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J Bone Joint Surg Am. 1988;70:347-356.

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Publisher Information

The Journal of Bone and Joint Surgery
20 Pickering Street, Needham, MA 02492-3157
www.jbjs.org

Metallic Wear in Failed Titanium-Alloy Total Hip Replacements

A HISTOLOGICAL AND QUANTITATIVE ANALYSIS*

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ABSTRACT: We conducted extensive histological examination of the tissues that were adjacent to the prosthesis in nine hips that had a failed total arthroplasty. The prostheses were composed of titanium alloy (Ti-6Al-4V) and ultra-high molecular weight polyethylene. The average time that the prosthesis had been in place in the tissue was 33.5 months (range, eleven to fifty-seven months). Seven arthroplasties were revised because of aseptic loosening and two, for infection. In eight hips cement had been used and in one (that had a porous-coated implant for fifty-two months) no cement had been utilized.

Intense histiocytic and plasma-cell reaction was noted in the pseudocapsular tissue. There was copious metallic staining of the lining cells. Polyethylene debris and particles of cement with concomitant giant-cell reaction were present in five hips. Atomic absorption spectrophotometry revealed values for titanium of fifty-six to 3700 micrograms per gram of dry tissue (average, 1047 micrograms per gram; normal, zero micrograms per gram), for aluminum of 2.1 to 396 micrograms per gram (average, 115 micrograms per gram; normal, zero micrograms per gram), and for vanadium of 2.9 to 220 micrograms per gram (average, sixty-seven micrograms per gram; normal, 1.2 micrograms per gram). The highest values were found in the hip in which surgical revision was performed at fifty-seven months. The concentrations of the three elements in the soft tissues were similar to those in the metal of the prostheses.

The factors to which failure was attributed were: vertical orientation of the acetabular component (five hips), poor cementing technique on the femoral side (three hips), infection (two hips), and separation of a sintered pad made of pure titanium (one hip). A femoral component that is made of titanium alloy can undergo

severe wear of the surface and on the stem, where it is loose, with liberation of potentially toxic local concentrations of metal debris into the surrounding tissues. It may contribute to infection and loosening.

Titanium alloys have attracted considerable attention in the development of surgical implant materials because of their excellent mechanical properties, resistance to corrosion, and biocompatibility^{1,3,27,40}. A number of designs of titanium alloy (Ti-6Al-4V) total hip prostheses are available³². That alloy has the advantage of reducing the incidence of fracture of the stem as compared with models that are made of other alloys³⁶. It has a lower modulus of elasticity than stainless steel and cobalt-chrome^{30,35,40,41}.

The designs include the DF-80 (Zimmer; Warsaw, Indiana), ES-30 (Biomet), 6Ti/32 (Zimmer) (6032), STH (Zimmer), and HGP (Zimmer). The wear properties of titanium alloy and of ultra-high molecular weight polyethylene have been studied extensively⁸. Under certain laboratory conditions, Ti-6Al-4V is more susceptible to severe abrasive corrosive wear than is 316 stainless steel or cobalt-chrome alloy, but the exact conditions in clinical practice under which the threshold for breakdown of the titanium alloy is crossed are not understood²⁴. To our knowledge, in only one report that was devoted to titanium prostheses (seven hips) were the clinical findings as well as descriptions of the prostheses at surgical revision given in detail. The macroscopic findings in these hips indicated that there was no evidence of abnormal wear after the implants had been in the patients for eleven to fifty-seven months⁸.

Materials and Methods

At The Hospital for Special Surgery, we observed that there was black staining in the soft tissues that were adjacent to failed Ti-6Al-4V alloy implants at the time of revision surgery. The purpose of this report is to present the histological features of the soft tissues adjacent to the total hip-replacement components that were composed of titanium alloy and polyethylene and to document the amounts of the metal in those tissues. Between August 1985 and February 1986, tissues were obtained from nine such hips in eight patients. A brief summary of each case history follows.

* No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article. No funds were received in support of this study.

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CASE 1. A seventy-three-year-old woman who had a twenty-year history of rheumatoid arthritis was first seen at our institution thirty-two months after a total hip replacement in which a titanium femoral component was inserted. She complained of pain when walking. Radiographs made just before our revision arthroplasty showed that the acetabular component had been oriented 55 degrees from the horizontal and that there was loosening of both components, with subsidence of the femoral component. A radiolucent zone, more than two millimeters in width, was present in all three zones on the acetabular side. Preoperative cultures and cultures of material that was obtained at surgical revision were negative for bacteria. Both components were revised. At operation, the synovial lining was noted to be darkly stained.

CASE 2. A seventy-three-year-old man who had osteoarthritis was seen thirty-four months after total hip arthroplasty. He complained of a six-month history of pain when walking. There had been no fever or chills. Radiographs revealed that the femoral component was loose. The acetabular component, which had been placed too high and too far laterally, was well fixed. Preoperative and intraoperative cultures were negative for infection. At revision, gray staining of the synovial tissue was noted. Only the femoral component was replaced. Two months postoperatively, the patient complained of severe pain in the hip, and infection with *Staphylococcus epidermidis* was diagnosed. The patient was treated with débridement and intravenous administration of antibiotics.

CASE 3. A sixty-two-year-old man who had idiopathic osteonecrosis had total hip replacement at The Hospital for Special Surgery. The initial radiographs revealed excellent position and cementing technique. He was free of pain for four years, but then increasing pain developed when walking. He denied having fever or chills. Radiographs that were made fifty-seven months after the arthroplasty revealed loosening and subsidence of the femoral component. Intraoperative cultures were negative for infection. At surgical revision, intense black staining of the tissue adjacent to the components was observed. Only the femoral component was loose, and it was replaced.

CASE 4. A sixty-five-year-old woman who had osteoarthritis was seen thirty-one months after total hip replacement. She had had severe pain for eight months, with episodes of fever and chills. All attempts at passive motion of the hip elicited pain, and radiographs revealed gross loosening of both components. Culture of material obtained from aspiration of the hip joint preoperatively grew *Staphylococcus aureus*. At operation, the hip joint was found to be grossly purulent. There was intense black staining of the soft tissues of the joint capsule, which was severely distended because of the infection. A Girdlestone procedure was done, and the patient was successfully treated for the infection with intravenous administration of nafcillin.

CASES 5 AND 6. A fifty-seven-year-old man who had osteoarthritis first came to see us after bilateral total hip arthroplasty. The left hip had been replaced seventeen months earlier and the right, twenty-eight months earlier, but neither hip had been free of pain during this interval. He had no fever or chills. Radiographs revealed that there was poor cement technique on the femoral component bilaterally.

Radiolucent lines around the cement were evident in zones 2 to 6 on the right and zones 1 to 7 on the left¹⁶. Each acetabular component was well fixed, but neither was oriented properly (55 degrees from the horizontal on the left and 48 degrees, on the right). Preoperative and intraoperative cultures were negative for infection. At staged revision (four months apart), the femoral components were found to be grossly loose. The soft tissues adjacent to the components were gray.

CASE 7. An eighty-four-year-old woman who had Paget disease and osteoarthritis was seen eleven months after total hip arthroplasty. She had had pain on walking ever since the operation but had not had fever or chills. Radiographs revealed loosening and subsidence of the femoral component. The acetabular component, which was oriented 64 degrees from the vertical, was well fixed. Preoperative and intraoperative cultures were

negative for bacteria. At the revision procedure, both components were found to be loose and were replaced. No unusual staining of the synovial tissue was noted.

CASE 8. A sixteen-year-old girl had severe degenerative joint disease secondary to a failed Chiari osteotomy for congenital dysplasia of the hip. She had total hip arthroplasty using custom-made components. The femoral component was a press-fit model with a stem of titanium alloy that was covered with sintered pure-titanium wire mesh anteriorly and posteriorly in its proximal one-quarter. The ball for the femoral head was composed of titanium alloy that had been cold-welded onto a tapered neck. The acetabular component was made of polyethylene and was cemented.

The patient did well for four years and then began having pain when walking. Radiographs demonstrated subsidence of the femoral component. Preoperative and intraoperative cultures were negative for infection. At the revision procedure, the titanium mesh on the anterior part of the stem was found to be partially detached, and both components were loose. They were replaced with press-fit components. The soft tissue of the joint lining was found to be stained dark gray.

CASE 9. A seventy-five-year-old man who had osteoarthritis was seen by us twenty-three months after a total hip arthroplasty. The postoperative course had been complicated by posterior dislocation two weeks after the operation; this had been treated by trochanteric advancement. The patient continued to complain of pain and was unable to bear weight on the limb. Eight months postoperatively, a mixed infection with *Enterobacter* and *Enterococcus* was diagnosed, and the patient was treated with débridement and intravenous administration of antibiotics for six weeks.

When we first saw the patient, there was resistance to any motion of the hip, but there was no active drainage. Radiographs showed that the components were in good position, and there was no radiographic evidence of loosening. Cultures of material that was aspirated from the hip joint were positive for *Enterococcus* and *Enterobacter*. Resection arthroplasty and thorough débridement were done, followed by six weeks of intravenous administration of antibiotics. Because of the relatively poor success rate for surgical revision in the presence of a mixed gram-negative infection, we elected not to implant another prosthesis at that time.

In seven hips, the prosthesis that had been used for the index total hip arthroplasty was the 6032 type, which has a stem of titanium alloy, a thirty-two-millimeter head of titanium alloy, and a polyethylene acetabular component. In Case 1 a carbon-fiber-reinforced polyethylene acetabular component was used. In Case 3 the prosthesis was a DF80 femoral component with a twenty-eight-millimeter head, both composed of titanium alloy. In Case 8 the femoral component was custom-made. The stem was composed of titanium alloy, and commercially pure titanium wire was sintered on the anterior and posterior aspects of the proximal one-quarter of the stem. A twenty-eight-millimeter femoral head of titanium alloy had been cold-welded to a Morse taper neck, which articulated with a carbon-fiber-reinforced polyethylene acetabular component.

Collection of Specimens

At the index operations, the hip joint was inspected and specimens of soft tissue were obtained from areas adjacent to the prosthetic collar, neck, and acetabulum and from the bone-cement interface. The specimens were two to five millimeters thick and, with one exception, did not include the outer layer of the pseudocapsule (the tissue farthest from the surface of the components). In the hip from which this outer layer was obtained (Case 4), the entire

TABLE I

Case	Specimen*	Polyethylene	Cement	Metal	Giant-Cell Reaction	Titanium ($\mu\text{g/g Dry Tissue}$)	Aluminum	Vanadium	Ti:Al:V Ratio
1	A	+	-	++	\pm	227	27	50	4.5:0.5:1
	B	+	+	+	\pm	366	33	75	4.9:0.4:1
	C	+	+	++	-	280	20	66	4.3:0.3:1
2	A	+	-	++	+	243	37	18	13.4:2:1
	B	+	-	++	+	148	28	12	12.5:2.4:1
3	A	+	+++	++	+++	3700	396	220	16.8:1.8:1
	C	++	-	++	-	1083	130	78	13.9:1.7:1
	D	+	+++	++	+++	2298	215	122	18.8:1.8:1
4	A	+++	-	+++	++	1750	206	82	21.5:2.5:1
	B	+	-	++	+	2009	249	103	19.5:2.4:1
	E	+++	-	+++	+++	1360	152	72	19.2:1:1
5	A	-	-	-	+	579	78	34	17.2:3:1
	B	-	-	+	+	737	78	38	19.2:1:1
	D	-	+++	+	++	869	59	41	21:1.4:1
6	A	+	+	+	+				
	B	+	-	+	+				
	C	-	-	+	-				
7	B	-	-	-	-	50	17	3	16:5.4:1
	C	-	-	-	-	60	2	3	21:0.8:1
8	B	\pm	+++	+++	-	3420	4	36	96:0.1:1
	C	\pm	+++	+++	-	1800	26	23	80:1.2:1
	D	\pm	+	+++		2648	55	112	24:0.5:1
9	A	+	+	-	-	125	15	7	18:2.1:1
	B	+	+	-	+	56	16	3	11:5.5:1
	F	+	+		-	32	13	5	11:2.6:1

* A = Pseudocapsule adjacent to the prosthetic collar, B = pseudocapsule adjacent to the prosthetic neck, C = synovial tissue adjacent to the cup, D = membrane between the femoral component and the medullary canal, E = granulation tissue adjacent to the acetabulum, and F = bone from the calcar femorale.

thickness of the capsule was black, and the black tissue entered the pelvis. One sampling technique affected the results of the quantitative analysis because the soft tissue that was closest to the components was more heavily stained with black than was the deeper fibrous tissue of the pseudocapsule. One specimen of bone from the calcar femorale was retrieved from one patient.

The specimens were fixed in 10 per cent buffered formalin, and representative samples were selected for analysis. The analytical methods included light and electron microscopy, energy-dispersive analysis of radiographs, and atomic absorption spectrophotometry.

For routine histological examination, five-micrometer-thick serial sections were made from paraffin-embedded specimens. All sections were studied by light and polarized-light microscopy and were graded using a modification of the method of Willert and Semlitsch³⁸.

For energy-dispersive analysis of x-rays, paraffin-embedded sections of tissue were taken from the same block that had been used for histological analysis. The sections were placed on carbon planchets, the embedding medium was removed, and the planchets were mounted on aluminum stubs. The specimens were desiccated and then coated with approximately 200 angstroms of palladium. They were then examined by the scanning electron microscope (Amray 1000A; Bedford, Massachusetts) and probed by an energy-dispersive analyzer (EDAX 9100/40; Prairie View, Illinois).

Tissue from eight hips (all but Case 6) was available

for atomic absorption spectrophotometry, the blocks being those that were used for light microscopy. A specimen of tissue was removed from the formalin-fixed block and was dissected with plastic instruments to obtain a specimen that weighed 250 to 500 milligrams. It was placed in a polyethylene vial and dried in an oven at 75 degrees Celsius for thirty-six hours. The dried tissue was then weighed and was transferred to a clean polyethylene vial. One milliliter of 50 per cent hydrogen peroxide was added to the vial, which was heated in an oven at 55 degrees Celsius to digest the tissue. Frequent inspection and agitation to disperse the froth were essential to avoid loss of material. Additions of one-milliliter volumes of hydrogen peroxide were made when indicated to completely digest the organic matter. After digestion was complete, the temperature was raised to 75 degrees Celsius and the sample was evaporated to dryness. The digestion procedure took approximately thirty hours. The residue was dissolved in two milliliters of 8N nitric acid and allowed to stand at room temperature overnight. Additional dilutions of the solutions for analysis of the content of titanium, aluminum, and vanadium were made with deionized distilled water.

The amounts of titanium, aluminum, and vanadium were measured by flameless atomic-absorption spectrophotometry using a Zeeman 5000 graphite furnace (Perkin-Elmer; Norwalk, Connecticut). Standard curves (zero to 200 milligrams per liter for titanium and vanadium and zero to fifty milligrams per liter for aluminum) were prepared using

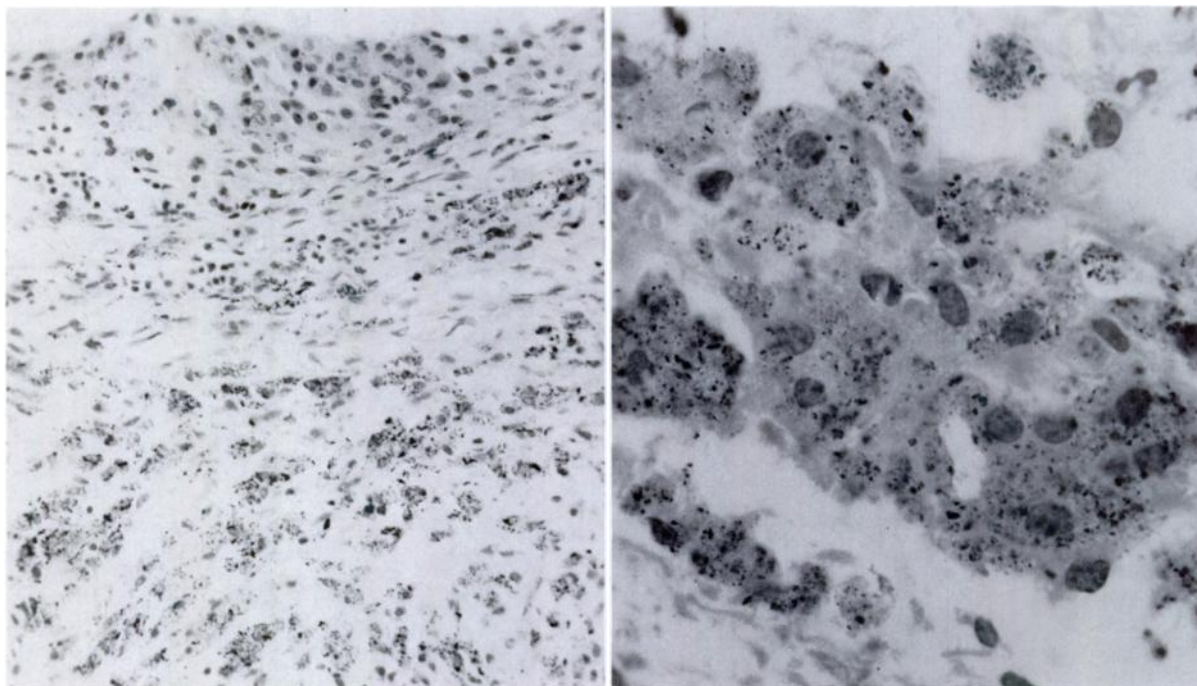


FIG. 1-A

FIG. 1-B

Figs. 1-A and 1-B: Case 3.

Fig. 1-A: Photomicrograph of the synovial layer, showing occasional synovial cells and almost all of the subsynovial histiocytic cells laden with black, opaque metallic debris (hematoxylin and eosin, $\times 22.5$).

Fig. 1-B: Higher-magnification photomicrograph, showing metallic debris within histiocytes (hematoxylin and eosin, $\times 1000$).

control preparations of tissue that had been subjected to the same digestion procedure, dissolution with nitric acid, and dilution. Samples of formalin and cement were also tested, as well as fresh cement and stock formalin solution. Titanium and vanadium were measured during atomization of the sample from the wall of pyrolytically coated graphite tubes, while the L'Vov platform (Perkin-Elmer) was used for the measurement of aluminum. Details of the methods have been submitted for publication elsewhere².

To determine whether the amount of the metal in the samples could be attributed to corrosion or wear, the ratios of titanium to aluminum and of titanium to vanadium were calculated (Table I). The relative percentages were calculated and then were compared with the percentages of the elements in the alloy (90 per cent titanium, 6 per cent aluminum, and 4 per cent vanadium, 22.5:1.5:1).

Two of the retrieved femoral components were analyzed for chemical composition and were found to conform to the published chemical specifications of the American Society for Testing and Materials³³. In the Department of Biomechanics at The Hospital for Special Surgery, all of the femoral prostheses were examined by light microscopy (with a magnification factor of ten) and were found to have scratches (of undetermined depth) on the head. There also was some burnishing of both the head and the stem.

Results

Histological Findings

In all hips, the soft tissue was diffusely tan-gray, fre-

quently with extensive dark-gray areas. The consistency of these tissues ranged from soft to slightly firm, and there were focal gritty areas. Fragments of bone or cement were present in occasional specimens.

Histologically, the synovial lining showed a slight proliferative reaction, with moderate hypertrophy of the synovial cells but without substantial hyperplasia. The subsynovial layer and the capsular tissue had been mostly replaced by a histiocytic infiltrate. The cytoplasm of a few synovial cells and most of the histiocytes in the subsynovial tissue contained numerous black, opaque, irregular particles (metal) (Figs. 1-A and 1-B), measuring approximately one to two micrometers in diameter. In addition, there were focal foreign-body giant cells containing large, irregular clefts that were thought to be due to polyethylene (Fig. 2-A). In two hips (Cases 1 and 8), there were larger, solid-black fragments that were thought to be carbon fibers. They were five to ten micrometers wide and fifty to seventy micrometers long. In addition, large empty foci that had scalloped edges and a surrounding giant-cell reaction were considered to be due to methylmethacrylate.

Polarized light provided a better appreciation of the foreign materials that were seen. The opaque black intracytoplasmic particles (metal) were refractile due to diffraction of light from their irregular edges. Many of the colorless defects, which were seen in the giant cells as well as in the mononuclear histiocytes, were strongly birefringent (polyethylene fragments) (Fig. 2-B). The large black fragments that were seen in two hips (Cases 1 and 8) diffracted light

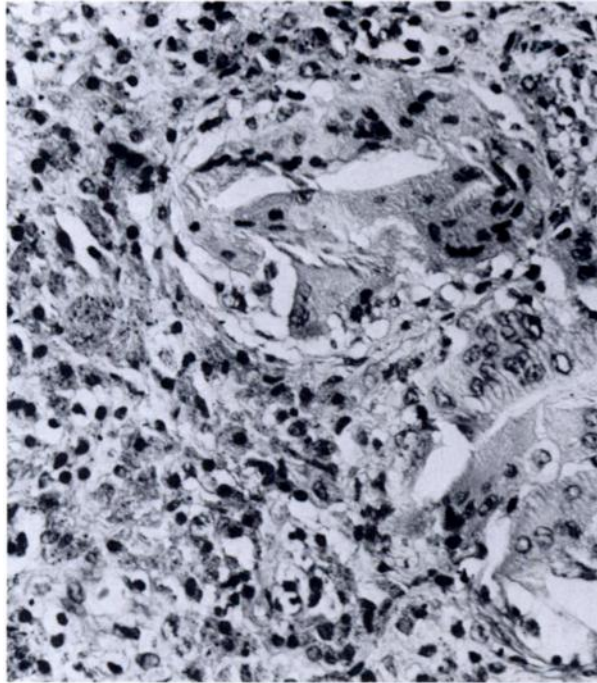


FIG. 2-A

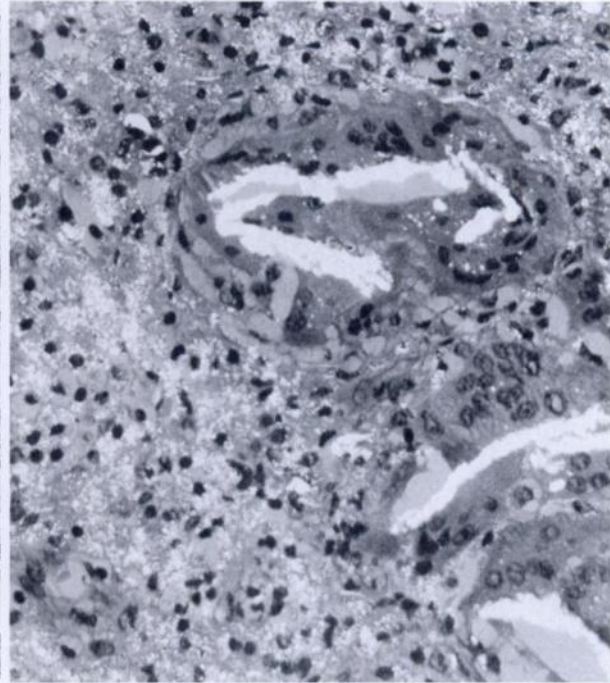


FIG. 2-B

Figs. 2-A through 2-D: Case 4.

Fig. 2-A: Photomicrograph showing histiocytes with metallic debris and giant cells with cleft-like spaces and fragments of polyethylene (hematoxylin and eosin, $\times 250$).

Fig. 2-B: Photomicrograph made with polarized light, showing the edge effect of metallic debris and the bright appearance of polyethylene (hematoxylin and eosin, $\times 250$).

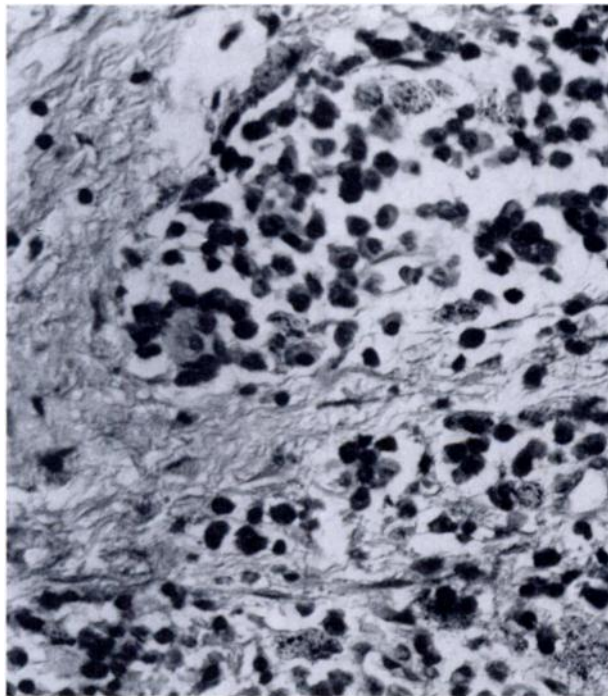


FIG. 2-C

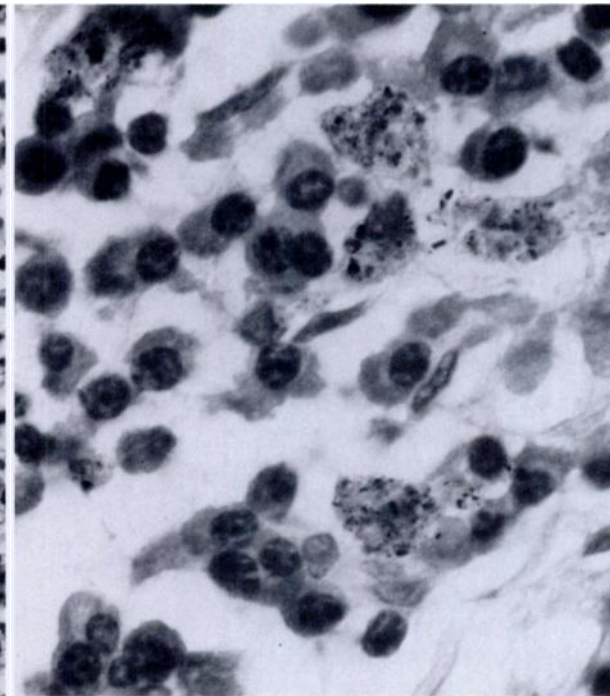


FIG. 2-D

Fig. 2-C: Photomicrograph showing diffuse lymphoplasmacytic infiltrate (hematoxylin and eosin, $\times 200$).

Fig. 2-D: Higher-magnification photomicrograph, showing the presence of metallic debris within histiocytes, associated with lymphoplasmacytic reaction (hematoxylin and eosin, $\times 1000$).

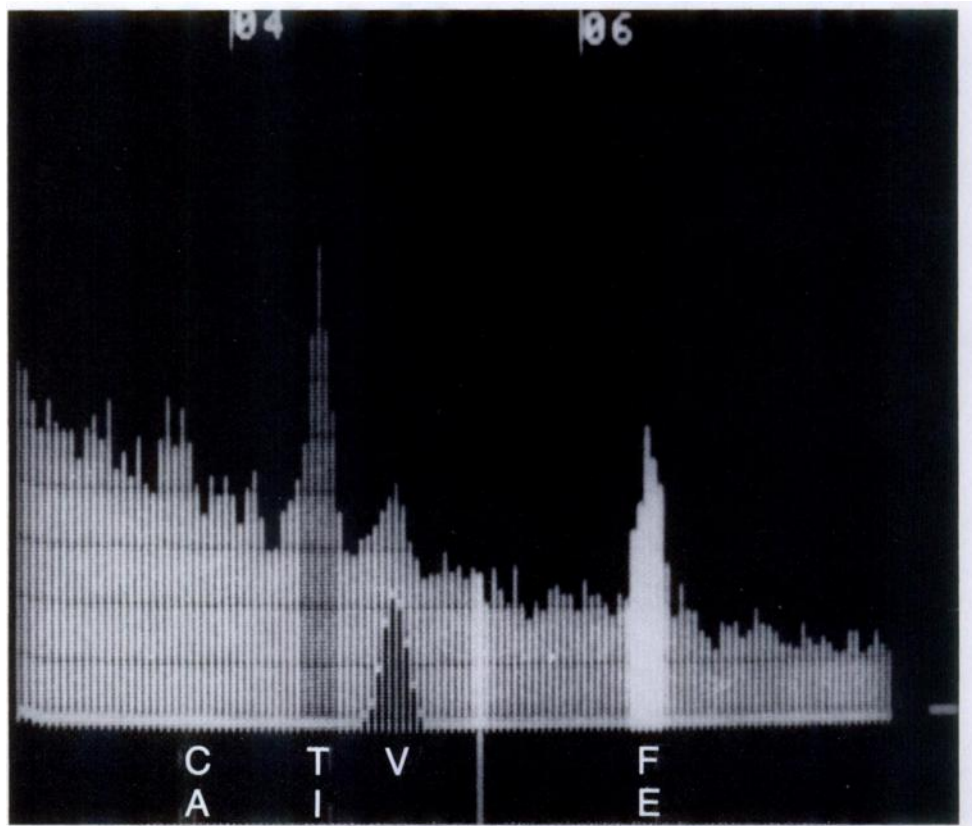


FIG. 3

Energy-dispersive analysis of x-rays. There are peaks for calcium (CA), titanium (TI), vanadium (V), and iron (FE). The vanadium is overlapped by the titanium beta peak.

from their edges (carbon). The large empty spaces did not show any diffractile material and those spaces were considered to be consistent with spaces from which (barium) cement had been dissolved.

Focal necrosis was seen in all of the hips; either it involved the synovial villi or it occurred as areas of central necrosis in the subsynovial tissue.

Polyethylene debris was observed in all hips except two (Cases 5 and 7). In those two hips, the implant had been in place for fewer than eighteen months. Cement debris was noted in six hips and was absent from three (Cases 2, 4, and 7); this could not be adequately explained. Metal debris was observed histologically by light microscopy in all hips but two (Cases 7 and 9); it was thought to be directly related to the low tissue burden of metal, confirmed by atomic absorption spectrophotometry.

The pseudocapsule around the collar and neck of the prosthesis was composed mostly of dense, fibrous connective tissue that had a marked histiocytic and giant-cell response. The reaction was similar to that seen in the subsynovial tissue in both the degree and the amount of foreign-body material that was present in the cells. In four of the hips (Cases 1, 2, 3, and 8) in particular there was severe scarring and histiocytic infiltration. Two hips (Cases 5 and 6) showed a predominant histiocytic response. One hip (Case 4) was striking in that the fibrous connective tissue

appeared to be almost completely replaced by foreign-body giant cells. The cytoplasm of these giant cells was entirely filled with black (metal) debris and occasional clear refractile (polyethylene) fragments.

Two hips (Cases 3 and 4) were remarkable for their infiltrate of plasma cells and lymphocytes (Fig. 2-C) surrounding metal-filled histiocytes (Fig. 2-D). This reaction was not predominantly perivascular or perilymphatic in location. Three hips (Cases 4, 7, and 9) showed acute inflammation: cultures were positive in only two (Case 4, *Staphylococcus aureus*, and Case 9, *Enterococcus* and *Enterobacter*). In one patient (Case 2) an infection developed two months after the revision procedure.

Histologically, the bone-cement interface was similar to the synovial tissue with regard to particulate debris and cell type. However, there was considerably more cement debris with concomitant giant-cell reaction.

The decalcified sections, including the one specimen of bone from the calcar femorale, showed occasional reactive bone formation, but in no hip was there any evidence of marked resorptive activity. In one hip (Case 4), polyethylene and metal debris was seen in the bone marrow.

In summary, all of the tissue that had been adjacent to a prosthesis showed, to varying degrees, a prominent histiocytic response to metal debris, along with a histiocytic and foreign-body giant-cell reaction to polyethylene and

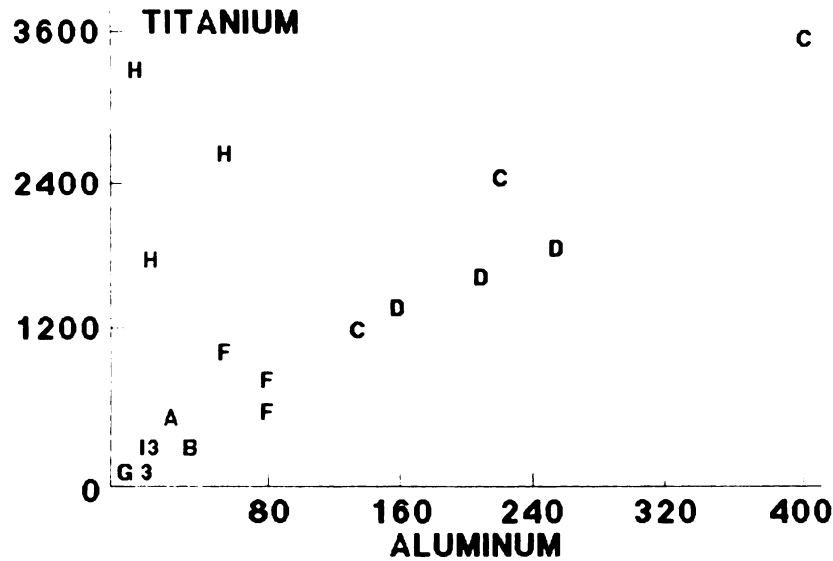


FIG. 4-A

Each letter represents a case number: A — Case 1, B — Case 2, C — Case 3, D — Case 4, F — Case 5, G — Case 7, H — Case 8, and I — Case 9. The two number 3's on the lower left represent six samples for which the values were too low to be plotted.

methylmethacrylate. In only one hip was metal demonstrated in the bone marrow. A lymphoplasmacytic reaction was seen in two hips, with no evidence of infection or history of allergy in one of them. In two hips (Cases 3 and 4), staining for aluminum at the calcification front of the calcar femorale was negative. The particulate debris, especially metal, could be recognized by light microscopy, but polarization microscopy enhanced our appreciation of how much metal had been worn away.

Energy-dispersive analysis of the x-rays of each specimen demonstrated a titanium peak that varied in height. Specimens from four hips (Cases 1, 2, 4, and 5) showed small peaks for aluminum. A peak for vanadium could not be identified because of the overlap of the titanium beta

peak with that of vanadium (Fig. 3). Therefore, the data for vanadium are not tabulated (Table I). Since energy-dispersive analysis is qualitative, the quantitative levels of elements could not be determined by this method. Thus, the findings by energy-dispersive analysis confirmed the presence of metal in all hips.

Measurable values for titanium, aluminum, and vanadium in soft tissue were found in all hips (Table I). The levels of titanium ranged from 49.8 micrograms per gram of dry tissue (Case 7) to 3700 micrograms per gram of dry tissue (Case 3). The specimen of bone from one hip (Case 9) contained 32.1 micrograms of titanium per gram of dry tissue. For the failed arthroplasty with an uncemented porous-coated prosthesis (Case 8), the values for titanium

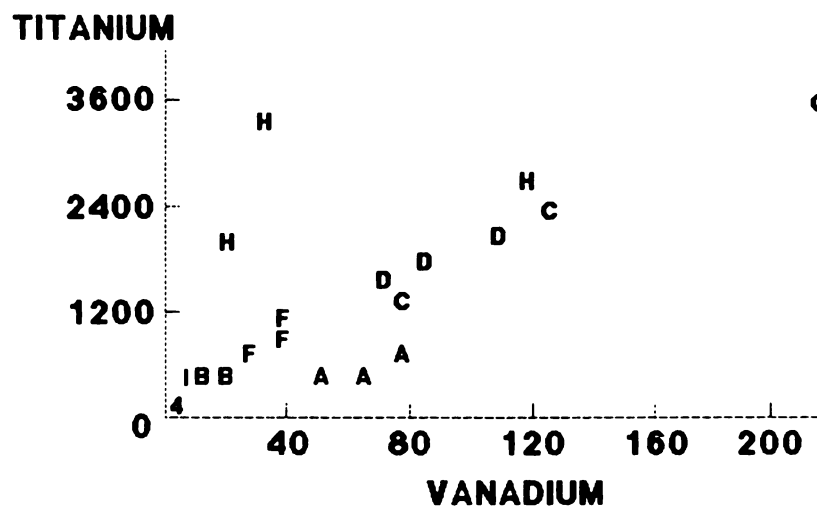


FIG. 4-B

Each letter represents a case number: A — Case 1, B — Case 2, C — Case 3, D — Case 4, F — Case 5, G — Case 7, H — Case 8, and I — Case 9. The number 4 on the lower left represents four samples for which the values were too low to be plotted.

ranged from 1800 to 3420 micrograms per gram of dry tissue, depending on the locations from which the specimens were taken. For all hips the values for aluminum ranged from 2.1 to 396 micrograms per gram of dry tissue. For Case 8 values of 4.1 to 54.7 micrograms per gram of dry tissue were recorded. For all hips the values for vanadium ranged from 2.9 to 220 micrograms per gram of dry tissue. For Case 8 values of 22.5 to 112.3 micrograms per gram of dry tissue were recorded. The control value for vanadium was 1.26 micrograms per gram of dry tissue, whereas those for titanium and aluminum were zero.

In all of the hips except one hip (Case 8), the ratios of values for the three principal elements of the alloy were close to those of the alloy itself. For the subset of hips that had a cemented prosthesis, linear-regression analysis was performed on the data that had been obtained by atomic absorption spectrophotometry. The results were highly significant ($p < 0.0001$), with r values of 0.989 for the ratio of titanium to aluminum and 0.938 for the ratio of titanium to vanadium (Figs. 4-A and 4-B). In one hip (Case 1), however, the ratio of titanium to vanadium was much lower than for all of the other hips, so atomic absorption spectrophotometry was repeated on specimens from that hip. The findings were consistent. In Case 8 (the failed arthroplasty with a porous-coated prosthesis), the ratio of titanium to vanadium was higher than in any other hip.

Determinations of titanium, aluminum, and vanadium contents were also made on samples of cement that had been retrieved from the hips and on formalin in which the specimens had been prepared. All values were less than 0.5 microgram per gram.

Discussion

The phenomenon of dark staining of soft tissues immediately adjacent to static implants made of titanium or titanium alloy is well known. Meachim and Williams performed a combined histological, metallurgical, and clinical study of tissue from nineteen hips from which a static titanium implant had been removed²⁶. No implant showed corrosion, and the authors concluded that, in some patients, titanium can be liberated into adjacent tissues even in the absence of visible corrosion or fracture of the implant. Even in so-called static devices, wear may occur (for example, as the result of relative movement of the implant against bone or of screws against the bone or the plate). Therefore, wear should not be ruled out as a source of contamination of tissue. Meachim and Williams used neutron-activation analysis to estimate the amounts of titanium in the tissues adjacent to the implants. They found considerable variation from individual to individual in the amounts of titanium that were released, and there was no correlation between the titanium content of the tissue and the length of time that the implant had been in the body²⁶. Dobbs and Scales described the case of a patient who had a titanium replacement for the distal part of the femur, used in combination with a cobalt-chrome bearing at the knee⁹. The bearing broke and had to be replaced. At operation, the interior of the capsule

surrounding the titanium component was found to be black, but the black material appeared to be completely tolerated by the patient's body.

In the present study, periprosthetic tissue from a group of patients who had a failed total hip arthroplasty in which the prosthesis was made of titanium alloy and polyethylene was analyzed. It is well known that the causes for failure of a total hip replacement include young age, excessive weight or activity, poor bone stock, improper anatomical reconstruction, inadequate prosthetic position, design or material failure, poor surgical or cementing technique, and infection^{5,19,29}. In eight of the nine hips in our study, one or more of these factors pertained. Five hips had a vertically oriented acetabular component and one hip had high placement of the acetabular component. Evidence of poor cementing technique was seen about the femoral stem in three hips, and there were two infections.

Only in one hip (Case 3) did we consider the reconstruction to have been excellent. The patient had a satisfactory clinical and radiographic result at first, but a year later there was radiographic evidence of failure.

As has been mentioned, Clarke et al. reported on seven hips from which titanium alloy and polyethylene components were removed at the time of surgical revision, eleven to fifty-seven months after implantation. No evidence of metallic sludge, no black staining, and no abnormal wear phenomena¹⁹ were found. The causes of clinical failure in those hips were loosening of the femoral component in four hips and femoral fracture, acetabular loosening, and subluxation in one hip each.

Dobbs and Scales studied a similar device that was removed after two and one-half years of service. It did show evidence of metallic wear, and they suggested that as much as a few tenths of a micrometer of prosthetic head had been removed⁹. They stated that blackening of tissues adjacent to titanium implants was observed in several cases and suggested that a bearing surface other than titanium alloy be used to articulate with the polyethylene, especially when acrylic cement is used. Three-body simulation with an unphysiological load has demonstrated abrasion of titanium alloy against polyethylene, the abrasion being worse when acrylic particles were present⁸.

The exact composition and structure of the particles that were released from the prosthesis or other implants, in other studies and in our own, is controversial. Two interacting mechanisms are thought to be causative: corrosion, with shedding of the passivating layer at the articular surface, and wear. Meachim and Williams studied the soft tissues adjacent to nineteen static implants from humans and found variations in the amount of titanium that had been released; there was no obvious correlation between the concentration of titanium in the tissue and the length of time that the prosthesis had been in the body²⁶.

Using a canine model, Ducheyne et al. demonstrated no measurable amount of titanium in the osseous tissue surrounding a smooth, press-fit cylinder of Ti-6Al-4V, but they found titanium in amounts of as much as 2100 nano-

grams per gram of dry osseous tissue surrounding a porous implant. The method of study included neutron-activation analysis¹⁰. Clinically, in the system that uses Ti-6Al-4V alloy and ultra-high molecular weight polyethylene, oxide particles at the interface abrade the metallic surface implant, removing other oxide and alloy, with generation of more oxide as the surface attempts to repassivate.

In vivo corrosion of a titanium alloy was demonstrated by Woodman et al., in a study of the porous ingrowth in cemented titanium prostheses in baboons³⁹. A marked elevation of titanium content in the lungs and spleen occurred: seventy-six months after the implantation procedure, the value was 968 micrograms per gram of dry weight in the lungs and 90.63 micrograms per gram of dry weight in the spleen³⁹. Substantially elevated levels of aluminum were also found in the serum, lungs, and regional lymph nodes. The level of vanadium in the lungs reached a peak of twenty-seven micrograms per gram of dry weight at six months but decreased to control values thereafter. There was no titanium, aluminum, or vanadium in the muscle adjacent to the implant at any time during the experiment.

The ratios of titanium, aluminum, and vanadium in our data were fairly constant in the synovial specimens and resembled those in the parent metal. The metallic debris in those specimens most probably was generated by wear rather than by pure corrosion. The excessively high concentration of titanium relative to aluminum and vanadium in the one exceptional hip (Case 8, the failed arthroplasty with a porous-coated femoral component) was to be expected because the porous surface was composed of pure titanium wire. Its wear properties, incidentally, are inferior to those of titanium alloy⁹.

Solar et al. proposed a model of surface corrosion and wear of titanium alloy to explain the findings of titanium in tissue adjacent to the implant^{34,35}. They suggested that on all surfaces there is a passive layer composed of microscopic oxide needles and a smooth planar oxide. At surface irregularities, the oxide needles are broken off by friction or dissolved *in vivo*, providing the source of titanium in the tissue. As wear particles are generated, a new surface area for dissolution of the elements becomes available. Corrosion then can become substantial. Rae was unable to detect any solubility of titanium or aluminum in fetal calf serum at 210 days, while vanadium was highly soluble (28.6 micromoles per milliliter)^{30,31}. Therefore, it may be concluded that the different elements of the alloy are handled differently *in vivo*, and this may explain, in part, the variations in ratios that we found and the early disappearance of vanadium from the lungs that was described by Woodman et al.³⁹. The question remains as to how biologically active (toxic) these three metals are^{6,7,11,14,15,17,25,37}. There is controversy in the literature regarding the ionic characteristics of the metal that is liberated from the surface of the implant, and this con-

trovery cannot be resolved except by extensive toxicological investigations¹⁰.

Previous studies of stable titanium-alloy implants have demonstrated that the local biocompatibility of the alloy is excellent^{4,13,23}. *In vivo*, titanium and some of its alloys may be the most biocompatible, corrosion-resistant metallic implant materials that are in use^{18,20-22}. Laing reported that the reaction of tissue to titanium in the absence of wear is minimum in both humans and animals²¹. Dobbs and Scales reported that even in blackened tissues adjacent to titanium implants no adverse response by tissue was noted histologically, nor was there any evidence of sensitivity to the metal⁹. Laing et al. reported that the reaction of tissue to titanium and to its alloy Ti-6Al-4V is extremely benign and that there is less fibrosis than is seen with other metals²².

In contrast, we found a major histological response in the tissues; namely, an abundance of histiocytes and giant cells. In the two patients who had the highest recorded content of aluminum and vanadium in the tissue, the tissue contained so many plasma cells that we found the reaction to be consistent with either an allergic or a chronic inflammatory etiology.

It is difficult, if not impossible, to separate the individual reactions of the tissue to the various materials (metal, cement, and polyethylene). With regard to the metal, the values that we recorded were higher than in previous reports^{12,39}. However, the method of collecting the tissue should be taken into consideration. The values we obtained may reflect only the content in the soft tissue that lay closest to the prosthesis, and the variability in the tissue burden of metal even in the same patient (Cases 3, 4, and 8) also might be attributable to sampling variation.

In conclusion, our study demonstrated that when a titanium total hip prosthesis has failed, whatever the reason, copious metallic debris can be generated, and while this may be locally irritating and possibly toxic to the surrounding tissues, and while these effects may contribute to loosening, we could not demonstrate such a contribution. Even in the well cemented total hip replacement, the layer of titanium oxide passivating the surface is continually rubbed off the head of the femoral component as it articulates with the acetabular component, thus exposing progressively deeper zones of the implant. This process, called corrosion — wear only nanometers deep — causes the continual release of particles of titanium alloy into the tissues. The process is exacerbated if the stem of the prosthesis becomes loose in the medullary canal. Whether the process, involving exposure of large areas of surface of the particles, does permit dissolution of extremely high concentrations of the elements into the surrounding tissues and tissue fluids is not known, but it is possible. Carbon-reinforced polyethylene should not be used with titanium alloy because it may enhance the abrasive effect.

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