

Early failure of metal-on-metal bearings in hip resurfacing and large-diameter total hip replacement

A CONSEQUENCE OF EXCESS WEAR

D. J. Langton,
S. S. Jameson,
T. J. Joyce,
N. J. Hallab,
S. Natu,
A. V. F. Nargol

From North Tees and Hartlepool NHS Trust, Stockton-on-Tees and Centre for Rehabilitation, Newcastle University, Newcastle upon Tyne, England

■ D. J. Langton, MRCS(Eng), Orthopaedic Research Registrar
 ■ S. S. Jameson, MRCS(Eng), Specialist Registrar
 ■ A. V. F. Nargol, FRCS(Tr & Orth), Consultant Orthopaedic Surgeon
 Joint Replacement Unit
 ■ S. Natu, FRCPATH, Consultant Histopathologist
 Department of Histopathology
 University Hospital of North Tees, Hardwick, Stockton-on-Tees TS19 8PE, UK.

■ T. J. Joyce, PhD, Lecturer in Biomechanics
 Centre for Rehabilitation and Engineering Studies, School of Mechanical & Systems Engineering
 Stephenson Building,
 Claremont Road, Newcastle University, Newcastle upon Tyne NE1 7RU, UK.

■ N. J. Hallab, Associate Professor
 Department of Orthopaedic Surgery
 Rush University Medical Center,
 1735 W. Harrison MC 107,
 Chicago, Illinois 60612, USA.

Correspondence should be sent to Mr D. J. Langton; e-mail: djlangton22@doctors.org.uk

©2010 British Editorial Society of Bone and Joint Surgery
 doi:10.1302/0301-620X.92B1.22770 \$2.00

J Bone Joint Surg [Br]
 2010;92-B:38-46.
 Received 29 April 2009;
 Accepted after revision 27 August 2009

Early failure associated with adverse reactions to metal debris is an emerging problem after hip resurfacing but the exact mechanism is unclear. We analysed our entire series of 660 metal-on-metal resurfacings (Articular Surface Replacement (ASR) and Birmingham Hip Resurfacing (BHR)) and large-bearing ASR total hip replacements, to establish associations with metal debris-related failures. Clinical and radiological outcomes, metal ion levels, explant studies and lymphocyte transformation tests were performed. A total of 17 patients (3.4%) were identified (all ASR bearings) with adverse reactions to metal debris, for which revision was required. This group had significantly smaller components, significantly higher acetabular component anteversion, and significantly higher whole concentrations of blood and joint chromium and cobalt ions than asymptomatic patients did (all $p < 0.001$). Post-revision lymphocyte transformation tests on this group showed no reactivity to chromium or cobalt ions. Explants from these revisions had greater surface wear than retrievals for uncomplicated fractures. The absence of adverse reactions to metal debris in patients with well-positioned implants usually implies high component wear.

Surgeons must consider implant design, expected component size and acetabular component positioning in order to reduce early failures when performing large-bearing metal-on-metal hip resurfacing and replacement.

Although debris from metal-on-metal joint replacements may cause local tissue reaction,^{1,2} systemic effects have yet to be demonstrated. In the 1970s there were reports of large joint effusions and widespread tissue destruction following total hip replacement (THR) with McKee-Farrar devices.³ In 2005 Willert et al⁴ described the histological appearance of periprosthetic tissues surrounding failed metal-on-metal joint replacements and suggested a lymphocyte-dominant delayed-type hypersensitivity reaction, aseptic lymphocyte-dominated vasculitis-associated lesion (ALVAL), as a potential explanation. Because the clinical relevance of this testing remains uncertain, this continues to be a concern for surgeons implanting metal-on-metal devices, particularly when combined with the unknown incidence of such tissue reactions.

Pandit et al¹ used the term 'pseudotumour' to describe cystic and solid masses associated with resurfacing devices. They estimated that 1% of patients who have a metal-on-metal resurfacing develop a pseudotumour within five years and speculated that the adverse effects could be mediated by an allergic

response to 'normal' levels of metal debris, or could be caused directly by toxic concentrations of chromium (Cr) and cobalt (Co) generated from bearing surfaces experiencing abnormal wear. It remains unclear whether ALVAL is itself an integral factor in the mechanism of failure, or simply an associated observation in the capsular tissues. Without exception, the literature reports an increased incidence of these problems in women.^{1,2,5}

We sought to establish the rate of failure secondary to adverse reactions to metal debris (ARMD) in our patients, to identify relationships between this mode of failure and the wear rate of the prosthetic joint, and to provide a potential explanation for the increased incidence of this in women. There is currently no clear consensus in the literature defining the boundaries of the terms metallosis, ALVAL and pseudotumour. Reports suggest that tissues examined following revision surgery often exhibit a combination of the above pathologies.^{1,3,4} For the purposes of this paper we therefore use the acronym 'ARMD' as an umbrella term to describe joint failures associated with pain, a large sterile effusion of the hip and/or macroscopic necrosis/metallosis.

Table I. Patient demographics, component details and metal ion concentrations. All values are mean (range) unless marked with '§', in which case they are median values

	ASR*	BHR†	ASR THRs‡
Demographics			
Number	418	155	87
Age in yrs (range)	56 (28 to 77)	51 (32 to 67)	67 (25 to 85)
% female	44	43	61
Post-operative time in mths (range)	35 (8 to 57)	63 (57 to 85)	41 (10 to 57)
ASA¶ (range)	1.6 (1 to 3)	1.39 (1 to 2)	1.98 (1 to 3)
Femoral size in mm (range)	48.6 (39 to 59)	47.6 (38 to 58)	47.2 (39 to 57)
Inclination angle in degrees (range)	48.5 (31 to 70)	48.3 (32 to 70)	48.8 (36 to 76)
Anteversion angle in degrees (range)	20.4 (3 to 39)	19.9 (-5 to 39)	19.4 (-9 to 35)
Harris hip score (range)	94 (35 to 100)	97 (51 to 100)	76 (29 to 100)
Outcome scores			
Number of total ion results (bilateral patients)	138 (15)	90 (11)	19 (2)
Serum metal ion levels (range)	Cr (µg/l)§	4.46 (0.6 to 115)	4.42 (1.8 to 77)
	Co (µg/l)§	2.82 (0.4 to 228)	1.96 (0.7 to 190)
Whole blood metal ion levels (range)	Cr (µg/l)§	4.16 (1.5 to 69.8)	4.19 (2.37 to 40)
	Co (µg/l)§	2.74 (0.4 to 271)	1.80 (0.63 to 147)
Adverse reactions to metal debris failure at a minimum of six months (%)	3.2	0.0	6.0

* ASR, articular surface replacement

† BHR, Birmingham hip resurfacing

‡ THR, total hip replacement

¶ ASA, American Society of Anaesthetologists

Patients and Methods

The senior author (AVFN) used the Birmingham Hip Resurfacing (BHR, Smith & Nephew, Warwick, United Kingdom) implant from 2002 to April 2004, and the Articular Surface Replacement (ASR, DePuy International Ltd, Leeds, United Kingdom) thereafter. All patients were enrolled in a prospective study to monitor clinical, radiological and functional results. The femoral component of the ASR (ASR XL form), can also be used in combination with a stem (Corail or SROM, DePuy International Ltd) to articulate with the standard ASR resurfacing acetabular component. The articulating surfaces of both systems are therefore identical in terms of composition and manufacturing processes. For this reason we also considered patients with ASR THRs in this study. We have already described in full the differences in design of the ASR and BHR acetabular components.⁶

By January 2009, 505 ASR devices had been implanted (including 87 ASR THRs) and 155 BHRs prior to April 2004. Resurfacing procedures were carried out through a posterior approach and THRs through a direct lateral approach. The technique used for the resurfacing procedure has also been described previously.⁷ The majority of resurfacings were performed in patients under 65, but older men were included if they were considered biologically younger. Patient demographics can be seen in Table I. Patients were followed up at six weeks, three and six months, and annually thereafter. Harris hip scores⁸ (HHS)

and University of California, Los Angeles (UCLA) activity scores⁹ were recorded at one year for all patients.

Radiographic analysis. Weight-bearing, digital anteroposterior (AP) pelvic radiographs were obtained post-operatively and at subsequent visits. Assessment of acetabular component position was carried out using Einzel-Bild-Roentgen-Analyse software (University of Innsbruck, Innsbruck, Austria)^{10,11} using all available radiographs in order to improve accuracy.¹² Radiographic measurements were performed by two of the authors (DJL and SSJ), with mean values used for analysis.¹³ The theoretical distance of the articular contact patch to articular rim, which would be present in the standing position, was calculated for all patients using a method previously described.⁶

Metal ion analysis. *Blood.* From June 2007, Cr and Co ion levels in whole blood and serum were routinely analysed for each patient with a unilateral implant at a minimum of 12 months after surgery. Beyond this 'running-in' phase, implants are thought to reach a relatively steady state of wear.¹⁴⁻¹⁶ The sampling method has been described previously.¹³ All samples were frozen and sent for blinded trace element analysis to the Biochemistry Department at the Royal Surrey County Hospital, Guildford, United Kingdom. Samples were measured by inductively coupled plasma mass spectrometry.

Joint fluid. During revision surgery, joint fluid was sampled and analysed using the same technique and equipment as in collecting blood specimens. Where the

joint capsule was still intact, a cannula was inserted through the soft tissue prior to incision and drainage of the effusion.

Histopathological examination of tissues from revision procedures. Specimens were received in formalin from various sites within the neocapsule. They were routinely processed, embedded in paraffin and stained with haematoxylin and eosin. Histological analysis was carried out at $\times 2$, $\times 4$, $\times 10$, $\times 25$ and $\times 40$ magnification using a Nikon Eclipse 80i light microscope (Nikon Instruments Europe BV, Amstelveen, The Netherlands). A calibrated graticule was used for measurements. The various layers of the neocapsule were studied. Layer 1 consists of the surface membrane and was graded as type 1 to 4.¹⁷ Type 1 surfaces have an intact pseudosynovial membrane. Type 2 surfaces show a loss of the pseudosynovial membrane. Type 3 surfaces are associated with fibrin deposition in addition to the loss of the surface membrane, and in type 4 there is gross disruption of the surface membrane with fibrin deposition and fissuring. Layer 2 is the subsynovial layer, which usually contains the inflammatory infiltrate. Layer 3 is the vascular layer, which contains the perivascular lymphocyte cuffing. Layer 4 is the deeper layers containing muscle fat and fibrous tissue. The thickness of the histiocyte band containing particulate matter in Layer 2 was measured using the graticule. The presence of perivascular lymphocytic cuffing and its average thickness in layer 3 was also recorded.^{4,17} Patients who experience failure of their hip resurfacings secondary to a fractured neck of femur have tissue samples sent for routine analysis to exclude pathological causes. All tissue samples from metal-on-metal revision surgery are now graded histologically as described above.

Explant analysis. Since October 2007, explants retrieved at revision surgery have undergone analysis using a Zeiss TSK Rondcom60A (Carl Zeiss IMT Group, Minneapolis, Minnesota) roundness measuring machine, which has a resolution $> 1 \mu\text{m}$. Out-of-roundness (deviation in shape from a perfect circle) measurements were taken from three planes for each acetabular and femoral component. For acetabular components these planes were 3 mm, 7 mm and 11 mm below the rim. For the femoral components these planes were 3 mm, 7 mm and 11 mm from the 'pole' of the head. Modern manufacturing of resurfacing hip prostheses allows acetabular and femoral components to be produced with an out-of-roundness $< 5 \mu\text{m}$. Explanted components with greater out-of-roundness values imply that either material has been removed locally (wear) or the component has been distorted.

Lymphocyte transformation tests. All patients who had undergone surgery for failure of their metal-on-metal prostheses secondary to ARMD were invited to attend a clinic for metal allergy testing. Blood samples were obtained for metal-lymphocyte transformation tests assays (Rush University Medical Center, Chicago, Illinois).¹⁸ Along with the patients with failed joints, asymptomatic patients with the highest blood metal ion

levels were also invited to attend to give samples. Because of the cost and logistics of running such tests, this clinic was conducted on a one-off basis and therefore only six ARMD patients were able to attend on the relevant day. The time interval between revision surgery and blood sampling ranged from one day to 19 months.

Statistical analysis. This was carried out using SPSS version 16 (SPSS Inc., Chicago, Illinois). The Mann-Whitney U test was used to identify significant differences between groups with non-parametric data (Cr and Co concentrations; comparison of ARMD joint orientations with controls) and two sample *t*-tests were used to compare groups with parametric data. The relationship of the blood and joint fluid to metal ion concentrations was examined with Spearman's rank correlation. Differences were deemed statistically significant if the *p*-value was < 0.05 . Survival was calculated using the Kaplan-Meier method and 95% confidence intervals were calculated.

Results

Patients presenting with pain. A total of 16 patients presented with groin pain. All had an ASR *in situ*. Of these, 14 were women. The symptoms and clinical findings were similar, although six patients described deterioration soon after the operation, and the rest had initially been satisfied but developed pain between two and 25 months post-operatively. Of this group, 13 patients have been revised and the remaining three are awaiting revision. This represents a revision rate of 3.2% (35 months, 8 to 57) for our ASR resurfacings and 6% (41 months 10 to 57) for our ASR THRs as a result of ARMD. Pain was localised in the groin and aggravated by straight leg raising, and a 'clicking' or 'clunking' sensation was often described. In each case the WBC, ESR and CRP were normal.

Each patient underwent aspiration of the hip under fluoroscopic guidance, yielding large volumes of yellow/green fluid which was occasionally bloodstained. There was no microbial growth in any of the samples. In one patient, radiographs revealed radiolucent lines in three acetabular zones and the joint was subsequently found to be loose at revision. In the other patients the radiographs showed no evidence of loosening.

In the first patient who underwent revision there was gross swelling of the pseudocapsule and a large volume of the fluid bathing the implant and tracking into the psoas tendon. These findings have been published previously.⁷ Similar appearances were seen at the other 12 revision operations, with varying degrees of tissue necrosis around the implant. At one revision of an ASR resurfacing the pressure of the hip fluid had created a fistula through the abductor musculature. In was a further patient a pre-operative ultrasound scan showed a mass consistent with the description of a pseudotumour.¹ It was 11 cm \times 3 cm \times 4 cm in size, cystic in nature, and found to communicate with the hip joint. At revision an undisplaced fracture of the femoral neck was also noted.

Table II. Femoral sizes, acetabular component orientation and metal ion concentrations of the patients with adverse reactions to metal debris (ARMD) compared to the remainder of the articular surface replacement (ASR) cohort. Mean values are given for size and angles, with median values given for metal ion concentrations with ranges in parentheses

	ARMD	Asymptomatic ASRs	p-value
Femoral size (mm)	44.9 (41 to 51)	48.62 (41 to 59)	< 0.001
Inclination angle of acetabular component (°)	52.5 (42 to 70)	48.4 (25 to 68)	0.076
Anteversión angle of acetabular component (°)	27.4 (18 to 39)	19.7 (-5 to 40)	< 0.001
Whole blood Cr (µg/l) (range)	29.3 (3.89 to 41.8)	3.89 (1.51 to 69.8)	< 0.001
Whole blood Co (µg/l) (range)	69 (7.82 to 99.1)	2.67 (0.38 to 271)	< 0.001
Serum Cr (µg/l) (range)	33.6 (3.84 to 67.5)	4.23 (0.58 to 115)	< 0.001
Serum Co (µg/l) (range)	29.7 (4.95 to 96.6)	2.67 (0.38 to 228)	< 0.001

A patient with a 'late' (46 months) fracture associated with gross metallosis had been entirely satisfied at two years post-operatively. He played football on a weekly basis. Routine blood metal ion analysis prior to his fracture had shown whole blood Cr and Co levels to be elevated at 29 µg/l and 69 µg/l, respectively. As he was asymptomatic, a decision was taken to simply observe him, but unfortunately he began to develop acute pain prior to a fracture being identified. A CT scan confirmed a fracture in the presence of a well-placed femoral component, which had been implanted without evidence of notching. At revision, the periprosthetic tissues were stained black, but there was no gross joint effusion. This patient has been included as a failure secondary to ARMD, making a total of 17 from this cause.

Joint orientations and metal ion concentrations. The mean anteversion angles of the acetabular component and the joint sizes in the ARMD group were significantly different from those in the remainder of the ASR cohort (Table II). Blood metal ion concentrations in the ARMD group were greatly increased, with the median blood Co ion level 20 times greater than in the asymptomatic group. Levels of Cr and Co in the joint fluid were also significantly increased in the ARMD group compared to those obtained from patients undergoing revision for other reasons (Fig. 1).

Histopathology. Histopathological analysis of tissue samples from ARMD patients consistently showed widespread infiltration of histiocytes with areas of tissue necrosis. In many cases the histiocytes were seen to contain small unidentified black particles consistent with the description of metal particulate debris.⁴ Most viable tissue samples exhibited areas with high numbers of lymphocytes forming cuffs around vascular tissue to a greater or lesser extent, and synovial ulceration was also frequently seen. These characteristics are consistent with the description of ALVAL.⁴ The extent of histiocyte and lymphocytic infiltration was recorded for each patient, along with the circumference of the observed lymphocytic cuffs. Examination of capsular tissues obtained at revision surgery for an uncomplicated fracture did not show lymphocytic cuffing (Table III).

Explant analysis. The maximum out-of-roundness value for each available explant can be seen in Table IV. The ARMD

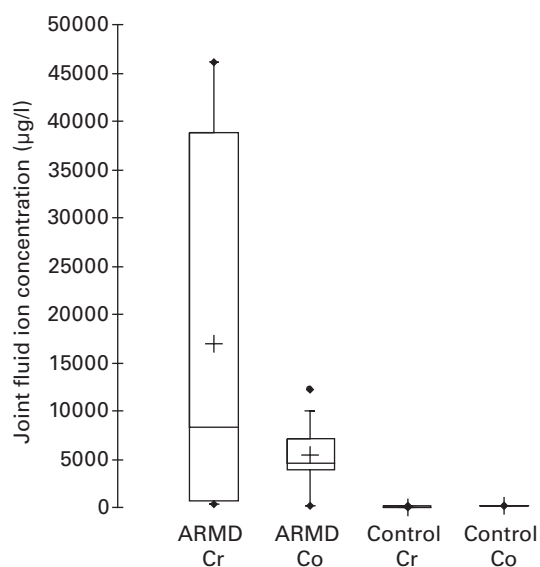


Fig. 1

Figure showing the comparison of metal ion concentrations in the joint fluid in patients with adverse reactions to metal debris and two controls (two Birmingham hip resurfacing patients revised for severe neck narrowing and another aspirated for suspicion of infection). The inferior, middle and superior horizontal lines of the boxes represent the first quartile, median and third quartiles. The ends of the 'whiskers' correspond to the limits of the data, beyond which values are considered anomalous. The mean is displayed with a +, outliers with *, and upper and lower values with •.

explants showed high out-of-roundness values compared to those obtained from explants retrieved for revision for an uncomplicated fracture. Although they can be caused by deformation secondary to the manufacturing and/or implantation processes, the low maximum out-of-roundness values for the fracture explants strongly suggest that an unexpectedly high rate of wear *in vivo* resulted in the out-of-roundness of the ARMD explants. The out-of-roundness traces of the acetabular components indicated that wear occurred at the edge of the component. The traces of the femoral components indicated a variety of wear patterns. Some showed localised wear on the superior surface, but others implied a more complex pattern, which is the subject of continuing research.

Table III. Histology results and comparison with clinical data. The last three results are given as controls. Zero months indicate that the patient was never free of pain post-operatively

Case	Gender	Allergies/ Atopic condition	Onset of pain post initial surgery (mths)	Onset of pain to revision (mths)	Layer 1	Layer 2	Layer 3		Comments
					Layer 1 surface membrane	Histiocyte sheet thickness (mm)	Lymphocytes	Lymphocyte cuff thick- ness (mm)	
1	F	Codeine	0	19	Type 4 extensive	3	Absent	0.05 to 0.15	
2	F	Nil	3	33	Type 4 extensive	0.5	Marked	0.2 to 0.25	Lymphocytic cuffs have occasional germinal centres
3	F	Septtrin	2	30	Type 3 and type 4	2	Moderate	0.05 to 0.15	Biopsy from first revision showed only necrosis
4	F	Morphine	0	36	Type 3 and focal type 4	1	Absent	Absent	> 200 ml of fluid at revision
5	F	Elasto-plast	7	29	Type 4 massive	NA*	NA	NA	Necrosis only, no viable tissue
6	F	Penicillin	0	12	Type 3 and type 4	2	Moderate	0.1 to 0.15	The cuffs form a rosary bead appearance
7	F	Elasto-plast	6	12	Type 4 massive	1.5	Moderate	0.25 to 0.3	Extensive necrosis
8	F	Asthma, hayfever	25	2	Type 3 and type 4	2.5	Mild	0.2 to 0.35	By far the thickest cuffs
9	F	Tramadol, suncream	0	8	Type 3 and type 4	3	Mild/moderate	0.05 to 0.15	Metallic sheen seen grossly
10	F	Asthma	0	17	Type 3 and type 4	0.9 to 2	Mild	0.15 to 0.2	
11	M	Sun cream	8	1	Type 4 massive	2.5	Moderate	0.15	Massive area of necrosis
12	F	Nil	0	2	Type 4 massive	NA	NA	NA	Necrosis only
13	M	Nil	35	3	Type 4 extensive	2	Mild	0.25 to 0.3	11 cm × 3cm × 4 cm pseudo-tumour
14	M	Nil	46 [†]	1	Type 4 massive	3	Mild	0.05 to 0.15	No features of ALVAL, [†] severe neck narrowing
15	F	Nil	48	2					No features of ALVAL, early fracture
16	M	Nil	No pain	0					No features of ALVAL, early fracture
17	F	Nil	52	2	Type 2	0.5	Absent	0.15 to 0.2	Sepsis

* NA, not applicable

†patient sustained a fracture at 46 months

† ALVAL, aseptic lymphocyte-dominated vasculitis-associated lesions

Metal-lymphocyte transformation tests. None of the ARMD samples showed increased lymphocyte reactivity to Cr or Co *in vitro*, or demonstrated an elevated incidence of metal sensitivity above that of the general population (10% to 15%).¹⁸ Only one ARMD patient showed metal reactivity, which was a mild response to aluminium, molybdenum and nickel (Table V).

Discussion

In this series we have described a failure rate as a consequence of ARMD of 3.2% in our ASR resurfacing group, and 6.0% in the ASR THR group. This amounts to a failure rate of 3.4% for all patients with ASR prostheses in this study. These figures are likely to represent the 'best case scenario'. Based on our experience, which is consistent with the reports in the literature,¹ metal debris-related complications may take several years to develop. The absence of ARMD in the BHR group, despite patients being drawn from the same geographical pool, suggests there is no genetic predisposition to this condition.

We have previously shown that smaller ASR components are particularly sensitive to position in terms of metal ion release.¹³ Our results have been corroborated by another

centre.¹⁹ We have now shown that ASR patients experiencing joint failure as a consequence of ARMD have significantly smaller, suboptimally orientated acetabular components than do asymptomatic patients. Concentrations of blood and joint metal ions in failed cases were significantly increased compared to those in patients who were pain free. Explant analysis of the available failed ARMD joints confirmed greater wear than expected for the duration *in situ*, as out-of-roundness values are a direct indication of the wear depth on the different components. Maximum out-of-roundness values of ARMD femoral components were markedly elevated compared to those of explants retrieved following fracture, including a femoral component that was retrieved following a fracture two years post-operatively. We conclude that an increase in the production of metal debris increases the risk of adverse local tissue reactions. There are reports of adverse immune responses leading to failure of MoM joints where subsequent retrieval analysis showed only minimal wear on the bearing surfaces.²⁰ The absence of the condition in our study group with BHR implants or larger/well-positioned ASRs suggests that these cases represent a minority group of sensitive patients who go on to develop ARMD despite relatively low levels of metal debris.

Table IV. Comparison of maximum out-of-roundness values for the analysed adverse reaction to metal debris failures with those retrieved following fracture

Implant*	Time in situ (mths)	Reasons for revision	Max out of roundness (head) (μm)	Max out of roundness (acetabular component) (μm)
ASR	28	Pain, effusion	31.3	
ASR	18	Pain, effusion	17.7	14.8
ASR THR	36	Pain, effusion	38.8	
ASR	8	Pain, effusion	91.8	64
ASR	27	Pain, effusion	38	28.8
ASR	35	Pain, pseudotumour	12.9	
ASR	14	Pain, effusion	3.69	6.86
ASR	46	Late fracture	66.9	
ASR	17	Pain, effusion	32.9	23.1
ASR	2	Fracture	1.8	
ASR	8	Fracture	3.1	
ASR	0	Fracture	2.5	
ASR	2	Fracture	1.7	
ASR	24	Fracture	2.7	
ASR	6	Fracture	2	

* ASR, articular surface replacement; THR, total hip replacement

Table V. Metal-lymphocyte transformation (LTT) results. Time indicates number of months after revision surgery when blood samples were taken

ARMD* failures	Cr	Co	Time	LTT results†
			19	No reactivity
	34.9	96	12	No reactivity
	64.8	217	12	No reactivity
			7	Mild reactivity to A1, Mo, Ni
	3.89	20.9	7	No reactivity
	6.4	8.0	1 day	No reactivity
Asymptomatic high ions	26	46.4	42	Mild reactivity to Ni
	69.8	271	41	No reactivity
	38	81	30	Mild reactivity to Ni, Fe
Asymptomatic low ions	2.89	1.04	38	Mild reactivity to Co, Cr, Ni. Moderate to Mo
	3.4	1.5	6	No reactivity

* ARMD, adverse reaction to metal debris;

† A1, aluminium; Mo, molybdenum; Ni, nickel; Fe, iron

Levels of blood metal ions correlate well with articular wear in retrieved components, and can therefore be used as a surrogate marker *in vivo* wear.²¹ We can use this information to propose an explanation for the increased incidence of ARMD in the ASR group. BHR acetabular components provide a greater arc of cover than do ASR components. For example, the coverage provided by the average female BHR (size 52 mm) acetabular component in this series is 162°, with the equivalent ASR component (size 52 mm) providing 151° of cover. Therefore, in components matched for size and orientation, articular contact will take place closer to the rim of an ASR acetabular component. This 'edge loading' effect has been shown in numerous retrieval studies to be strongly associated with increased articular wear,^{5,22} and this is consistent with the results of our explant analyses. We have previously published work

proposing that the location of the articular contact patch in the standing position of the patient is crucial in the development of high wear states.⁶ The closer this patch lies to the rim of the acetabular component the greater the chance of increased blood metal ion levels. Figure 2 shows the calculated mean contact patch to rim distances for ASR and BHR patients (men and women) in our series. The smaller the mean contact patch to rim distance the greater the incidence of ARMD. Women are exposed to higher concentrations of metal ions owing to a combination of factors: increased mean acetabular component inclination and anteversion, and a reduced mean joint size (Table II). Anatomical studies also show that the average female patient has a greater degree of femoral anteversion, which could also lead to posterior impingement and microseparation, a process implicated in increased wear.²³ It has been reported that high

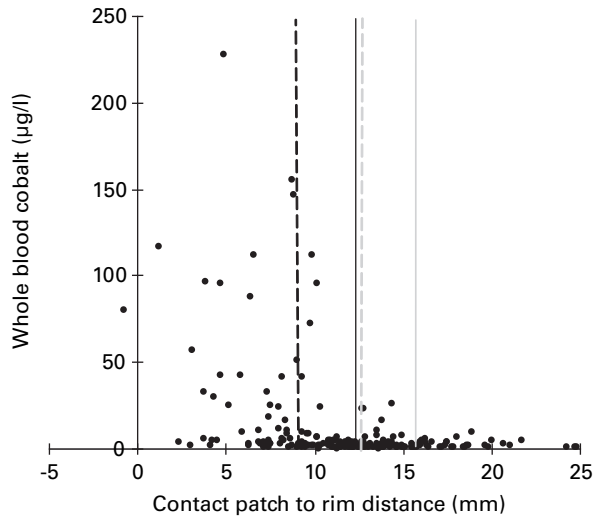


Fig. 2

Scatter plot showing all metal ion results for all unilateral implants in this study. Grey vertical lines represent the mean male (solid line) and female (broken line) Birmingham hip resurfacing patients' calculated contact patch to rim distances. The black vertical lines represent the equivalent articular surface replacement resurfacing patients. Note that the articular surface replacement total hip replacement contact patches for men and women are omitted because of their almost identical values to the articular surface replacement resurfacing male and female patient groups.

metal ion concentrations are associated with disturbing amounts of tissue necrosis, even when the patient remains asymptomatic.²¹

Some individuals and populations (e.g. women) have a greater predisposition to have or develop metal-associated delayed-type metal hypersensitivity, possibly as a consequence of prior metal sensitisation caused by jewellery²⁴ or, environmental exposure. Metallic ions purportedly become bound to plasma proteins, and the resulting complexes may stimulate an immune response.²⁵⁻²⁷ Furthermore, this reaction is metal specific, and the observed reactivity correlates with serum levels of metal ions *in vivo*.²⁸ However, the results we obtained from the lymphocyte transformation test studies were not consistent with this idea. The lack of lymphocyte reactivity to Cr and Co ions implies that if an immune response is the pathogenic factor in the development of an effusion, necrosis and pain, then it is likely to be a localised response rather than a pre-existing or systemic sensitivity. The fact that two of the patients with ARMD in this series had bilateral implants but only unilateral symptoms lends support to this theory. However, localised immune responses may act to sequester activated lymphocytes to the site of the joint inflammation and lead to fewer available peripherally primed circulating lymphocytes for lymphocyte transformation testing, and hence a non-elevated systemic response *in vitro*.²⁹

The unsatisfactory outcome in the two patients described in this series who were revised to metal-on-metal bearings, appear to favour the existence of a localised persisting

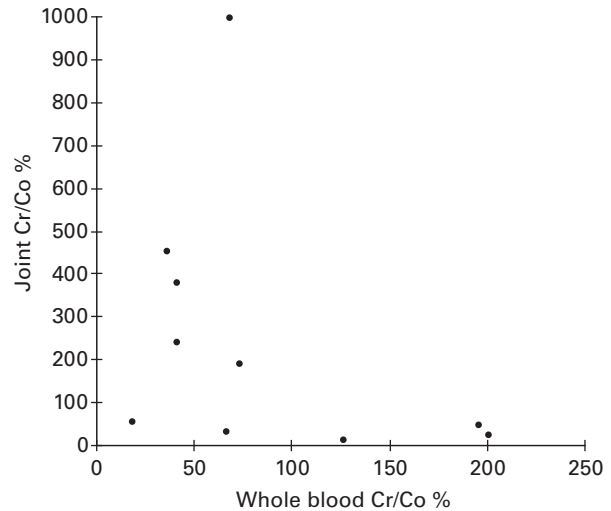


Fig. 3

Scatter plot showing joint fluid metal ion concentrations *versus* blood metal ion concentrations. Spearman's rank correlation = -0.599, $p = 0.09$. Included here are two results from one Birmingham hip resurfacing patient revised for severe neck narrowing and another aspirated for suspicion of infection.

immune response.⁷ Newly published results³⁰ have implicated a mediated response to Co-Cr-Mo alloy particles as a potentially important factor in reactions to metal debris. This type of reactivity, which has been shown to be critical to sensitivity responses to other non-metal antigens, would fit with the appearance of the ARMD tissues, which show heavy histiocyte infiltration. However, there is also accumulating evidence to show that massive concentrations of Cr and Co ions in the joint fluid could alone explain the observed micro- and macroscopic tissue necrosis.^{31,32}

The relationship between blood and joint concentrations of metal ions is unexpected and warrants further investigation. In patients with the highest concentrations of joint metal ions, Cr ions predominate, with a concentration around four times that of Co. In the blood of the same patients, the opposite is true, with Co concentrations two to three times those of Cr (Fig. 3). Only when blood metal ions are present in high concentrations do they reflect the ratios of the metal alloy from which they are released (Co:Cr 2.4:1). We acknowledge the small size of our data set, but the results do appear to suggest that Cr is sequestered in and around the joint space, with Co apparently more easily released into the circulation. Transmission electron microscope studies of metal particulate matter from tissues retrieved at revision surgery for failed joints at other centres, have shown that these particles are composed almost entirely of Cr, mostly in the form of a product of corrosion, chromium orthophosphate.^{33,34}

Early failure as a consequence of ARMD is probably multifactorial. Modifiable factors such as the orientation of the acetabular component and implant design conspire

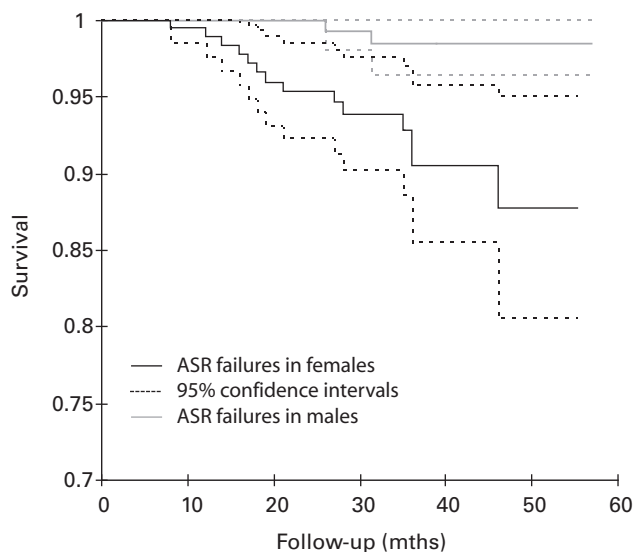


Fig. 4

Kaplan-Meier survival chart of the articular surface replacement (ASR) failures secondary to adverse reactions to metal debris in the < 49 mm femoral head group versus the ≥ 49 mm heads. Broken lines represent 95% confidence intervals. The minimum follow-up for inclusion was six months.

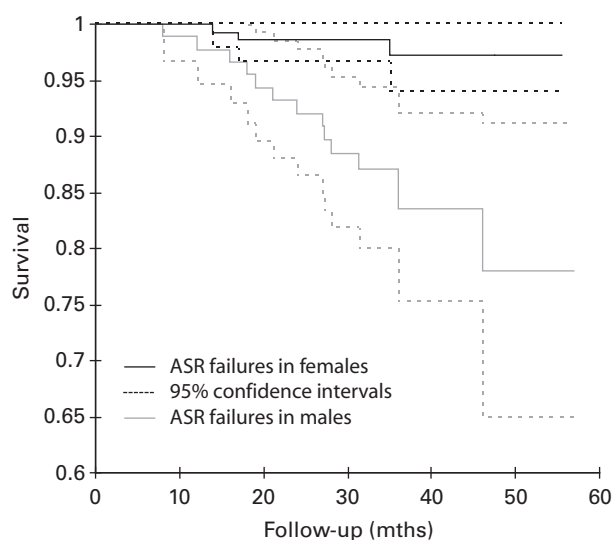


Fig. 5

Kaplan-Meier survival chart of the articular surface replacement patients with a calculated contact patch to rim distance > 10 mm (black) versus < 10 mm (grey). Broken lines represent 95% confidence intervals. Minimum follow-up for inclusion was six months.

with non-modifiable factors, including component size and host tolerance/response, to determine the success or failure of the resurfacing procedure. We have an unacceptably high failure rate secondary to ARMD in patients with small ASR bearings (Fig. 4). We have previously identified what we believe to be the optimal orientation for the ASR acetabular

component and highlighted the relatively small margins of error involved when attempting to reduce blood metal ion concentrations.¹³ This investigation has described the clinical consequences of the resultant increase in articular wear when these boundaries are exceeded (Fig. 5). Numerous studies have shown that surgeons cannot consistently achieve the desired acetabular component orientation,^{34,35} and our own experience is consistent with the literature. Surgeons must consider implant design, expected component size and positioning of the acetabular implant in order to reduce early failures when performing large-bearing metal-on-metal hip resurfacing and THR.

Supplementary material



Appendices giving further information on proliferation assay and hip joint contact are available with the electronic version of this article on our website at www.jbjs.org.uk

The author or one or more of the authors has received or will receive benefits for personal or professional use from a commercial party related directly or indirectly to the subject of this article. In addition, benefits have been made or will be directed to a research fund, foundation, educational institute, or other non-profit organisation with which one or more of the authors are associated.

References

- Pandit H, Glyn-Jones S, McLardy-Smith P, et al. Pseudotumours associated with metal-on-metal hip resurfacings. *J Bone Joint Surg [Br]* 2008;90-B:847-51.
- Ollivere B, Darran C, Barker T, Nolan J, Porteous MJ. Early clinical failure of the Birmingham metal-on-metal hip resurfacing is associated with metallosis and soft-tissue necrosis. *J Bone Joint Surg [Br]* 2009;91-B:1025-30.
- Jones DA, Lucas HK, O'Driscoll M, Price CHG, Wibberley B. Cobalt toxicity after McKee hip arthroplasty. *J Bone Joint Surg [Br]* 1975;57-B:289-96.
- Willert HG, Buchhorn GH, Fayyazi A, et al. Metal-on-metal bearings and hypersensitivity in patients with artificial hip joints: a clinical and histomorphological study. *J Bone Joint Surg [Am]* 2005;87-A:28-36.
- De Haan R, Campbell PA, Su EP, De Smet KA. Revision of metal-on-metal resurfacing arthroplasty of the hip: the influence of malpositioning of the components. *J Bone Joint Surg [Br]* 2008;90-B:1158-63.
- Langton DJ, Sprowson AP, Joyce TJ, et al. Blood metal ion concentrations post hip resurfacing arthroplasty: a comparison of the Articular Surface Replacement and Birmingham Hip Resurfacing devices. *J Bone Joint Surg [Br]* 2009;91-B:1287-95.
- Jameson SS, Langton DJ, Natu S, Nargol AVF. The influence of age and sex on early clinical results after hip resurfacing: an independent centre analysis. *J Arthroplasty* 2008;23(Suppl 1):50-5.
- Harris WH. Traumatic arthritis of the hip after dislocation and acetabular fractures: treatment by mold arthroplasty: an end-result study using a new method of result evaluation. *J Bone Joint Surg [Am]* 1969;51-A:737-55.
- Zahiri CA, Schmalzried TP, Szczechowicz ES, Amstutz HC. Assessing activity in joint replacement patients. *J Arthroplasty* 1998;13:890-5.
- Stoel B, Biedermann R, Auckenthaler T, et al. Ante- and retroversion measurement of cups by EBRA. *J Bone Joint Surg [Br]* 2001;83-B(Suppl II):179.
- Biedermann R, Tonin A, Krismer M, et al. Reducing the risk of dislocation after total hip arthroplasty: the effect of orientation of the acetabular component. *J Bone Joint Surg [Br]* 2005;87-B:762-9.
- Langton DJ, Sprowson AP, Mahadeva D, et al. Cup anteversion post hip resurfacing arthroplasty: validation of EBRA and presentation of a simple clinical grading system. *J Arthroplasty* 2009; in press.
- Langton DJ, Jameson SS, Joyce TJ, Webb J, Nargol AVF. The effect of component size and orientation on the concentrations of metal ions after resurfacing arthroplasty of the hip. *J Bone Joint Surg [Br]* 2008;90-B:1143-51.
- Back D, Young DA, Shimmin AJ. How do serum cobalt levels change after metal-on-metal hip resurfacing? *Clin Orthop* 2005;438:177-81.
- Heisel C, Streich N, Krachler M, Jakobowitz E, Kretzer JP. Characterization of the running-in period in total hip resurfacing arthroplasty: an in vivo and in vitro metal ion analysis. *J Bone Joint Surg [Am]* 2008;90-A(Suppl 3):125-34.
- Daniel J, Ziaee H, Pradhan C, McMinn DJ. Six-year results of a prospective study of metal ion levels in young patients with metal-on-metal hip resurfacings. *J Bone Joint Surg [Br]* 2009;91-B:176-9.

17. **Davies AP, Willert HG, Campbell PA, Learmonth ID, Case CP.** An unusual lymphocytic perivascular infiltration in tissues around contemporary metal-on-metal joint replacements. *J Bone Joint Surg [Am]* 2005;87-A:18-27.
18. **Hallah NJ, Anderson S, Caicedo M, et al.** Immune responses correlate with serum-metal in metal-on-metal hip arthroplasty. *J Arthroplasty* 2004;19(Suppl 3):88-93.
19. **De Haan RD, Pattyn C, Gill HS, et al.** Correlation between inclination of the acetabular component and metal ion levels in metal-on-metal hip resurfacing replacement. *J Bone Joint Surg [Br]* 2008;90-B:1291-7.
20. **Campbell P, Beaulé PE, Ebraamzadeh E, et al.** A study of implant failure in metal-on-metal surface arthroplasties. *Clin Orthop* 2006;453:35-46.
21. **De Smet K, De Haan R, Calistri C, et al.** Metal ion measurement as a diagnostic tool to identify problems with metal-on-metal hip resurfacing. *J Bone Joint Surg [Am]* 2008;90-A(Suppl 4):202-8.
22. **Morlock MM, Bishop N, Zustin J, et al.** Modes of implant failure after hip resurfacing: morphological and wear analysis of 267 retrieval specimens. *J Bone Joint Surg [Am]* 2008;90-A:89-95.
23. **Nevelos J, Ingham E, Doyle C, et al.** Microseparation of the centres of alumina-alumina artificial hip joints during simulator testing produces clinically relevant wear rates and patterns. *J Arthroplasty* 2000;15:793-5.
24. **Hallah N, Merritt K, Jacobs JJ.** Metal sensitivity in patients with orthopaedic implants. *J Bone Joint Surg [Am]* 2001;83-A:428-36.
25. **Merritt K, Rodrigo JJ.** Immune response to synthetic materials: sensitization of patients receiving orthopaedic implants. *Clin Orthop* 1996;326:71-9.
26. **Yang J, Black J.** Competitive binding of chromium, cobalt and nickel to serum proteins. *Biomaterials* 1994;15:262-8.
27. **Yang J, Merritt K.** Production of monoclonal antibodies to study corrosion of Co-Cr biomaterials. *J Biomed Mater Res* 1996;31:71-80.
28. **Hart AJ, Hester T, Sinclair K, et al.** The association between metal ions from hip resurfacing and reduced T-cell counts. *J Bone Joint Surg [Br]* 2006;88-B:449-54.
29. **Caicedo MS, Desai R, McAllister K, et al.** Soluble and particulate Co-Cr-Mo alloy implant metals activate the inflammasome danger signaling pathway in human macrophages: a novel mechanism for implant debris reactivity. *J Orthop Res* 2009;27:847-54.
30. **Allen MJ, Myer BJ, Millett PJ, Rushton N.** The effects of particulate cobalt, chromium and cobalt-chromium alloy on human osteoblast-like cells in vitro. *J Bone Joint Surg [Br]* 1997;79-B:475-82.
31. **Rae T.** The toxicity of metals used in orthopaedic prostheses: an experimental study using cultured human synovial fibroblasts. *J Bone Joint Surg [Br]* 1981;63-B:435-40.
32. **Huber M, Reinisch G, Trettenhahn G, Zweymüller K, Lintner F.** Presence of corrosion products and hypersensitivity-associated reactions in periprosthetic tissue after aseptic loosening of total hip replacements with metal bearing surfaces. *Acta Biomaterials* 2009;5:172-80.
33. **Shahgaldi BF, Heathley FW, Dewar A, Corrin B.** In vivo corrosion of cobalt-chromium and titanium wear particles. *J Bone Joint Surg [Br]* 1995;77-B:962-6.
34. **McCullum DE, Gray WJ.** Dislocation after total hip arthroplasty: causes and prevention. *Clin Orthop* 1990;261:159-70.
35. **Hassan DM, Johnston GH, Dust WM, Watson F, Dolovich AT.** Accuracy of intraoperative assessment of acetabular prosthesis placement. *J Arthroplasty* 1998;13:80-4.