Extensive metallosis and necrosis in failed prostheses with cemented titanium-alloy stems and ceramic heads

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We describe three prostheses with cemented titanium-alloy stems and Al₂O₃ ceramic femoral heads which had to be revised after a mean period of implantation of 78 months. In each case, the neck of the prosthesis had been so severely worn that the profile was elliptical rather than circular. There was severe metallosis of the periprosthetic tissues. Metal particles isolated from the tissues were approximately one nanometre in size and the ratios of titanium, aluminium and vanadium in the particles were the same as in the original alloy. Histologically, the high concentration of metal particles masked the presence of high-density polyethylene (HDP) debris, but again particles about one nanometre in size were isolated from the tissues. The severe necrobiosis and necrosis noted were consistent with other reports of the presence of extensive wear particles in periprosthetic tissues. Wear is presumed to have occurred as a result of mismatch between the shape or size of the taper cone and the femoral head, or to changes in the geometry of loading due to migration of the cup. To facilitate early intervention, patients with this design of prosthesis should be monitored radiologically.

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The rate of wear of a prosthetic femoral head is usually low, but it can accelerate as metal wear particles themselves abrade the articulating surfaces.1

Wear-resistant materials, such as cobalt-chromium-molybdenum alloy, stainless steel or ceramic, make good articulating surfaces. Titanium alloys are better suited for the manufacture of the anchoring surface of the femoral stem.2-4 In a cemented prosthesis, wear is generally caused by movement of the metal against the polymethylmethacrylate (PMMA) cement. When the morse taper cone exactly fits the head, it is unlikely to wear,1 but any mismatch between the surfaces may produce metal wear particles. The process begins as the hard ceramic head abrades the softer layer of titanium oxide of the femoral neck. If extensive fretting disrupts this layer the underlying alloy, which is even softer, is exposed and the rate of wear increases.

We have encountered three cases of extensive wear in femoral prostheses with titanium alloy stems and ceramic heads.

Patients and Methods

Between September 1996 and March 1998 we undertook revision operations on three women who had undergone total hip arthroplasty for osteoarthritis of the left hip at a mean of 78 months earlier (66 to 94), because of severe pain due to aseptic loosening of both the femoral and acetabular components. The femoral component in all three was a cemented titanium-aluminium-vanadium (Ti6Al4V) self-locking stem (Cremascoli, Milan, Italy). The size and origin of the high-density polyethylene (HDP) acetabular cups varied. Table I gives details of the patients and Table II of the original implants.

We subjected the removed implants to stereomicroscopy (ZH10; Olympus Hamburg, Germany) and then scanning

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Table I. Details of the three patients

<table>
<thead>
<tr>
<th>Case</th>
<th>Gender</th>
<th>Age (yr)</th>
<th>Weight (kg)</th>
<th>Side</th>
<th>Prosthesis in situ (mth)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>88</td>
<td>55</td>
<td>L</td>
<td>66</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>79</td>
<td>65</td>
<td>L</td>
<td>73</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>59</td>
<td>82</td>
<td>L</td>
<td>94</td>
</tr>
</tbody>
</table>
electron microscopy (SEM). After cutting the taper carefully from the stem we used energy-dispersive x-ray analysis (EDA) to determine the composition of the surface (Link ISIS 300; Oxford Instruments, Oxford, UK). Sections of the HDP cup approximately 1 cm wide were cut, sonicated, attached to an SEM stub and sputter-coated with gold for SEM (JSM 5800; JEOL, Tokyo, Japan).

**Histological analysis.** Samples of periprosthetic tissue obtained during revision were fixed in 10% formalin.

### Table II. Details of the removed prostheses

<table>
<thead>
<tr>
<th>Case</th>
<th>Stem</th>
<th>Neck</th>
<th>Head</th>
<th>Acetabulum</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ti6Al4V, cemented, width 12.5mm, length 117mm, Cremascoli self-locking</td>
<td>14/16 Al2O3,</td>
<td>32 mm,</td>
<td>Cemented, No 50, Protek (Bern, Switzerland)</td>
</tr>
<tr>
<td>2</td>
<td>Ti6Al4V, cemented, width 10mm, length 112mm, Cremascoli self-locking</td>
<td>14/16 Al2O3,</td>
<td>32 mm,</td>
<td>Cementless, No 64, LIMA (Milan, Italy)</td>
</tr>
<tr>
<td>3</td>
<td>Ti6Al4V, cemented, width 12.5mm, length 117mm, Cremascoli self-locking</td>
<td>14/16 Al2O3,</td>
<td>32 mm,</td>
<td>Cemented, No 54, Protek (Bern, Switzerland)</td>
</tr>
</tbody>
</table>

### Table III. Classification of histological samples for cases 2 and 3 according to the modified Mirra classification

<table>
<thead>
<tr>
<th>Histology</th>
<th>Case 2</th>
<th>Case 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute inflammatory cells</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mononuclear histiocytes</td>
<td>3+</td>
<td>3+</td>
</tr>
<tr>
<td>Chronic inflammatory cells</td>
<td>1+</td>
<td>0</td>
</tr>
<tr>
<td>Giant cells (multinucleated histiocytes)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Metal particles</td>
<td>3+</td>
<td>3+</td>
</tr>
<tr>
<td>PMMA globules</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Necrosis</td>
<td>3+</td>
<td>3+</td>
</tr>
<tr>
<td>Necrobiosis</td>
<td>3+</td>
<td>3+</td>
</tr>
</tbody>
</table>

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**Fig. 1**

Radiographs of the implant a) 73 months (case 2) and b) 94 months (case 3) after implantation.

**Fig. 2**

Photographs showing that a) because of abrasion by the ceramic head, the femoral neck has become elliptical rather than circular and b) the ceramic head has subsided on to the femoral stem.
embedded in paraffin, sectioned at 5 μm, stained with haematoxylin and eosin, and examined under light and polarised light microscopy. We stained selected samples with Oil Red O to detect HDP particles. A modification of the Mirra classification\(^5\) (Table III) was used to assess acute and chronic inflammatory cells, the number of mononuclear histiocytes and giant cells, the number and location of metal and PMMA particles, as well as areas of necrosis and necrobiosis.

**Particle isolation.** We used the method of Campbell et al\(^6\) to isolate HDP and metal particles simultaneously. Approximately 2 to 3 g of periprosthetic tissue were digested by 5N NaOH at 65°C. We added 5 ml of 5% sucrose to the digest, which was then centrifuged for one hour at 6000 x g. After removal of the supernatant, the sucrose was rinsed from the particles with distilled water. The particles were heated to 80°C for one hour, then 3 ml of propanol were added after sonification and the solution centrifuged for one hour at 4000 x g. The HDP particles separated out, forming a thin white band on top.

The metal particles were collected from the sediment and transferred to a separate vial. For SEM analysis, we filtered 100 to 500 μl of the particles through 0.2 μm Nucleopore polycarbonate filter paper (Costar, Pleasanton, California). The filter was dried, attached to an SEM stub and coated with gold. The composition of the particles was verified by EDA.

The HDP particles were dried in air, tableted with KBr, and then subjected to Fourier transform infrared (FTIR) spectroscopy (FTIR 1725-X; Perkin Elmer, Norwalk, Connecticut). We measured spectra in the range of 400 to 4000 cm\(^{-1}\). We used the FTIR spectrum for 5 μm of HDP powder (catalogue no. S-395-N2; Shamrock Technologies, Denkers International, Zevenaar, Holland) as a reference.

**Chemical analysis.** We added 1 ml of concentrated analytical grade HN0\(_3\) to the tissue sample. This became a transparent solution after heating to 37°C for several hours. The concentrations of Ti, Al and V were measured by inductively-coupled plasma atomic emission spectrometry (Plasma 40, Perkin Elmer) and electrothermal atomic absorption spectrometry (Zeeman 8279; Hitachi, Tokyo, Japan).

**Results**

**Radiological findings.** Preoperative radiographs of two of the three patients showed that the implants had displaced from their original position. Aseptic loosening was shown by radiolucent zones. In one patient (case 2) loosening had caused the acetabular cup to shift into varus. As the diameter of the femoral neck had worn down, the ceramic head subsided on to the stem (Fig. 1a). Subsidence was even more apparent in the third patient, although the acetabular cup had remained in its original position (Fig. 1b).

**Metal wear.** Severe deformation occurred as the ceramic head abraded the superolateral part of the femoral neck. In the three patients as the diameter of the three femoral necks wore down from their original 14 mm to 11 mm, 11.5 mm and 9 mm, respectively, they became elliptical rather than circular (Fig. 2a). Figure 2b shows how the ceramic head subsided on to the femoral stem. In Figure 3a, the machining marks are still visible on the inferomedial part of the neck. By contrast, Figure 3b shows irregularities on the surface of the superolateral part of the neck, and the machining marks have been worn away by the ceramic head. EDA of the inferomedial and superolateral parts of the neck confirmed that their composition was identical, with Ti 89.8wt%, Al 6.4wt% and V 3.8wt%. All three ceramic heads were marked with black tracks, probably from metal particles trapped between the head and the acetabular cup (Fig. 2b).
At revision, we found extensive black staining in the periprosthetic tissues. It was more distinct around the femoral canal, where some tissue was completely black, but was also present in the cement mantle of the acetabular cup.

Individual metal particles isolated from the periprosthetic tissues varied from 20 to 50 nm in diameter, but they often aggregated into clusters (Fig. 4a). EDA confirmed that the composition of the metal particles corresponded to the base Ti6Al4V alloy (Fig. 4b). The gold signal concealed the vanadium signal.

The acetabular membrane of the first patient had concentrations of metal of Ti 30.4 ppm, Al 3.3 ppm, and V 0.6 ppm, a ratio of Ti:Al:V of 88:9:3. In the tissue samples from the femoral canal the concentration of these metals increased by up to three orders of magnitude, but the ratio remained the same.

HDP wear. Figure 5a shows the deeply scratched surface of one of the HDP acetabular cups, with delamination developing. Magnification revealed crumbling of the surface and formation of submicron HDP particles (marked S in Figure 5b). Campbell et al. classified these particles as granules and beads (marked G and B, respectively, in Figure 6a). Although we isolated no particles larger than one nanometre in size, we noted some larger, elongated wear particles (marked E in Figure 5b) several micrometres long. The composition of the HDP particles was confirmed by FTIR spectrum analysis (Fig. 6b).

Histological analysis. We found extensive metallosis and necrosis but HDP wear particles were absent. Table III classifies the histological samples. All tissue samples showed metallosis (Fig. 7a), corresponding to the so-called jet-black histiocytes (+3, >100 visible black particles/histiocytes). Metal debris was stored intracellularly, mostly within mononuclear histiocytes and widely deposited.

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extracellularly. Necrosis was extensive (+3, >1 cm of necrosis/slide). When necrobiosis was incomplete, we observed macrophages containing metal particles and dying or ghost nuclei, but when complete only a network of collagen fibres with ghost outlines of histiocytes remained and metal debris lay in the tissue or within ghost outlines of formerly viable histiocytes (Fig. 7b). Complete necrosis was characterised by acellular debris (results not shown) and the absence of a network of collagen fibres. In some samples there was occasional evidence of tumoral calcinosis-like necrosis.

Under polarised light we saw no HDP particles in histiocytes or giant cells (Table III). Oil Red O staining was positive in samples with slate-blue histiocytes, but negative in samples with jet-black histiocytes. Because we had already identified HDP particles in these tissues, however, we believe that the high density of metal particles masked the HDP.

Discussion

Metallosis is defined as aseptic fibrosis, local necrosis, or loosening of a device secondary to metal corrosion and release of wear debris.7-9 Although a prosthesis with an Al2O3 ceramic head and titanium-based femoral stem should give long-term reliability several cases of severe metallosis have been reported.10-13 We have described three cemented femoral implants with Ti6Al4V stems and Al2O3 heads which had to be replaced after a mean time of implantation of 78 months. Loosening of the prosthesis was accompanied by severe deformation of the femoral neck and an accumula-
tion of wear debris in the periprosthetic tissues.

The histological picture was one of necrosis and necrosis. HDP and PMMA particles are known to stimulate production of multinucleated cells. We rarely saw multinucleated cells which seems to indicate that metal particles do not stimulate their production. Necrosis, however, has been shown to accompany failure of the implant in several studies, 14-16 and metal debris apparently stimulates a reaction which leads to necrosis of the surrounding tissues. This reaction may not be due solely to the metal. In our study, all three types of wear particle, namely, metal, HDP and PMMA, were present and possibly active.

Titanium has long been regarded as inert and biocompatible. Accumulation of titanium in the tissues is not considered to be detrimental to health. 17 Titanium particles and ions, however, can induce the release of potentially osteolytic cytokines in vitro. 18-20 Further, titanium may suppress expression of the gene that codes for collagen in osteoblast-like cells. 21 Jacobs et al 22 reported raised levels of serum titanium in patients with loose implants. Case et al 23 found that wear particles from loosened prostheses caused necrosis, fibrosis and other structural changes in regional lymph nodes, the liver and the spleen.

In our three cases, conclusions based solely on histological evidence could have been misleading since the metal particles appear to have masked the HDP particles, but we were able to isolate the latter from periprosthetic tissues.

We found the three principal elements of the alloy in the particles in ratios corresponding to the composition of the alloy itself, indicating that the metal debris was generated by wear rather than by corrosion. Other authors have noted similar findings. 14,15,24

We do not know why these three implants wore so badly. Around the same time, two other prostheses of the same type had to be replaced because of loosening, but no comparable wear of the femoral neck was evident. We assume that the severe wear resulted from mismatching the size and angles of the femoral heads and taper locks. Loosening and migration of the cup change the relationship between the acetabular and femoral components, giving rise to instability, abrasion and wear. Once the hard ceramic head starts to rub against the softer titanium alloy, large quantities of metal debris are released into the surrounding tissue. In all three of our cases, a taper of 14 to 16 mm and a cone of 22 mm had been used. Our study was too small to indicate whether this particular combination would invariably lead to severe wear, but the failure of the implants raises doubts about the reliability of this design. We believe that further investigation of the long-term effects of wear is important and recommend that patients with this type of prosthesis should be monitored radiologically so that early intervention can be planned if necessary.

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References