ABSTRACT
The metal-on-metal articulations in total hip arthroplasty (THA) were widely used between 1960 and 1975. The McKee-Farrar and other first-generation prostheses failed at a high rate because impingement caused early component loosening. The problem of early component loosening was corrected by improved component design and better manufacturing quality. Second-generation metal-on-metal total hip replacements have experienced short and medium-term success as assessed by Harris Hip Scores and patient self-assessment. The combined annual linear wear of the metal-on-metal femoral head and acetabular insert is less than 10 mm and osteolysis has only rarely been observed in association with well-fixed metal-on-metal total hip replacements. Hypersensitivity is not a common cause of loosening with second-generation hip replacements and remains to be proven as a definitive diagnosis in unusual cases of unexplained pain. More than 40 years of use has demonstrated no increase in the incidence of renal failure or cancer in patients with metal-on-metal total hip replacements. The scientific evidence of the results using the metal-on-metal articulations would recommend its continued use in any patient who does not have compromised renal function.

INTRODUCTION
A high rate of early component loosening with metal-on-metal total hip replacements and the superior clinical results of the Charnley prosthesis during the 1970s discouraged the continued use of the metal-on-metal articulation. August1 reported a high loosening rate in patients with the McKee-Farrar total hip arthroplasty and concluded that equatorial bearing and high friction moments contributed to failure at the bone-cement interface. Evans et al.2 suggested that metal sensitivity caused obliteration of the blood flow to bone and bone necrosis was responsible for aseptic loosening. Walker et al.3 demonstrated that mechanical failure caused loosening when impingement of McKee-Farrar femoral neck against the rim of the acetabular component compromised component fixation. Retrieved total hip replacement components and periprosthetic tissue provided important information to determine what caused the high rate of aseptic loosening observed with the use of first-generation metal-on-metal hips. Equatorial bearing and jamming was suspected but the study of retrieved implants never demonstrated this mechanism of failure. All of the retrieved total hip prostheses had polar bearing and a diametrical clearance of 120 mm or greater between the ball and socket.4,5 Low wear has been a consistent finding with cobalt-chrome on cobalt-chrome total hip articulations. Anissian et al.6 found that the metal-on-metal hip prosthesis generates 100-fold less wear debris than metal-on-polyethylene in hip simulator studies. The combined annual linear wear rate for both first and second generation metal-on-metal articulations is reported to be from 1 to 6 mm according to implant retrieval studies.7,8,9,10 Low in vivo wear rates were measured in both the McKee-Farrar and Metasul retrievals and durability of the bearing surface was established by the study of implants retrieved from patients more than 20 years after the index operation.11 The histological response of tissues around metal-on-metal hips is different than the response of periprosthetic tissues to polyethylene wear debris.11,12 Macrophages and giant cells that are associated with osteolysis are not prevalent around retrieved metal-on-metal components.

Periprosthetic tissue specimens around revised metal-on-metal hips demonstrated fibrous tissue and little inflammation in some hips and perivascular lymphocytic infiltrates with plasma cells in others. Hypersensitivity reaction has not caused a high rate of component loosening or a high incidence of unexplained pain with the use of second-generation metal-on-metal total hip replacements.13,14,15,16 There is growing evidence that the smaller volume of wear debris generated by metal-on-metal bearing couples results in a lower incidence of osteolysis.17 Bone loss observed in association with well-fixed metal-on-metal hips has been limited to
calcar resorption from stress shielding. The radiographic findings with metal-on-metal bearings do not resemble those seen in patients with osteolysis from polyethylene debris. There is one published case report of osteolysis in a patient with a well-fixed metal-on-metal hip.

Zimmer reports that more than 250,000 of the Metasul articulations have been sold worldwide since November 1988 and eight manufacturers currently offer metal-on-metal articulations for hip replacement and surface replacement arthroplasty.

The purpose of this review is to describe causes of component loosening and describe the improvements that corrected the problem, review current in vivo wear data, provide evidence that the incidence of overall osteolysis has decreased with the use of metal-on-metal articulations, and show that hypersensitivity is not proven to be a definitive diagnosis in unusual cases of unexplained pain.

We have experience with 582 patients (619 Metasul articulations), and the majority of published data of four years or more are on this articulation couple, so the results of Metasul will be the focus of this review.

**LOOSENING**

First generation metal-on-metal THAs failed due to acetabular and femoral component loosening at a higher rate than Charnley’s prostheses. Dandy and Theodorou reported the loosening rate in 739 McKee-Farrar THRs with 3.1% for the femoral component and 4.4% for the acetabular component at 2 to 7 year follow-up. In a study of 230 McKee-Farrar prostheses, August reported 50% femoral component loosening, 51% acetabular component loosening, and 67.7% overall loosening at an average follow-up of 13.9 years. Dobbs introduced survivorship to the orthopaedic literature with a study of 273 Stanmore THRs. The Stanmore femoral component had a similar design to the McKee-Farrar and a similar poor survival rate of 53% at 11 years. Despite the similar pattern of early failure reported by each of these investigators, the cause of loosening was poorly understood.

In 1974, Peter Walker suggested that impingement was a reason for loosening and demonstrated that the neck of the femoral component made repeated contact against rim of the acetabular component. The design flaw was the large diameter femoral neck and unfavorable head/neck ratio of the McKee-Farrar, Stanmore, and similarly designed total hip prostheses. Szuszczewicz observed that metalosis, component loosening, and progressive pelvic osteolysis was caused by impingement in one patient with failed bilateral McKee-Farrar hips. During the past two decades, designers of total hip prostheses have come to understand that bearing surface damage, component loosening, and hip dislocation are all potential consequences of hip component impingement.

Second generation metal-on-metal THAs were introduced with more favorable head-neck ratios and the incidence of impingement and aseptic loosening has decreased. Second generation metal-on-metal hips do not have a high failure rate due to aseptic loosening. Recent studies with second-generation metal-on-metal prostheses show a low rate of aseptic loosening that is not higher than the rate reported with metal-on-polyethylene. Improved component design has diminished, but not eliminated impingement as a contributing factor in cases of aseptic loosening.

Inadequate diametric clearance can contribute to loosening by causing equatorial contact, high torque, and jamming. In a hip simulator wear test, Farrar et al. demonstrated that a complete seizure was observed after 20,000 cycles for the samples having a negative diametral clearance (-40 and -74 µm). Semlitsch reported the analysis of six retrieved Huggler and 11 Müller prostheses and demonstrated diametral clearance in the range 120-200 µm, with one bearing couple having a diametral clearance of 500 µm. McKellop et al. retrieved McKee-Farrar hips and reported a diametral clearance of 127-386 µm, with one outlier with an extreme clearance of 1.75 mm. None of these specimens had equatorial contact and the author is not aware of any report of retrievals with inadequate diametral clearance that caused jamming and loosening.

Jones et al. believed that cobalt toxicity was responsible for component loosening in a series of loose McKee hip arthroplasties. Willert continues to support the possibility of a lymphocyte-dominated immunological response as an uncommon cause of loosening. The experience with second-generation metal-on-metal hip prostheses suggests that if hypersensitivity is a cause of loosening, then its prevalence is low. Both first and second-generation metal-on-metal total hip replacements generate a similar volume of wear debris, but the high loosening rate that was observed with first-generation metal-on-metal hips was not been observed with the use of second-generation hips. The low loosening rates observed with second-generation metal-on-metal hips suggest that it is unlikely that the high rate of loosening with the use of first-generation implants was caused by an allergic reaction to metal debris. Better component design, including a more favorable head-neck ratio, and a decreased incidence of impingement probably contributed most to the improved loosening rates, and components designed with an unfavorable head/neck ratio are no longer used.
WEAR

Cobalt-chrome bearings demonstrate wear well below the annual linear wear of 100 µm per year that is considered to be the threshold for osteolysis. A combined annual linear wear below 10 µm has been observed in hip simulator wear tests and substantiated by analysis of retrieved first and second-generation hip replacement articulations. Wear of this magnitude cannot be measured radiographically, so assessment of wear in vivo has been done on implants obtained during revision hip surgery and on autopsy retrievals. The earliest reports of wear from metal-on-metal retrievals were anecdotal in character and based on small numbers of failed implants. Smith described eight patients revised for loosening of Gaenslen cups mated to Austin-McCormick femoral prostheses. The retrieved prostheses showed virtually no visible signs of wear and the tissues involved about the metal showed little staining, discoloration, or pathologic changes to indicate wear. Walker et al. analyzed wear of 12 retrieved McKee-Farrar prostheses using low power microscopy, scanning electron microscopy, and surface profilometry. Three types of wear were described: type 1, a surface with initial scratching, type 2, a surface in which the scratches had been smoothed or polished, and type 3, a smooth surface (after scratching) showing signs of deterioration. The depth of wear estimated by stylus profilometry was estimated to be 1 µm. When modern techniques to analyze wear were applied to retrieved first-generation implants similar low wear measurements were obtained. Jantsch et al. reported an annual linear wear of 1 µm for three McKee-Farrar hips retrieved 14 years after implantation. Using a coordinate measuring machine Schmalzreid et al. found a combined annual linear wear of 4.2 µm more than 20 years after implantation of five McKee-Farrar hips. The annual linear wear rate was below 5 µm for 11 Mckee-Farrar and for six Huggler prostheses that were implanted for an average of 11 years (range 3-20). The consistently low in vivo wear rates established by retrieval studies of first-generation metal-on-metal total hip replacements stimulated interest in reintroducing metal-on-metal as wear resistant articulation.

Second-generation metal-on-metal hip prostheses were manufactured using modern techniques in order to promote lubrication and further decrease wear. The Metasul bearing surface was manufactured as a wrought-forged, high-carbon cobalt-chrome, and the diametral clearance was approximately 100 µm. Wrought-forged cobalt chrome alloys are harder, and have better abrasive and adhesive wear characteristics than cast alloys. High-carbon cobalt-chrome (0.20-0.25% C) alloys were developed to induce a lower wear rate than a low-carbon cobalt-chrome (0.05-0.08% C) alloys. Hip simulator studies have shown that a small clearance decreases the wear of metal-on-metal bearings, but clearance must be sufficient to prevent jamming. Seiber et al. reported the wear of 118 retrievals with the Metasul articulation couple as 5 µm 3 to 8 years after implantation. Rieker et al. reported the results of 172 Metasul couples with an annual linear wear rate of 6.2 µm. Recent published reports have all shown that the annual linear wear is below 10 µm with the use of second-generation implants. Although laboratory studies indicated that the wear of second-generation metal-on-metal THRs should be lower than that of first-generation devices, retrieval analyses do not indicate superiority in this regard.

OSTEOLYSIS

Metal-on-metal articulations were reintroduced to address the emerging problem of osteolysis. August defined bone erosions adjacent to the components and/or a change in position of the McKee-Farrar components as loosening. In that study, bone erosions were not considered to be osteolysis. Using those criteria, 67.7% of the patients had radiographic evidence of loosening and none had osteolysis. In a study by Zahiri et al. of 15 hips with McKee-Farrar THAs still in place at 21 to 26 years postoperatively, only 4 of the 15 (25%) had some osteolysis. In that study, 10 periprosthetic tissue specimens were obtained from a group of 15 patients that had revision of a McKee-Farrar hip replacement. Chronic inflammation (lymphocytes, and plasma cells) was minimal to absent in all cases. Multinucleated histiocytes (foreign body-type giant cells) were mostly found along the edges of polymethylmethacrylate globules. These radiographic findings and the histological findings demonstrated that the response of the human body to metal debris from the McKee-Farrar total hip replacements could be distinguished from the response to polyethylene wear debris. Published reports with the use of second-generation metal-on-metal prostheses indicate that osteolysis is only rarely observed in association with well-fixed components. In our report of 156 patients (161 hips), only calcar resorption in nine hips (5.5%) (with no other osteolytic lesions) was observed at an average of seven years follow-up. Calcar resorption was a focal radiolucent area seen immediately beneath the collar of the femoral stem, identified by its location between the calcar cortical bone, and the medial stem. The radiographs of eight of the hips showed radiolucent lesions that had a maximum size of 2 x 2 mm. One patient had a lesion that grew to 2 x 2 cm five years after the index hip operation. Nine other recent clinical studies with
radiographic follow-up of second-generation metal-on-metal hip replacements report no osteolysis.\textsuperscript{11,14,15,23,35,40,41} Beaulé\textsuperscript{18} reported one case of osteolysis in a patient with a well-fixed, cementless, Zweymuller stem coupled with a Metasul metal-on-metal bearing. In that report, localized osteolysis was identified on the plain radiographs at the tip of the Zweymuller, Ti alloy stem. At the time of revision surgery minimal bearing surface wear was visible and there was no metallic staining of the capsule or acetabular membrane. Specimens of tissue from the hip capsule and the femur in the area of osteolysis showed only small numbers of inflammatory cells, such as macrophages and no lymphocytic infiltrations or granulomas. The authors concluded that this was not a typical case of particulate-induced osteolysis as seen with polyethylene wear debris. Joint fluid pressure within the effective joint space was implicated as the cause of the osteolytic lesion. The predominantly histiocytic inflammation with abundant giant cells that is associated with metal-on-polyethylene debris is a not observed in association metal-on-metal wear debris.

**HYPERSENSITIVITY**

Evans et al.\textsuperscript{2} were recognized as the first to draw attention to the possibility that metal toxicity occurred after total hip replacement using metal-on-metal bearings. They suggested that in certain patients, the release of metal from a prosthesis may result in tissue sensitization and that this was detected clinically by a skin patch test in which a soluble salt of the metal was used as the test object. They reported that the release of metal from prostheses in metal-sensitive patients caused obliterative changes in blood vessels supplying the bone into which the prosthesis was implanted. According to this theory, metal sensitivity caused bone necrosis and loosening of the McKee-Farrar prostheses. Jones et al.\textsuperscript{20} reported cobalt toxicity in seven patients that had failure due to aseptic loosening after McKee hip arthroplasty from nine months to four years after the index total hip replacement. Six of these patients were cobalt-positive, but nickel- and chrome-negative on patch testing. In patients with McKee-Farrar or Charnley prostheses, these authors suggested that cases of aseptic loosening were caused by sensitivity of the tissues to one of the metals in the alloy of which the prosthesis is composed. Several authors have reported on the histological appearance of periprosthetic tissues obtained from the area around early metal-on-metal joint replacements and they did not identify any lymphocytic or plasma-cell infiltration of the periprosthetic tissues.\textsuperscript{11,26,32} Wilert et al.\textsuperscript{30} analyzed tissues that had been retrieved from fourteen hips in which a contemporary metal-on-metal joint replacement had failed after an average of thirty months in vivo. The investigators found a perivascular lymphocytic infiltrate, which they suggested was similar to that found in association with a type-IV hypersensitivity reaction. The histopathological changes in the soft tissues were characterized by few wear particles and granulomas compared to tissues obtained from patients with osteolysis from polyethylene debris. Davies et al.\textsuperscript{12} also reported an unusual lymphocytic perivascular infiltration in tissues around contemporary metal-on-metal joint replacements. The lymphocytic infiltration was more pronounced in samples obtained at the time of revision for aseptic loosening than in samples retrieved at the time of autopsy or during arthrotomy for reasons other than aseptic failure. The authors did not know the prevalence or clinical implications of the findings, but suggested that they may represent a novel mode of failure for some metal-on-metal joint replacements.

The diagnosis of hypersensitivity was considered as a possible explanation for the high rate of failure of first-generation metal-on-metal total hip replacements. The low incidence of loosening or clinical symptoms reported with the use of second-generation metal-on-metal prostheses suggests that hypersensitivity is not a common problem that leads to failure and that it should only be considered a diagnosis of exclusion in a small number of patients with unexplained pain. In a study by Dorr et al.\textsuperscript{16} of 213 hips with a Metasul articulation, two patients (1%) were explored and had exchange of a metal-on-metal bearing surface with a preoperative diagnosis of hypersensitivity. Tissue and serum samples were sent to the laboratory for examination and neither patient had positive serum levels that indicated allergy to the implant. One patient had perivascular lymphocytes in only one of seven tissue samples, and the other patient had lymphocytes in four of five specimens. Neither patient had relief of pain more than one year after exchange of the metal-on-metal bearing surface for a metal-on-ceramic bearing. Pain was completely relieved in one patient two years the index hip operation following an operation for degenerative disease of the lumbar spine. The authors concluded that neither case qualified as a definitive diagnosis of hypersensitivity. There have never yet been reported cases of hypersensitivity that included a symptomatic patient, positive serologic testing for hypersensitivity, and tissue specimens that substantiated the diagnosis of a hypersensitivity reaction.

**DISCUSSION**

The clinical results of metal-on-metal have been studied for more than 40 years, including second-generation metal-on-metal results that are approaching 20 years
in Europe and 10 years in the United States. We here review the status of metal-on-metal total hip articulations based primarily on the clinical performance reported in human subjects. It is now generally accepted that the early loss of fixation observed with first-generation metal-on-metal hips was due primarily to poor component design, and this problem was corrected by improved second-generation implants designs. The combined annual linear wear rate for metal-on-metal hip replacements in vivo is well established and it has been consistently reported to be below 10 μm. Osteolysis has been a rare radiographic finding during the first 10 years of reports with the use of second-generation metal-on-metal hips. Tissue specimens demonstrate that the histological response that defines polyethylene induced osteolysis is not found in association with well-fixed metal-on-metal total hip replacements. The current diagnosis based on pathological findings of lymphocytes adjacent to blood vessels in capsules of retrievals and it is not a common cause of hip pain or component loosening.

For more than three decades, the problem of aseptic component loosening was poorly understood and several theories were proposed. The Charnley prosthesis was referred to as a low friction arthroplasty and the relatively higher friction of metal-on-metal articulations demonstrated by the pendulum that lead some investigators to suspect that high friction was the cause of early loosening. Retrieval studies that examined both first and second-generation metal-on-metal hips did not identify increased friction as a cause of failure. All metal-on-metal specimens retrieved during the past 40 years have demonstrated polar bearing. Polar bearing and increased diametral clearance have been shown in simulator studies and by retrievals to cause higher bearing surface wear rates, however, none of the retrieved couples that had a wide diametral clearance failed as a direct result of excessive wear. The optimal diametral clearance for total hip replacement articulations is reported to be between 50 and 100 μm. Retrieved specimens with diametral clearances greater than 100 μm demonstrated more wear than couples with smaller clearance, however, combined annual linear wear was still below 10 μm. It is now generally accepted that the high rate of early loosening observed with first-generation total hip replacements was not due to clamping or jamming of the articulation couple. The problem of early metal-on-metal component loosening was corrected when implants were redesigned. The low wear of metal-on-metal articulations was established both in vitro and in vivo. There are no reports of catastrophic failure or wear-through. Based on the published annual linear wear rates established for metal-on-metal, a well-fixed hip replacement could function in an active patient for more than thirty years without wearing out. Attention has turned away from the problems of early failure due to loosening or late failure due to wear. The focus today is on evaluating potential problems that might occur as the result of metal-on-metal wear debris and metal ions. It is well established that small cobalt and chromium particles and ions are generated by the metal-on-metal bearing surface, widely distributed throughout the body through the bloodstream and the lymphatics, and excreted in the urine. Serum, blood, and urine samples consistently demonstrate elevated levels of chromium and cobalt compared to the levels measured in patients with metal-on-polyethylene implants. The clinical significance of these elevated ion levels is unknown. Long-term follow-up of patients with first generation metal-on-metal total hip replacements, and short-term follow-up of patients with second-generation metal-on-metal implants have not demonstrated any unique complications. In spite of the concerns of some authors that complications such as cancer or hypersensitivity would occur, currently none have been reported clinically. It is likely that large, long-term, multi-center studies will be necessary to identify any increased risk of local or systemic disease caused by the use of metal-on-metal bearing surfaces for total hip replacement.

There is no radiographic evidence the wear debris being produced at the metal-on-metal interface leads to the occurrence of osteolysis. In the author's study of 161 total hip arthroplasties (154 patients), the only bone erosion that was measured was calcar resorption. It was not possible to determine whether this calcar resorption was from stress shielding or particulate debris. Other authors have not classified calcar resorption as osteolysis. Small focal radiolucent areas that were seen under the collar of 9 out of 161 hips were not considered in the definition of osteolysis. Malone et al. defined relatively small punched-out areas of bone loss under the collar as typical zone 7 osteolytic lesions. Goetz's description of osteolysis included only those lesions that caused scalloping of the endosteal cortex. These findings are in agreement with other authors who have reported cementless metal-on-metal hip arthroplasty without any osteolysis at five and six year follow-up. Longer follow-up is necessary to determine if the low incidence of osteolysis will continue beyond the first decade. The Metasul articulation has been implanted in patients in Europe since 1988. The author is not aware of any reports of the incidence osteolysis. Hypersensitivity has been suggested as a possible unique complication and cause of failure for metal-on-metal hip arthroplasties. Hypersensitivity is a diagnosis described by Willert, based on the occurrence of lymphocytes adjacent to blood vessels in capsules of
retrievals from failed metal-on-metal hip arthroplas-
ties. Hallab et al. described a triple assay technique
for the evaluation of metal induced, delayed type hy-
persensitivity responses in patients with total joint ar-
throplasty. The most conclusive result using this assay
would be a strongly positive response to all three as-
pects of the triple assay technique to both cobalt and
cromium ions. To our knowledge, there have been no
reports of unexplained pain associated with radiographic
evidence of implant loosening, supported by a positive
response to the triple assay technique. Reports with the
use of second-generation metal-on-metal prostheses in-
dicate that unexplained pain occurs only rarely and loose
prostheses are uncommon and therefore the diagnosis
of hypersensitivity as a clinical problem remains elu-
sive.

The potential for permanent biological fixation with
noncemented components, combined with a bearing
surface that does not fail due to wear or osteolysis,
makes it conceivable that total hip replacements im-
plants could survive in active patients for more than 30
years. If the clinical results are as good as metal-on-
polyethylene articulations, the mechanical complications
are no greater, and there is no observed increased inci-
dence of adverse biological reactions, then continued
use of metal-on-metal articulation couples is justified.

REFERENCES