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Accumulation in Liver and Spleen of Metal Particles Generated at Nonbearing Surfaces in Hip Arthroplasty

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Abstract: Systemic migration of metal particles generated at nonbearing surfaces rather than the intended primary bearing was studied in postmortem specimens from 30 patients with total hip arthroplasty. Using light and electron microscopy with x-ray microanalysis, submicrometer metal particles were identified within macrophages in the liver and/or the spleen in 11 of 15 patients with a revised arthroplasty and in 2 of 15 patients with primary hip arthroplasty. The macrophages formed focal aggregates in the organs without apparent toxicity. Fretting at ancillary fixation devices, loose components, and modular connections can generate a substantial volume of debris. These particles are in addition to those generated at the bearing surfaces, further increasing both the local and systemic particulate burdens. While all components can be associated with the distant spread of particles and metal ions, it is the environment of revision arthroplasty that provides the greatest potential for the generation and systemic dissemination of wear debris. The long-term effects of accumulated wear particles in the liver and spleen are unknown. **Key words:** wear, particles, systemic dissemination, granuloma, implant retrieval, hip arthroplasty.

Wear products, including metallic ions and particulate debris, are generated at the primary bearing surfaces of hip arthroplasty prostheses when they are functioning as designed. Unintended wear modes at the primary bearing involve either third-body particles interposed between the bearing surfaces, or rubbing of 1 bearing surface against a nonbearing surface [1]. The present paper focuses on the effects of yet another wear mode that does not involve the intended articulating surfaces at all, but rather is a consequence of unintended motion between 2 nonbearing surfaces. Wear between nonbearing surfaces can occur at modular connections [2], at interfaces between the prosthesis and cement or bone [3], and with ancillary devices employed to reattach the trochanter or to stabilize periprosthetic fractures or bone grafts [4,5].

The granulomatous response to high concentrations of wear particles in the surrounding tissues has been associated with osteolysis and aseptic loosening of prosthetic components, limiting the life of joint arthroplasties [6]. Consequently, considerable efforts have been directed toward reducing wear as well as understanding and possibly moderating the local cellular reactions to wear particles. More recently, it has been recognized that, in addition to local accumulation of debris, wear products are

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disseminated systemically and stored in distant organs, raising concern over potential effects on organ function [7–9].

The purpose of this study was to determine the prevalence of and histological response to accumulation in the liver and spleen of metal wear particles generated specifically between 2 nonbearing surfaces. Postmortem specimens from 30 patients who had hosted primary or revised total hip arthroplasties were studied. Visceral organs, periprosthetic tissues, and retrieved prosthetic components as well as ancillary fixation devices were examined.

Materials and Methods

Accumulation in the liver and spleen of metal particles generated between nonbearing surfaces was investigated in 30 patients with total hip arthroplasty prostheses who had consented to collection of tissue samples and prosthetic devices following their demise (Table 1) [10]. Material from 18 of these patients, reported in part previously [8], was reexamined in the present study with a focus on metal particles generated between nonbearing surfaces. The other 12 (patients 8–10, 14, 20, 21, 23, 25, 27–30) represent completely new material that has since become available from our retrieval program.

Specimens from the major lobes of the liver, the spleen, and the implants with adjacent tissues were collected postmortem from each patient. Clinical data obtained from office notes, operative reports, and clinical radiographs were reviewed. The prevalence of metal wear particles in the liver and spleen, the elemental composition of and histological response to the particles as well as the surfaces at which they had been generated were determined.

Seventeen male and 13 female patients were studied. The mean age at death was 73 years (range, 43–91). The cause of death was cardiac disease in 13 patients, metastatic carcinoma in 10, pneumonia in 2, and 1 each of various other pathologies in the remaining 5 patients. No death was related to a joint arthroplasty.

Fifteen of the patients had hosted a primary hip arthroplasty for a mean time of 5.8 years (range, 3.6–14.3) (Table 1). Two patients had bilateral primary hip implants; and 1 patient also had a primary knee arthroplasty. Femoral reconstruction consisted of a stem inserted with cement in 8 patients and without cement in 7. The acetabular components consisted of a porous-coated hemispherical cup with a modular polyethylene liner that had been inserted with screws in 12 patients and without screws in 2. In 1 other patient, an all-polyethylene component had been implanted with the use of bone cement. The most recent Harris hip score was 84 (range, 62–100) for the 13 patients for whom this information was available.

The other 15 patients had hosted hip arthroplasties in which 1 or more of the components had been revised (Table 1). Two of these patients had bilateral revised hip arthroplasties. Three patients also had a primary joint arthroplasty in the contralateral hip or in a knee. The mean time since the index hip arthroplasty was 19.3 years (range, 4–30); and the mean time since the last revision operation was 7.5 years (range, 0.1–13). The mean Harris hip score was 80 (range, 59–98) for the 12 patients for whom these scores were available.

Fourteen of the 15 patients with revised arthroplasties had a complex history of multiple failures of their hip reconstructions and multiple revision operations. The primary reason for revision was aseptic loosening of cemented components in 12 patients, osteolysis in 1, and periprosthetic fracture in 1. Five of the patients with multiple revisions ultimately required a femoral allograft-prosthesis composite, 4 required a femoral strut allograft, 3 an acetabular allograft, 1 a proximal femoral arthroplasty prosthesis, and 1 patient had multiple revisions without the use of allograft bone. Patient 23 had a single revision operation for aseptic loosening of an Austin Moore stem that was converted to a hybrid total hip arthroplasty.

Ancillary fixation devices were used in 13 of the 15 patients in whom implants had failed and been revised and in none of the patients hosting 1 or more primary hip arthroplasties. Stainless steel plates and screws were used to stabilize femoral allograft-prosthesis composites in 5 patients. Stainless steel wires and mesh or cobalt-chromium-nickel-tungsten alloy cable grip systems were employed for reattachment of the trochanter or as cerclage wires to stabilize bone allografts in 11 patients.

The harvested tissues and prosthetic devices were evaluated with the use of radiological, histological, and microanalytical techniques previously described [2,8,11]. High-resolution radiographs were obtained of the isolated specimens of the implants and surrounding bone to assess the nature of the bone-implant interface. The prosthetic components with the adjacent bone and soft tissues were studied histologically to determine the nature of implant fixation, possible loosening, or implant failure [11].

Samples from several locations in each liver and spleen were examined using correlated light microscopy of stained histological sections and back-

Table 1. Patient Data and Metal Particles From Nonbearing Surfaces in the Liver and Spleen

Patient	Gender, Age at Death (yrs.)	Duration (mos.)	Hip Score at Last Exam (points)*	Composition of Femoral Component†	Composition of Acetabular Component†	Ancillary Fixation Devices†	Wear Particles in Liver†	Wear Particles in Spleen†
Primary hip								
1	F, 64	43	100	CoCrMo	Ti, TiAlV screws	—	nd	nd
2	M, 91	44	62	CoCrMo	Ti, TiAlV screws	—	nd	Ti, TiAlV
3	F, 86	46	95	CoCrMo	Ti, TiAlV screws	—	nd	nd
4	M, 74	48	69	CoCrMo	Ti, TiAlV screws	—	Ti, TiAlV	nd
		48	70	CoCrMo	Ti, TiAlV screws	—		
5	F, 83	54	79	CoCrMo	Ti, TiAlV screws	—	nd	nd
6	M, 71	54	83	TiAlV, Ti	Ti, TiAlV screws	—	nd	nd
7	M, 71	57	91	CoCrMo	Ti, TiAlV screws	—	nd	nd
8	M, 80	14	65	TiAlV	Ti, TiAlV screws	—	nd	nd
		59	67	TiAlV, Ti	Ti, TiAlV screws	—	nd	nd
9	M, 60	65	96	CoCrMo	TiAlV	—	nd	nd
10	M, 80	68	nr	CoCrMo	TiAlV	—	nd	nd
11	M, 54	78	98	TiAlV, Ti	Ti, TiAlV screws	—	nd	nd
12	M, 59	89	100	TiAlV, Ti	Ti, TiAlV screws	—	nd	nd
13	M, 71	99	100	TiAlV, Ti	Ti, TiAlV screws	—	nd	nd
14	F, 75	153	91	CoCrMo	Ti, TiAlV screws	—	nd	nd
15	F, 72	171	nr	TiAlV	UHMWPE	—	nd	nd
Revision hip								
16	M, 62	47	79	CoCrMo	Ti, TiAlV screws	FeCrNi plate/screws	nd	nd
17	F, 62	65	59	CoCrMo	Ti, TiAlV screws	FeCrNi plate/screws	CoCrMo	nd
18	M, 74	156	68	TiAlV, Ti	Ti, TiAlV screws	FeCrNi wires	nd	Ti, TiAlV
19	F, 67	198	93	TiAlV, Ti	Ti, TiAlV screws	—	Ti, TiAlV	nd
20	F, 80	204	66	CoCrMo	Ti, TiAlV screws	FeCrNi wires	nd	nd
21	M, 77	204	nr	CoCrMo	Ti, TiAlV screws	FeCrNi plate/screws	nd	FeCrNi
22	M, 76	204	89	TiAlV, Ti	Ti, TiAlV screws	—	nd	nd
23	F, 67	204	80	CoCrMo	Ti, TiAlV screws	CoCrNiW wires/mesh	CoCrMo	CoCrNiW, CoCrMo, Ti
24	F, 85	284	73	Ti6Al4V	Ti, TiAlV screws	FeCrNi wires, Ti staples	Ti	Ti
25	M, 43	288	nr	CoCrMo	Ti, TiAlV screws	CoCrNiW cable grip	nd	nd
26	F, 66	292	nr	FeCrNi	Ti, TiAlV screws	FeCrNi wires	nd	FeCrNi
		232	nr	FeCrNi	UHMWPE	FeCrNi wires		
27	M, 87	324	nr	TiAlV	TiAlV	CoCrNiW cables, FeCrNi wires	CoCrNiW, TiAlV	CoCrNiW, TiAlV
		312	nr	CoCrMo	TiAlV	CoCrNiW cables		
28	F, 79	324	86	CoCrMo	Ti, TiAlV screws	CoCrNiW cable grip, FeCrNi plate/screws	nd	CoCrNiW, CoCrMo, TiAlV
		312	87	CoCrMo	Ti, TiAlV screws	—		
29	F, 79	329	98	CoCrMo	Ti, TiAlV screws	CoCrNiW cable grip	nd	Ti
30	F, 91	356	76	CoCrMo	Ti, TiAlV screws	FeCrNi plate/screws	FeCrNi	FeCrNi
		12	nr	CoCrMo	none	—		

Abbreviations: CoCrMo, cobalt-chromium-molybdenum alloy; Ti, commercially pure titanium; TiAlV, titanium-6% aluminum-4%vanadium alloy; FeCrNi, stainless-steel alloy; CoCrNiW, cobalt-chromium-nickel-tungsten alloy; nd, not detected; nr, not recorded; F, female; M, male

*Harris hip score †Composition of retrieved components and particles in the liver and spleen.

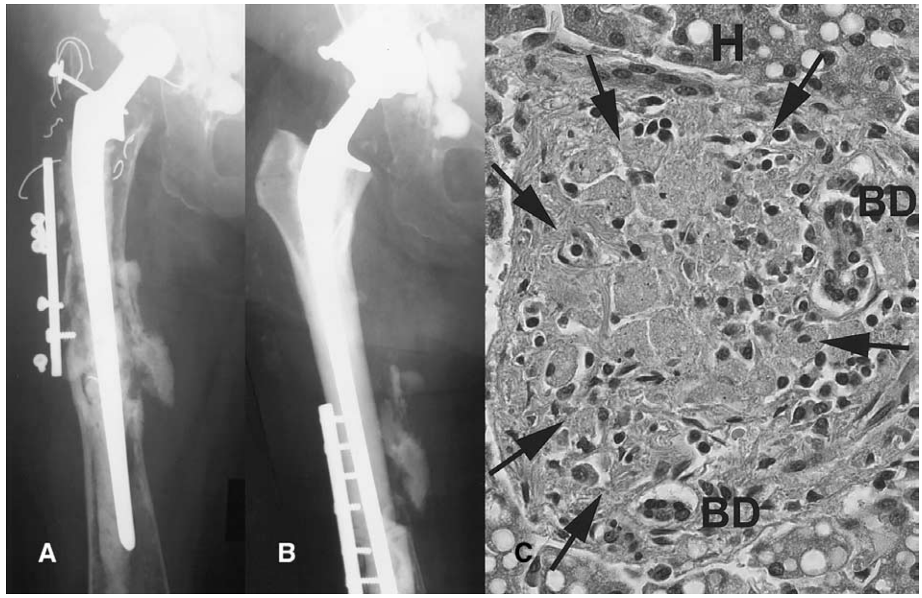

Fig. 1. Patient 30. (A) Preoperative radiograph of failed reconstruction for periprosthetic fracture showing loose and broken stainless steel hardware 12 years prior to this patient's demise. (B) Radiograph 10.5 years following successful reconstruction of the same femur using an allograft-prosthesis composite. (C) Postmortem photomicrograph of liver reveals cluster of pale-staining macrophages (arrows) containing minute stainless steel particles (presumably, some of which were generated 12 years earlier) filling the central portion of a portal tract. BD = bile ductule; H = hepatocytes. (Hematoxylin and eosin; original magnification ×300).

scattered-electron imaging of serial unstained sections with the use of energy dispersive x-ray analysis (models 8900RL and 6460LV; JEOL, Peabody, Mass.) [2]. Individual metallic particles, ranging in size from .1–10 micrometers, were identified, anatomically localized, and the histopathological response to the particles within the organ was characterized with regard to cellular infiltration, fibrosis, and necrosis. The periprosthetic tissues were studied in a similar manner.

Determination of the sources of the disseminated particles was accomplished in 2 ways. The source of stainless steel or cobalt-chromium-nickel-tungsten alloy particles in the organs of some patients was obvious because the ancillary fixation devices were the only parts fabricated from these alloys. For other metallic particles, the primary source of the specific particles found in the organs was determined by examination of the parts of the prostheses composed of the same material for evidence of surface damage and by identification of particles of the same material in the periprosthetic tissues [8].

Results

Seventy-three percent (11 of 15) of patients with a revised hip arthroplasty and 13% (2 of 15) of the patients with a primary hip arthroplasty had metallic particles in their liver and/or spleen that had been generated by wear between nonbearing surfaces. In the patients with a revised hip arthroplasty, the particles were present in the spleen alone in 5 patients, in both the liver and spleen in another 4 patients, and in the liver alone in 2 (Table 1). In the patients with primary hip arthroplasty, metal particles generated between nonbearing surfaces were detected in the liver of 1 patient and the spleen of another patient. The size of disseminated particles ranged from .1 up to 8 micrometers with most particles measuring less than 1 micrometer.

The nonbearing surfaces at which the disseminated metal particles had been generated included loosened components, ancillary fixation devices, and a well-fixed acetabular component and its fixation screws. In patients with a revised arthroplasty, metal alloy particles in the liver or spleen that had been identified as cobalt-chromium-molybdenum alloy, titanium-aluminum-vanadium alloy, or titanium were determined to have been generated due to loosening of a femoral component in 5 patients (Patients 17, 18, 23, 24, and 29) and loosening of both femoral and acetabular components in 1 (Patient 19). Particles of stainless steel alloy in the liver or spleen were generated due to fretting of ancillary fixation wires, plates, or screws in Patients 21, 26, and 30 (Figs. 1A and 1B). Cobalt-chromium-nickel-tungsten alloy particles in the organs were associated with cable grip systems in Patients 23 and 28 and with cerclage wires in patient 27 (Fig. 2A).

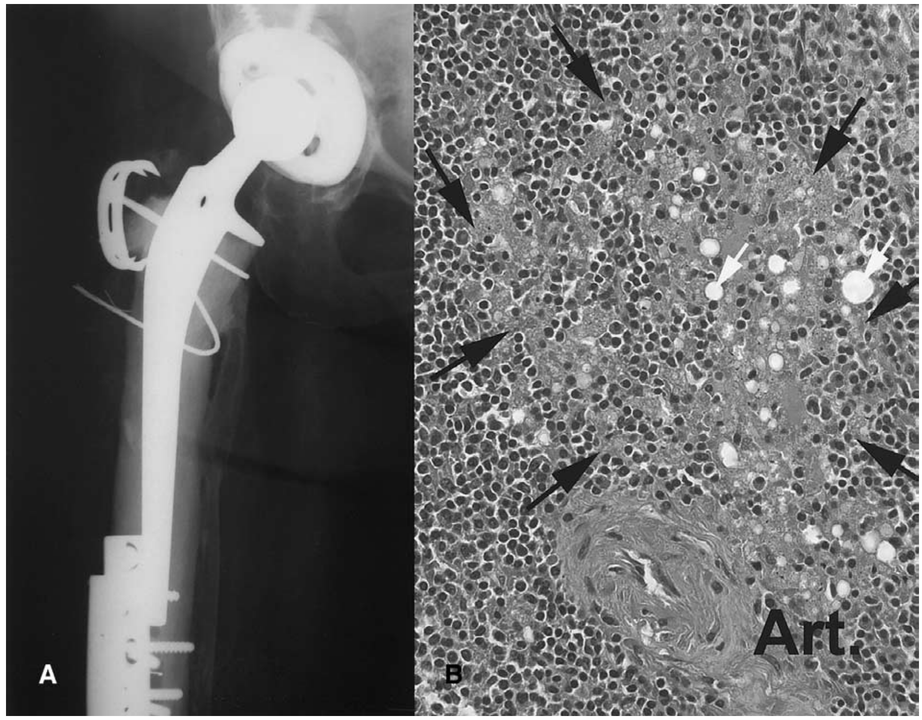

Fig. 2. Patient 28. (A) Radiograph demonstrates allograft-prosthesis composite with fixation plates and cobalt-chromium-nickel-tungsten alloy cable grip system with broken cable 1.7 years prior to the death of this patient. (B) Postmortem photomicrograph of white pulp of the spleen shows aggregate of macrophages (black arrows) containing abundant submicrometer particles of cobalt-chromium-nickel-tungsten alloy generated by the cables. Lipid droplets (white arrows) consistent with deposition of dietary saturated hydrocarbons such as mineral oil were also present. Art. = splenic arteriole. (Hematoxylin and eosin; original magnification ×200).

In 2 patients with primary arthroplasties, particulates in the organs included titanium-aluminum-vanadium alloy and titanium. In Patient 2, who had acetabular osteonecrosis following therapeutic pelvic irradiation, the source of the particles was a loose titanium acetabular component that showed no bone ingrowth in histological sections. In Patient 4, the particles were determined to have been generated at the junction between the titanium metal backing and titanium-aluminum-vanadium alloy fixation screws of an acetabular cup that appeared stable on clinical and specimen radiographs and had extensive bone ingrowth in the histological sections.

In the liver, the metal particles were found within macrophages in focal clusters, most commonly in the portal tracts (Fig. 1C), but also distributed around venules in the parenchyma. In the spleen, macrophages containing metal particles were found primarily within the lymphatic sheaths surrounding arterial vessels, where they formed foreign body granulomas (Fig. 2B). Metal particles that had been generated at nonbearing surfaces were often accompanied by apparent polyethylene particles. In the spleen of Patient 28, fragments of graphite fibers from a failed polyethylene-graphite acetabular cup removed 10 years earlier were also present.

The orthopedic wear debris was found intermixed with particulates of environmental origin such as silicates, some of which contained variable levels of titanium or aluminum. In the spleen, the granulomas frequently demonstrated variably sized lipid droplets consistent with deposition of dietary saturated hydrocarbons such as mineral oil [12] (see Fig. 2B). The concentrations of these accumulated iatrogenic and environmental materials in the liver and spleen ranged from relatively low to moderate. No toxic effects related to the particles were apparent in the histological sections of the liver and spleen.

Discussion

Wear between nonbearing surfaces can be a major source of particulates that migrate to and are stored in the liver and spleen. These particles are in addition to the local and systemic burden of polymeric and metallic debris that may be normally produced at the bearing surfaces of joint arthroplasties. In this study, metallic particles generated between nonbearing surfaces were present in the liver and/or spleen of 73% of patients with a prior failure and revision of their hip arthroplasty, and in 13% of patients with a primary reconstruction. Metallic particles generated from nonbearing surfaces were not detected in the liver or spleen of patients whose prosthetic components were apparently well fixed at the time of their demise, but metal and polyethylene particulates from the wear of bearing surfaces were found in the organs of some of these patients in varying concentrations.

The metallic particles detected in the liver and spleen that had been generated at nonbearing surfaces were mainly due to aseptic loosening of a femoral or acetabular component, fretting between parts of ancillary fixation devices such as wires, cables, plates, and screws, or wear at the junction between the metal backing of a stable acetabular cup and its fixation screws. These determinations were made 2 ways. The source of stainless steel or cobalt-chromium-nickel-tungsten alloy particles in the organs of some patients was obvious because the ancillary fixation devices were the only parts fabricated from these alloys. For other metallic particles, the primary source of the specific particles found in the organs was determined by examination of the parts of the retrieved prostheses composed of the same material for evidence of surface damage and by identification of particles of the same material in the periprosthetic tissues [8]. The precision of the latter method was greatest in patients with primary arthroplasty and least in those patients who had had a series of failed arthroplasties and revisions for whom, in some cases, the composition of the previous prosthetic components was known with less certainty.

A relatively low concentration of orthopedic wear debris appears histologically to be tolerated in the liver and spleen. However, the effects of accumulating metallic debris over the long term are unknown. It is important to note that in this study, particles apparently generated by previous component failure or fretting of ancillary fixation devices were still present in the liver or spleen after a decade or more. This finding suggests that particle deposition in the organs is cumulative. Accumulation of particles over decades may be particularly relevant for patients with long histories of multiple failures and revisions of their arthroplasties, in whom large amounts of particulates may be disseminated. High concentrations of exogenous particulates in the liver and spleen, including metallic debris from joint arthroplasties, are of concern because of the potential to induce granulomas that might, in some rare cases, compromise organ function [8,13].

Two living patients with malfunctioning hip arthroplasties and very high concentrations of disseminated metal wear particles in the liver or spleen have been studied previously by our laboratory. The first patient had extensive infiltration of titanium alloy particles in the liver and a serum titanium value approximately 1,000 times higher than that of control individuals without a titanium prosthesis [8,9]. Serum liver-function markers were normal; and a needle biopsy specimen of the liver showed only mild chronic portal inflammation and very mild nonspecific lobular hepatitis, findings that were also compatible with this patient's history of chronic hepatitis-C infection. In this patient, a heavy particulate burden was apparently tolerated in the liver, at least up to the time of the examination.

In the second living patient, dissemination of metallic wear debris, generated at the connection of a modular ceramic head and the neck taper of a titanium alloy stem, was associated with a visceral granulomatous reaction requiring operative and medical treatment [8,13]. The patient was a 61-year-old male who presented with an aseptically loosened titanium-alloy femoral stem and unexplained fatigue, weight loss, and hepatosplenomegaly 8 years following primary total hip arthroplasty. Examination of operative biopsy specimens revealed epithelioid granulomas containing abundant particles of titanium-aluminum-vanadium alloy in the abdominal lymph nodes, liver, and spleen. In the liver, there was mild bile-duct hyperplasia and moderate fibrosis. The patient recovered following revision of the loosened component, splenectomy, and a course of steroid therapy.

Besides the liver and spleen, other distant organs may also accumulate disseminated wear products. Possible titanium alloy wear debris has been reported in bone marrow of the iliac crests of 2 patients with failed hip or knee arthroplasty [14]. There remains a paucity of data concerning the distribution of wear debris in organs such as the brain, lungs, heart, kidneys, or bone marrow at sites remote from the implanted limb. Evaluation of these additional organs and postmortem material from patients who have hosted improved conventional and alternate bearing devices is essential to completing an inventory of the body burden of particulate and other forms of metallic, ceramic, and polymeric debris in patients with modern total joint arthroplasties.

Both single-particle and bulk analytical techniques, each with their own advantages and limitations, can be employed in a complementary manner to estimate the metal content of distant organs. In the present study, correlated light microscopy, backscattered electron imaging, and energy dispersive x-ray analysis were effective in characterizing the histopathological response to particulates and in determining the elemental composition of various individual particles as small as .1 micrometers within the tissue. In this manner, submicrometer wear particles could be distinguished from co-mingled particles of environmental origin, including silicates containing titanium and aluminum, elements also present in orthopedic wear debris. Disseminated wear products may also exist as nanometer sized particles, which, when embedded in tissue, may elude detection by the electron microprobe [15]. Transmission electron microscopy, although not practical for scanning organ sections, can extend identification of individual particles to approximately 10 nanometers, and is useful for special studies of particulate debris such as selected area electron diffraction. Metallic degradation products may also exist as particles less than 10 nanometers and as organometallic complexes. For these reasons, trace metal analyses by atomic absorption spectroscopy or inductively coupled plasma mass spectroscopy have been used to determine the overall metal burden of an organ [16].

In conclusion, wear particles generated at nonbearing surfaces of revised or malfunctioning primary arthroplasties can constitute an important source of particles that disseminate to and accumulate in remote organs. These particles are in addition to those generated at primary bearing surfaces. The recognition that high concentrations of wear particles can occur in organs distant from the implant site is further impetus to reduce particle generation by joint arthroplasty devices, to maintain long-term clinical and radiographic follow up of patients with joint reconstructions, and to consider revision of the implant in patients in whom large amounts of debris may be generated. Indeed, while all components can be associated with distant spread of particles and metal ions generated by wear and corrosion, it is the environment of the revision arthroplasty that is more worrisome than the primary arthroplasty. Elevated serum and urine metal concentrations may help identify patients whose implants are generating a high volume of metallic wear debris [17]. It is also essential to continue the long-term study of disseminated wear debris to ascertain if there are direct biological effects of clinical importance beyond the rare case described above of a patient with mechanical failure of an implant in whom granulomas formed in the liver and spleen [18].

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