COMPOSITION AND MORPHOLOGY OF WEAR DEBRIS IN FAILED UNCEMENTED TOTAL HIP REPLACEMENT

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Interfacial membranes collected at revision from 11 failed uncemented Ti-alloy total hip replacements were examined. Particles in the membranes were characterised by electron microscopy, microchemical spectroscopy and particle size analysis.

Most were polyethylene and had a mean size of 0.53 μm ± 0.3. They were similar to the particles seen in the base resin used in the manufacture of the acetabular implants. Relatively few titanium particles were seen. Fragments of bone, stainless steel and silicate were found in small amounts.

Most of the polyethylene particles were too small to be seen by light microscopy. Electron microscopy and spectroscopic techniques are required to provide an accurate description of this debris.

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Total hip replacement (THR) is now entering its fourth decade of clinical success since the introduction of cemented low-friction arthroplasty by Charnley in 1960. Many designs, fixed with or without polymethylmethacrylate (PMMA) cement, are in routine clinical use. Most utilise an ultra-high-molecular-weight polyethylene (UHMWPE) acetabular surface articulating with either a metallic or a ceramic femoral head. Loosening, often accompanied by osteolysis, is a common cause of clinical failure. Even in the absence of frank loosening, isolated osteolytic lesions have been reported around cemented (Harris et al 1976; Carlsson, Gentz and Linder 1983; Huddleston 1988) and uncemented (Maloney et al 1990; Jacobs et al 1992) femoral stems. Willert and Semlitsch (1977) first suggested that the macrophage response to particulate wear debris was an important cause of osteolysis and led eventually to loosening. More recent studies (Goldring et al 1983; Maloney et al 1990) have supported this idea and animal experiments (Howie et al 1988; Goodman et al 1990) with simulated joint replacement devices have shown the same apparent clinical progression.

Particular debris-associated osteolysis was first ascribed to the fragmentation of PMMA about cemented devices (Vernon-Roberts and Freeman 1977; Willert and Semlitsch 1977) and came to be called 'cement disease' (Jones and Hungerford 1987). Recent clinical studies have shown, however, that similar phenomena occur around uncemented implants; this suggests a role for the UHMWPE and metal debris found in tissues retrieved during revision (Maloney et al 1990; Jacobs et al 1992). There is evidence that particles of different composition produce different cellular responses, both in vitro (Glant et al 1992; Pizzoferrato et al 1987; Shanbhag et al 1994) and in patients (Howie 1990; Forest et al 1991) but the relative importance of particulate species and particle size remains to be defined.

Surveys of the literature (Forest et al 1991; Amstutz et al 1992) have failed to provide guidance. Particles from all the prosthetic components, as well as a variety of apparently foreign materials, have been found in tissues around cemented and uncemented implants (Mirra et al 1976; Vernon-Roberts and Freeman 1977; Jacobs et al 1992). Most reports did not identify the mean size of each type of particle and there is little information on particle size distribution (Kossovsky et al 1991; Lee et al 1992) and none on size distribution of particles associated with failed uncemented THR.

We have examined the debris in interfacial membranes recovered at revision of uncemented Ti-alloy hip prostheses.

PATIENTS AND METHODS

Clinical material. Tissues from the bone-prosthesis interface were available from 11 patients whose arthroplasties were
Table 1. Details of 11 patients who had revision of a total hip replacement and the nature of the revised components

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age (yr)</th>
<th>Diagnosis*</th>
<th>Duration (mth)</th>
<th>Indication for revision</th>
<th>Implant†</th>
<th>DNA (mg/g)</th>
<th>Hydroxyproline (mg/g)</th>
<th>Polyethylene (Percentage)</th>
<th>Ca-P‡ (Percentage)</th>
<th>Ti (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>51</td>
<td>Failed THR</td>
<td>8</td>
<td>Aseptic loosening</td>
<td>Anat, CR</td>
<td>0.2</td>
<td>2.77</td>
<td>50</td>
<td>50</td>
<td>0</td>
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<tr>
<td>2</td>
<td>F</td>
<td>69</td>
<td>ON</td>
<td>28</td>
<td>Aseptic loosening</td>
<td>HG, CR</td>
<td>0.65</td>
<td>3.78</td>
<td>95</td>
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<td>0</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>54</td>
<td>OA</td>
<td>28</td>
<td>Aseptic loosening</td>
<td>Anat, CR</td>
<td>1.2</td>
<td>3.69</td>
<td>0</td>
<td>75</td>
<td>25</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>69</td>
<td>ON</td>
<td>62</td>
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<td>APR, CR</td>
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<td>6.74</td>
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<td>0</td>
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<td>5</td>
<td>M</td>
<td>60</td>
<td>Fracture</td>
<td>64</td>
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<td>HG, CR</td>
<td>nd</td>
<td>nd</td>
<td>90</td>
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<td>5</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>57</td>
<td>OA</td>
<td>65</td>
<td>Femoral osteolysis</td>
<td>HG, CR</td>
<td>nd</td>
<td>nd</td>
<td>70</td>
<td>20</td>
<td>10</td>
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<tr>
<td>7</td>
<td>F</td>
<td>60</td>
<td>OA</td>
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<td>Aseptic loosening</td>
<td>HG, CR</td>
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<td>3.6</td>
<td>85</td>
<td>10</td>
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<td>F</td>
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<td>71</td>
<td>Femoral osteolysis</td>
<td>HG, CR</td>
<td>nd</td>
<td>nd</td>
<td>70</td>
<td>20</td>
<td>10</td>
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<td>9</td>
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<td>46</td>
<td>OA</td>
<td>84</td>
<td>Aseptic loosening</td>
<td>Mark-II</td>
<td>nd</td>
<td>nd</td>
<td>90</td>
<td>10</td>
<td>0</td>
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<tr>
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<td>F</td>
<td>65</td>
<td>OA</td>
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<td>70</td>
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<td>0.78</td>
<td>85</td>
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</table>

* ON=osteonecrosis; OA=osteoarthrosis
† Anat=Anatomic prosthesis; HG=Harris-Galante prosthesis; Anatomics and HGs have Ti-6Al-4V stems with commercially pure Ti (Cp-Ti) fibre-mesh pads diffusion-bonded on the proximal aspect of the stem. They have modular cobalt (Co)-based alloy heads; CR=component revised; MPLE=modular polyethylene liner exchanged; HG-I and HG-II=Harris-Galante acetabular components (Zimmer, Indianapolis, Indiana); fabricated from a hemispherical Cp-Ti shell with a Cp-Ti fibre-mesh for tissue ingrowth. The titanium shell is stabilised with a variable number of Ti-6Al-4V screws; APR=modular Ti-alloy femoral stem and head with an uncemented Ti-alloy hemispherical shell and an UHMWPE insert; C-PE=non-metal-backed cemented polyethylene acetabular cup; ACT=threaded, uncemented Cp-Ti hemispherical shell with a UHMWPE insert (Biomet, Warsaw, Indiana); Mark I and Mark II=non-modular Ti-6Al-4V stems with a Cp-Ti fibre-mesh diffusion-bonded along the entire length of the anterior and posterior surfaces (Zimmer).
‡ bone mineral
§ not determined

revised at a mean of 62 months (8 to 114) after implantation (Table 1). The prostheses were uncemented and made of Ti alloy. Seven revisions were performed for aseptic loosening of the femoral stems, three for progressive endosteal erosions of the femur without loosening, and one to replace a loose acetabular component.

At revision, the membrane was curetted from the endosteal surface of the bone and prepared immediately for particle extraction. Figure 1 shows the particles in cells of one of these membranes. The particulate debris was extracted from 1 to 3 g (wet weight) of fresh tissue recovered from each patient.

The total DNA and hydroxyproline concentrations of the membranes were determined as an indication of their cellular and fibrous tissue (collagen) content (Downs and Willfinger 1983; Schwartz et al 1985).

**Extraction of particulate debris.** The tissues were rinsed in phosphate-buffered saline and hydrolysed in 4M KOH (2 ml/g of tissue) at 56°C for 48 hours. Aliquots of tissue hydrolysates (2 ml) were mixed with 6 ml of 95% ethanol, to aid sedimentation of debris, and centrifuged (1000 x g, for 1 hour). The debris was again suspended in fresh KOH and the hydrolysis continued for an additional 48 hours. Centrifuged pellets were washed three times by suspending the debris in distilled water for 8 hours at 37°C and the debris was then digested with pronase (Calbiochem, San Diego, California: 2000 U/ml, 50 mM Tris, 75 mM NaCl) for 24 hours at 37°C. During the first five minutes in pronase, it was subjected to ultrasound to separate the particles. The debris was again washed three times with distilled water and further purified by suspension in a mixture of equal volumes of ethanol and hexane in which it was spun vigorously. A white or cream-coloured fraction stabilised at the hexane-ethanol interface while the metal particles sedimented in the ethanol phase. The hexane (HF) and the ethanol (EF) fractions were collected separately. The HF was evaporated and the debris from both the HF and EF were incubated separately overnight in 4M KOH at 56°C. The fractions were washed three times in distilled water, subjected to ultrasound for four minutes and again suspended in ethanol.

**Photomicrograph of the interfascial membrane from case 5.** Numerous submicron birefringent particles are seen within cells.
Characterisation of particulate debris. Samples from each fraction were spread over super-smooth carbon stubs (Ted Pella, Redding, California) and dried overnight in a desiccator. They were coated with carbon and examined by scanning electron microscope (S120 Cambridge Instruments, Cambridge, Massachusetts). Secondary and backscatter electrons were used to discriminate the debris. Quantitative energy-dispersive X-ray analyses (EDX) (Tracer Northern, Middleton, Wisconsin) of individual particles or clusters were used to define elemental compositions. Samples of debris were spread on KCl discs (Analect, Irvine, California) and analysed in a Fourier transform infrared spectrometer (FTIR) (Analect, Irvine, California).

Criteria for identification of particles. Particles were identified as polyethylene if they met two criteria: 1) the EDX of particles was similar to that of the carbon stub background; and 2) the dominant peaks in FTIR matched a reference polyethylene spectrum. GUR 415 (Hoechst Celanese, Houston, Texas), a conventional medical grade polyethylene resin with an agglomerated particle size of 80 to 100 μm (Leigh et al. 1992), served as the reference for FTIR, SEM and EDX analysis.

Metallic and other particles were identified by their constituent EDX spectra. Particle size was measured from SEM micrographs as the mean of two orthogonal dimensions. When particles were clustered those with demarcated edges were measured, at least 150 particles per sample. Cumulative frequency distribution and percentiles were determined.

Control experiments. A specimen of human hip capsule from a patient undergoing primary hip replacement was treated with KOH and pronase, as described above, to verify the complete degradation of tissues in the extraction process and to determine whether any sediment resulted. Additional control studies were performed on commercially pure Ti particles (1 to 3 μm) (Johnson Mathey, Danvers, Massachusetts) treated with KOH in the same way as the tissues. The particle weight and morphology before and after treatments were determined.

RESULTS

In 10 of the 11 samples, 70% to 90% of the debris volume separated in the hexane phase and the remainder in the ethanol phase. In one sample (case 3), all the debris sedimented in the ethanol phase and in two samples (cases 1 and 4) in the hexane phase.

Debris from hexane fraction. Particles in the HF were white or cream-coloured and yielded pure polyethylene peaks on FTIR (Fig. 2) matching the reference spectra. The EDX spectra showed occasional small peaks of Si, S, Al and Ca. The particles in this fraction were thought to be polyethylene.

On SEM analysis, high magnification (> 10 000 x) was required to image these particles. Some clarity was lost, but their size and shape were more easily determined.

The polyethylene particles in seven of these ten fractions were spheroids 0.1 to 2.0 μm in mean dimension (Fig. 3a). Clusters of smaller particles were found with varying frequency among samples, interconnected with fibrils typically 0.2 to 0.3 μm wide and up to 10 μm long (Fig. 3b). The finer particles were aggregated as a carpet-like mesh of 50 to 80 μm. In addition, long cigar-shaped shards resembling rolled plates were seen 1 to 3 μm wide and 20 to 200 μm long. Approximately 92% of the particles were smaller than 1 μm, and had a mean size of 0.53 ± 0.3 μm (Fig. 4).

In the remaining three fractions (cases 1, 9 and 10), the particles were clustered in large masses which precluded the identification of individual particles.

SEM analysis of the reference polyethylene resin GUR 415 showed that its constituent particles, of about 80 to
Polyethylene particles isolated from the tissues showing (a) spheroids and (b) clusters of finer particles with bridging fibrils (arrow).

Cumulative frequency distributions and percentile plots of retrieved polyethylene particles.

100 µm, were not solid pellets but rather cauliflower-like aggregates of smaller particles (Fig. 5a). Higher magnification of these base resin grains confirmed the presence of unfused spherules of 0.77 µm ± 0.3 with interconnecting submicron fusion fibrils (Fig. 5b). Both these forms were frequently seen in our retrieved debris. Rose et al (1979) and Siegmann et al (1991) demonstrated similar forms of HiFax 1900 (Hercules) and GUR 412 (Hoechst-Celanese) base resins although the particle size distribution was not reported. Surface EDX analysis of the GUR 415 grains used in this study also revealed traces of Si, S, Al and Ca.

**Debris from ethanol fraction.** This fraction consisted of metallic pieces and cream-coloured dense fragments. The metal was identified as Ti and represented about 5% to 10% of the debris volume. These fragments were shaped like wire or flakes and had a maximum dimension of 10 to 400 µm. Ti-6Al-4V fragments could not be distinguished chemically from the Cp-Ti pieces due to the presence of extraneous Al, the low concentration of V and overlapping of the Ti[Kβ] and V[Kα] peaks. Analysis of standards suggests an EDX detection limit of 1% to 3%. Notwithstanding, Ti flakes approximately 200 to 400 µm in size and about 10 to 20 µm thick were presumed to originate from the Ti-alloy stem (Fig. 6a), whereas wire-form Ti-fragments 300 to 400 µm...
wide and of varying lengths (Fig. 6b) were believed to arise from the fibres of the mesh pad (approximately 250 μm in diameter).

Cream-coloured fragments, constituting up to 30% of the debris volume, were present in 9 of the 11 samples and consisted of calcium and phosphorus (Ca-P)-rich particles as detected by EDX. With a calcium to phosphorus ratio of 1.5, they were similar to bone mineral. Ca-P particles were 0.2 to 300 μm in diameter with the majority between 1 to 10 μm. The smaller particles were rounded and the larger ones were angular.

In addition to particles originating from the prosthetic components and bone, some ‘anomalous’ particles were detected in the EF. Silica was a common trace contaminant seen in every sample. In two cases (7 and 10) it was present up to 30% by atomic weight, chemically bound to Ca (predominantly as Ca- and Si-rich fragments) or to Ca-P particles (Fig. 7a). Fe-, Cr-, and Ni-containing particles with an EDH composition consistent with stainless steel were also observed (Fig. 7b). Ti flakes were often found with adherent layers of Ca and P, and Ca-P particles were found by EDX to have trace amounts of Ti and Fe.

The normal human hip capsule tissue was completely degraded by the extraction process leaving no sediment. Within experimental error (± 5%), all added Ti particles were retrieved after treatment with KOH. Comparative scanning micrographs of test particles confirmed that fine particles were not degraded and were still present.

There was a high variability in both the DNA and the hydroxyproline content of the membranes (Table I) and no correlation between the DNA or hydroxyproline content and the debris fraction of polyethylene retrieved from the tissues.

DISCUSSION

We found three types of particulate debris in interfacial membranes from failed uncemented Ti-alloy THRs. Listed in order of estimated volume they were polyethylene in fine particles and clusters, Ca-P-rich particles and Ti fragments. In addition, ‘anomalous’ particles including stainless steel and silicates were detected.

A comparison of the cumulative percentile plots of the retrieved polyethylene particles and the particles seen in the virgin GUR 415 resin (Fig. 8) revealed a similar particle.
distribution which suggests that submicron particles similar in size to those retrieved pre-exist in the base resin. This implies that complete incorporation of the fine particles may not occur during processing of the polyethylene into implant components and that degradation of bulk polyethylene by fatigue or wear may be facilitated by such structural imperfections. The fact that the retrieved particles were smaller than those in the base resin could be because of their attrition and oxidative degradation after their release into the joint space. Most acetabular components manufactured in the USA are made from GUR 415 resin, but other resins, such as GUR 412 (Hoechst-Celanese, Houston, Texas) and HiFax 1900 (Hercules, Magna, Utah), are also used. The fabrication of resin into solid forms, either by hot pressing or ram extrusion, is a complicated undertaking and involves several different companies. In our retrospective study, it was not possible to determine which combination of raw material, fabricator and fabrication process was used in the manufacture of each component. The morphology, however, of the three base resins used in the manufacture of the components in this study (HiFax 1900, GUR 412 and GUR 415) is qualitatively similar (Rose et al 1979; Seigmann et al 1991). The presence of Al, Ca, Si and Ti inclusions in the polyethylene debris is most likely explained by their presence as components of the Ziegler-Natta catalyst systems (Al, Ti around submicron silica core) and calcium stearate used in polyethylene manufacture (Dobbs, Scales and Wright 1977; Nusbaum et al 1979).

Ti flakes and wire-shaped fragments are probably products of abrasive wear of the femoral stem against the bone. This is supported by our frequent observation of an adherent layer of Ca-P-rich material on the Ti substrates. Significant numbers of fine Ti particles are reportedly present in blackened tissues around THA components (Black et al 1990; Witt and Swann 1991). It should be emphasised that tissues interfacing with the devices reported in this study had no visible discoloration.

To address the issue of experimental artifact, this study has shown that a control tissue (a hip capsule from a patient without an implant) undergoing identical processing had no sediment. Also, micron-sized Ti particles were not made soluble by KOH. Campbell, Ma and Belcher (1993) have also shown that strong alkali does not alter the morphology of micron-sized high-density polyethylene particles.

The Ca-P-rich particles which are assumed to be bone, represent either remnants from drilling, reaming and curet-
tage or the result of abrasion at the implant-bone interface. The presence of traces of Ca and P on Ti fragments may be due to the incorporation of Ca in the Ti oxide layer (Ishizawa 1992). Conversely, the presence of trace amounts of Ti on Ca-P particles may, as Blumenthal and Cosma (1989) have suggested, represent incorporation of Ti into nucleating hydroxypatite. Normal osteoid mineralisation and bone remodelling in the close vicinity of a metal stem and its wear products would make incorporation of metal atoms into the hydroxypatite crystal a possibility.

The stainless-steel particles observed were probably contaminants introduced from the surgical instruments but the presence of silicates, complexed with Ti and iron and also with Ca-P, is more perplexing. Al, Ca and Si particulate contamination has been detected on the surfaces of fresh stock and of retrieved Ti-alloy femoral components and has been attributed to sand blasting and other techniques used to produce textured implant surfaces (Black et al 1992; Ricci et al 1992). Such hard contaminants including Ziegler-Nata catalysts could lead to three-body wear in the joint, and could thereby contribute to the release of polyethylene particles. Another possible source of iron is the blood or the products of its degradation but this seems unlikely since most of the iron was associated with Cr and Ni in the proportions characteristic of stainless steel.

Recently, Lee et al (1992) have measured the sizes of polyethylene particles in tissues around cemented THR. They used light microscopy and described birefringent particles of 2 to 13 μm diameter which were assumed to be polyethylene. By contrast, we found that most of the polyethylene particles were not visible by light microscopy. This contradiction could be explained if the particles seen by Lee et al were in fact aggregates of smaller particles.

Most of the polyethylene, bone mineral and metal particles present in interfacial tissues are very small (< 1 μm). Larger fragments are also present, however, and although they are relatively few they contribute heavily to the total volume. Fragments larger than 7 μm are generally assumed to be too large to be phagocytosed by macrophages (Robert and Quastel 1963) and to contribute only minimally, if at all, to the biological responses (Glant et al 1993; Glant and Jacobs 1994) leading to osteolysis. Fine particles, seen in phagocytic cytoplasms in osteolytic tissues (Maloney et al 1990; Jacobs et al 1992), however, are believed to stimulate macrophages and lead to bone resorption (Glant et al 1993; Glant and Jacobs 1994; Shanbhag et al 1993).

Most of the particles retrieved from the interfacial membranes of THR revisions are submicron polyethylene and they resemble the particles seen in virgin resin. This finding may have important implications with regard to the mechanisms of UHMWPE wear. Other particles, including Ti, bone mineral, silicates and stainless steel are also present in the membranes around failed uncemented Ti-alloy THRs, but this study suggests that the most important particle is submicron polyethylene.

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REFERENCES


Fig. 8

Cumulative percentile plots of retrieved polyethylene and GUR 415 particles.
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