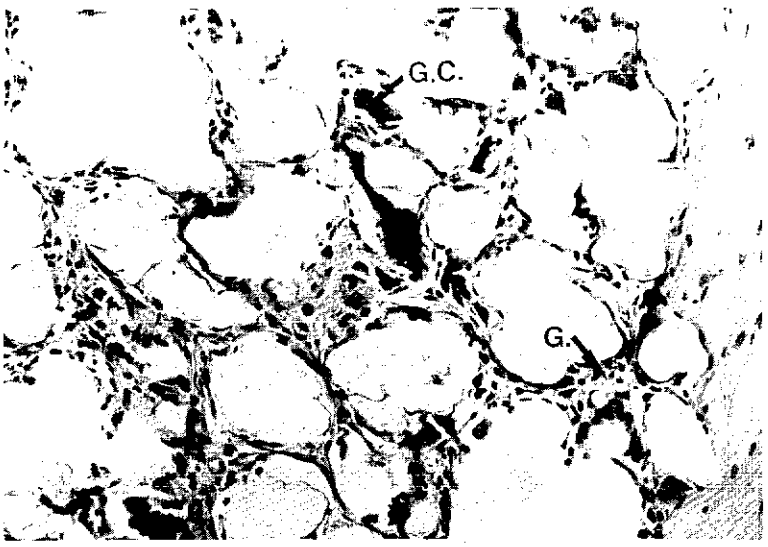

Fig. 7. Fibrous tissue proliferation is abundant around RCH-1000 particles implanted in muscle. This microphotograph shows some giant cells (g.c.) and small granuloma (g) formation. × 250.

produced considerable cellular reaction when implanted as powder samples (Table III). Ultrahigh molecular weight polyethylene was one exception; although prescribed as a well-tolerated material in solid form, it produced considerable inflammatory response and granuloma formation when tested in particulate form. This implies that wear products from this material might be reactive in the tissues provided that a sufficiently large volume of particles is present. Obviously, further clinical and laboratory work on the wear of ultrahigh molecular weight polyethylene is required to insure its safety when used in young and active individuals.

The use of Zircalloy as an implant material is clearly precluded by the local toxic response it induced. Zirconium, however, has been described by Laing[46] as well tolerated.

Polyimides (Vespel) have been suggested as a candidate for joint replacement applications due to their reputedly high wear resistance. They are used industrially as wear-resistant materials in dry types of bearings. In animal tissues in this study they consistently

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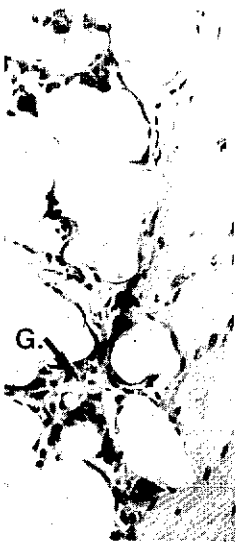

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exhibited a local toxic tissue response both in solid and in particulate form. Wear studies[2] indicated that polyimides were not superior to ultrahigh molecular weight polyethylene in wear behavior. It is felt for these reasons that their use in joint replacement as implants is contraindicated.

Teflon was implanted only in particle form. A consistently undesirable rich cellular response with small round cell infiltrates and occasional granuloma formation was observed. The findings confirmed the clinical experience of Charnley.[36]

Ceramics have been presented by many investigators as essentially inert and biocompatible, greatly superior to the metallic materials in current use. The results of this investigation do not support this assumption. The best-tolerated ceramics, titanium dioxide and titanium aluminate, exhibited tissue responses essentially similar to those of titanium or cast cobalt-chrome alloy and certainly not superior to them. In addition, some of the other ceramics tested including the glass ceramics were among the most reactive of the materials examined. Ceramics are brittle materials and in the authors' opinions, there is little justification for their use in skeletal weight-bearing applications.

The scarce pathology detected in the study of organs corresponds to the findings expected to occur spontaneously in laboratory animals.[47,48] The materials evaluated were thought to be relatively inert and were chosen for this study on that basis. The lack of systemic toxicity is therefore not surprising.

Carcinogenic and teratological effects are potential problems that must be considered in the overall biological acceptance of an implant material. Their evaluation was not a part of this study and no conclusions can be drawn in that matter from these results.

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