Total hip arthroplasty (THA) has been performed for nearly 50 years. Between 2006 and 2012, more than 600,000 metal-on-metal THA procedures were performed in the United States. This article reviews the production of metal wear debris in a metal-on-metal articulation and the interaction of cobalt and chromium ions that ultimately led to a dramatic decline in the use of metal-on-metal THA articulations. Additionally, the article reviews mechanisms of metal wear, the biologic reaction to cobalt and chromium ions, the clinical presentation of failing metal-on-metal articulations, and current diagnostic strategies. Further, the article discusses the use of inflammatory markers, metal ion levels, radiographs, metal artifact reduction sequence magnetic resonance imaging, and ultrasound for failed metal-on-metal THA procedures. When adopting new technologies, orthopedic surgeons must weigh the potential increased benefits against the possibility of new mechanisms of failure. Metal-on-metal bearings are a prime example of the give and take between innovation and clinical results, especially in the setting of an already successful procedure such as THA. [Orthopedics. 2016; 39(6):371-379.]
ever, failures as a result of osteolysis and aseptic loosening persist. The metal-on-metal polyethylene articulation itself was producing polyethylene wear particles. These particles created osteolysis through a biological reaction mediated by receptor activator of nuclear factor κ-B kinase and receptor activator of nuclear factor κ-B ligand. The increased enthusiasm for the metal-on-metal bearing couple was founded on the principle of decreasing the amount of wear debris and eliminating osteolysis to increase implant longevity. Wear simulator data suggested that the volumetric wear of metal-on-metal bearing couples was more than 100-fold lower than that of metal-on-polyethylene bearing couples. This led to the conclusion that “metal implants seem to be worth considering in patients with long life expectancy.” Between 2006 and 2012, more than 600,000 metal-on-metal THA procedures were performed in the United States alone, with a peak in 2008, in which 40% of all primary THA procedures performed in the United States were metal-on-metal procedures. A dramatic decline in metal-on-metal THA procedures occurred after the US Food and Drug Administration recalled the Durom acetabular component (Zimmer, Warsaw, Indiana) in 2008 as well as the ASR Hip Resurfacing System and the ASR XL Acetabular System (DePuy, Warsaw, Indiana) in 2010. By 2012, the percentage of metal-on-metal THA procedures had plummeted to approximately 10% of all primary THA procedures performed in the United States.

Reported failure rates for metal-on-metal THA procedures are higher than those for other THA bearing surfaces, and the incidence of revision THA ranges from 1% to 29%, depending on the prosthesis type. Therefore, in patients undergoing metal-on-metal THA procedures, monitoring for adverse reactions or implant failure is recommended. Physicians must understand the management of metal-on-metal THA along with the underlying mechanisms of wear and the potential pathology. This article discusses the tribology, clinical manifestations, evaluation, and diagnosis of metal wear in THA.

**COMPOSITION OF METAL BEARING COUPLES**

The alloy (ASTM F75, ISO 5832-4) used to manufacture metal-on-metal bearing couples consists of 62% cobalt, 27% to 30% chromium, 5% to 7% molybdenum, and small amounts (≤1%) of nickel, iron, silicon, carbon, and manganese. Alloys with more than 0.2% carbon offer superior wear resistance compared with alloys with less than 0.08% carbon. Additionally, the way in which an alloy is processed into the final implant affects its wear characteristics. Cast or formed implants have superior wear resistance compared with wrought or shaped implants.

**PRODUCTION OF METAL DEBRIS**

There are numerous modes for wear, including adhesive, abrasive, third body, fatigue, and corrosion. In the case of metal-on-metal THA, adhesive wear predominates, although incorrect implant positioning leads to additional wear.

After initial placement of a metal-on-metal articulation, “bedding-in” occurs, with high wear conditions and particle production. During this time, the metal head wears into the metal acetabular liner until an “optimal contact area” develops, at which point the wear rate reduces as contact stress decreases and lubrication conditions improve. The bedding-in period lasts for the first million cycles in wear simulation or the first year after implantation in vivo. The amount of wear produced during the bedding-in period is dependent on radial clearance and sphericity, with more radial clearance and less sphericity increasing the rate of wear during the bedding-in period. Surface finish may also affect bedding-in, but metal bearings tend to self-polish over time.

The bedding-in period is followed by a much lower steady-state wear rate that continues for the life of the implant. The transition from the bedding-in period to the steady-state phase is a change in the mode of lubrication and friction for a metal-on-metal articulation from a relatively high-friction boundary lubrication phase to a relatively low-friction fluid-film lubrication phase. Steady-state wear is directly related to femoral head size. Although linear wear can be reduced by increasing the size of the femoral head, volumetric wear increases linearly. A 36-mm femoral head has nearly double the volumetric wear of an 18-mm femoral head.

Further, the amount and the location of the bearing contact area correlate with wear. The most effective type of bearing contact is a polar bearing. A polar bearing leads to proper bedding-in and steady-state wear, as described earlier. Acetabular component abduction/inclination greater than 50° increases edge loading and leads to a statistically higher volumetric wear rate. Lack of a fluid-film lubrication phase increases adhesive wear. Less than hemispherical acetabular components (ie, the component encompasses less than 180° of the theoretical sphere that predicts its diameter) are predisposed to being placed in excess abduction/inclination and on average produce higher serum metal ion levels. An equatorial bearing is created when a thin-walled monoblock acetabular component is deformed during insertion into underreamed acetabular bone. A complete lack of radial clearance leads to a total contact bearing. Both equatorial and total contact bearings lead to friction, seizing, and massively increased wear.

Corrosion plays a central role in metal ion production. Corrosion and wear act synergistically, leading to even greater metal breakdown in the presence of proteinaceous solutions. Tribocorrosion involves a variety of corrosive interactions,
including fretting, crevice corrosion, and galvanic corrosion. Tribocorrosion occurs during fluid-film lubrication, even when the metal components are not in contact. Tribocorrosion is the irreversible transformation of a material as a result of the simultaneous action of corrosion and wear that takes place in a sliding tribologic contact area. In the case of metal-on-metal articulations, the 2 metal surfaces and synovial fluid react to form a tribomaterial. This material has an acidic nanocrystalline structure and consists of metallic and organic constituents that are liberated into surrounding soft tissues. Damage to the surface oxide layer increases the susceptibility of the metal-on-metal articulation to metal ion release. Corrosion is not exclusive to metal-on-metal articulations and can occur at any modular segment, including the head-neck junction, and it leads to a similar presentation in metal-on-polyethylene articulations.

**Composition of Metal Wear Particles**

The principal advantage of metal-on-metal articulations is the production of fewer wear particles, leading to reduced osteolysis and aseptic loosening. Overall, the linear wear rate of a metal-on-metal articulation is 20 to 180 times lower than that of a metal-on-polyethylene articulation. This is equivalent to more than a 100-fold decrease in volumetric wear.

Metal particles are fundamentally different from polyethylene particles. Metal particles are round to oval, with irregular boundaries, and polyethylene particles are mostly granular or ellipsoidal. Metal particles are 10 times denser than polyethylene particles, approximately 9 g/cm³ and 0.9 g/cm³, respectively. The mean size of a metal particle is quite small, less than 50 nm in vitro and 20 to 80 nm in vivo. Polyethylene particles have a mean size of approximately 1000 nm (1 μm). Therefore, 1×10⁶ metal particles are generated per 1 mm³ volumetric wear of a metal-on-metal articulation, and 1×10¹³ polyethylene particles are generated per 1 mm³ volumetric wear of a metal-on-polyethylene articulation. Clearly, the fundamental premise that metal-on-metal bearing couples could decrease the number of wear particles and decrease wear-related complications was conceptually flawed. Metal-on-metal articulations produce more and smaller particles, creating more surface area per mass of particle than metal-on-polyethylene articulations.

Although metal-on-metal articulations generally produce smaller wear particles, larger, more irregular metal particles promote inflammation and tissue damage. Specifically, phagocytosis of large, irregular particles leads to lysosome destabilization in macrophages and cathepsin B-mediated production of interleukin-1β. This is followed by inflammation and cytokine release along with indirect promotion of osteoclast activity and osteolysis. Phagocytosis of small, round particles does not cause activation of this pathway. Thus, the balance between particle size and particle number in metal-on-metal articulations may lead to differing clinical outcomes.

**Figure 1:** A polar bearing leads to proper bedding-in and low steady-state wear as well as fluid-film lubrication (A). Increasing acetabular component abduction/inclination results in edge loading and prevents fluid-film lubrication, increasing adhesive wear (B). An equatorial bearing is created when a thin-walled monoblock acetabular component is deformed at the rim, resulting in friction, seizing, and increased wear (C). A total contact bearing is created when there is no radial clearance, resulting in friction, seizing, and increased wear (D). Black arrows indicate the area of contact between the metal head and the acetabular component. Green and red arrows indicate the clearance available for fluid ingress and egress to establish fluid-film lubrication.
Tribomaterials involve ionic and particulate cobalt and chromium. The relationship and the effects of these 2 forms are unclear. Metal particles are found more frequently in local tissue, whereas metal ions circulate throughout the body and are found in a variety of organs. Metal ions also conjugate with other molecules. Cobalt and chromium also have different ionic qualities. Chromium is less soluble and more likely to be phagocytosed, and cobalt is more soluble in serum and is found in greater concentrations in tissue and blood.

**Biology of Metal Wear Debris**

Cobalt and chromium ions are considered toxic at high concentrations, and ionic valence plays an important role in the degree of toxicity. Specifically, Cr⁶⁺ causes pulmonary epithelial cancer after inhalation, whereas Cr³⁺ is much more innocuous and is the ion that is released from orthopedic implants. Cobalt, however, is considerably more toxic, with systemic effects in metal-on-metal THA implants that include severe neurologic and cardiac manifestations. Overall, cobalt and chromium particles pose 3 main threats to human cells: genotoxicity, cytotoxicity, and hypersensitivity.

Although both cobalt and chromium are genotoxic, chromium is slightly more toxic than cobalt. The DNA damage is induced via oxidation. Additionally, cobalt and chromium inhibit DNA repair and cobalt inhibits topoisomerase II. In patients with a metal-on-metal implant, the leukocytes show a significant increase in the number of chromosomal translocations and aneuploidy cells compared with those in patients without a metal-on-metal implant. Even at concentrations considered “subtoxic,” cobalt and chromium nanoparticles and ions can cause significant DNA damage. However, the clinical significance of genotoxicity is unknown. A Finnish cohort study showed no increase in the incidence of any type of cancer in patients with metal-on-metal bearings. The mortality rate in patients with metal-on-metal articulation is equivalent to that in the general population.

Cobalt and chromium particles are cytotoxic, but cobalt is significantly more cytotoxic than chromium. Cobalt causes greater macrophage and lymphocyte death at lower concentrations. Cobalt induces a hypoxic-like state, with greater oxidative stress and upregulation of hypoxia-regulated gene products. Neither cobalt nor chromium inhibits osteoblast activity. In vitro, cobalt and chromium particles generated with a wear simulator reduced the viability of histocytes and fibroblasts by 97% and 95%, respectively. In sharp contrast, alumina ceramic particles decreased the viability of histocytes by only 18%, with no effect on the viability of fibroblasts. A retrieval study supported these results and found a tumoral calcinosis-like reaction along with necrosis and necrobiosis in histocytes that had taken up metal debris surrounding metal-on-metal implants.

Hypersensitivity is an overreaction of a specific immune system to an allergen. On the skin, this reaction is characterized by the “wheel and flare.” Metal hypersensitivity is a well-known and common condition, affecting approximately 10% to 15% of the general population. Nickel, which is used in cobalt-chromium alloys that are used to make metal implants, is the most common and potent immunologic sensitizing metal, followed by cobalt and chromium. Metal ions themselves are too small to arouse an immune response. These ions react with protein carriers, such as albumin, to denature the protein and form a hapten (ie, the complex between the metal ion and the carrier). Haptenes are antigens and are large enough to create a robust immune response.

Those who are sensitive to nickel often have cross-reactivity with cobalt and chromium. Patients who react to a hapten, such as chromium-albumin or cobalt-albumin, are actually eliciting an allergic response to the denatured carrier, in this case, albumin. Nickel, cobalt, and chromium denature carrier proteins in similar ways, and hence cross-reactivity occurs. Significantly, a higher incidence of sensitivity to nickel has been noted in patients with metal-on-metal THA procedures compared with control subjects, as quantified by lymphocyte transformation testing, although metal-on-metal THA function was independent of nickel hypersensitivity. Interestingly, the risk of revision THA is independent of metal hypersensitivity.

In those with hypersensitivity to nickel, cobalt, or chromium, a cell-mediated type IV hypersensitivity reaction occurs when small nickel, cobalt, and chromium particles form immunoreactive haptenes. The CD4⁺ T-lymphocytes are presented with a hapten through their interaction with a major histocompatibility complex class II molecule on an antigen-presenting cell, such as a macrophage. The hapten-sensitized CD4⁺ T-lymphocytes release interferon-γ. Interferon-γ activates macrophages that secrete various cytokines (granulocyte/macrophage-colony stimulating factor, tumor necrosis factor, and interleukins) and recruit cytotoxic T-lymphocytes involved in the cell-mediated type IV hypersensitivity reaction.

**Adverse Clinical Reactions to Metal Wear Debris**

Adverse reactions to metal debris and adverse local tissue reactions are clinical manifestations that occur as a result of metal wear debris. It is unknown how adverse reactions to metal debris and adverse local tissue reactions correlate with the biologic issues of genotoxicity, cytotoxicity, and hypersensitivity described earlier. Metal allergies are much more common in patients who undergo joint replacement than in the general population of those without an implant. This percentage is even higher in patients with a poorly functioning, painful metal-on-metal articulation. However, a study performed in Italy showed no proven cause-and-effect
relationship between immunosensitization and poor clinical outcomes. The umbrella of adverse reactions to metal debris and adverse local tissue reactions includes 2 major subgroups, soft tissue reactions and osteolysis (Figure 2).

Soft tissue reactions are also described as aseptic lymphocyte-dominated vasculitis-associated lesions. This is a histologic diagnosis that has been used to describe the clinical appearance of soft tissue necrosis and abnormal joint fluid at the time of revision. Willert et al. took tissue samples at the time of revision surgery in patients with metal-on-metal implants who had persistent or early recurrence of preoperative symptoms and found diffuse perivascular infiltrates of T- and B-lymphocytes along with plasma cells and an accumulation of macrophages with or without metal debris (Figure 3). Notably, tissues with aseptic lymphocyte-dominated vasculitis-associated lesions that contain lymphocytes have a significantly higher mean metal content than aseptic lymphocyte-dominated vasculitis-associated lesion-like tissues that contain macrophages.

Pandit et al. coined the term “pseudotumor” to describe large cystic lesions first noted in patients who had undergone metal-on-metal hip resurfacing. The histology of these lesions is similar to that described by Willert et al., although the lymphocytic infiltrate was much more diffuse and tissue necrosis was much more extensive. Pseudotumors can be quite large and have a varied presentation, including pain, nerve palsy, spontaneous dislocation, and a palpable mass. Since Pandit et al. first coined the term, pseudotumors have been noted not only in patients with metal-on-metal hip resurfacing but also in those with metal-on-metal THA implants and even metal-on-polyethylene THA implants. The prevalence of these lesions varies, with rates as high as 32% to 61% in asymptomatic patients after metal-on-metal THA. In some cases, the tumor is so large and destructive that a constrained liner is necessary at revision because of disruption of the abductors and surrounding soft tissue (Figure 4). Pseudotumors and elevated metal ion levels correlate with poor function.

Osteolysis is loss of bone caused by receptor activator of nuclear factor κ-B kinase and receptor activator of nuclear factor κ-B kinase ligand–dependent osteoclast resorption of bone. It can be seen on plain radiographs as cystic lesions or radiolucent regions near the femoral and acetabular components. Histologic findings in patients with failed metal-on-metal implants as a result of osteolysis and aseptic loosening are similar to those in aseptic lymphocyte-dominated vasculitis-associated lesions. Perivascular lymphoplasmacytic infiltrates and metal debris were seen in multiple studies, pointing to osteolysis as the bony continuum of the soft tissue manifestations of aseptic lymphocyte-dominated vasculitis-associated lesions.

### Presentation, Diagnosis, and Treatment

Algorithms created by the Hip Society provide a good framework for a system-
atic evaluation of painful metal-on-metal articulation of the junction. Physical examination and a thorough history are essential in the workup of painful metal-on-metal articulation of the junction. Patients who have a symptomatic metal-on-metal articulation present with hip or groin pain. Persistent pain or early recurrence of preoperative symptoms suggests infection or adverse reactions to metal markers or adverse local tissue reactions. Patients also may present with a palpable mass or fluid collection near the hip, with or without loss of hip abduction. Catching, locking, or crepitus is also common, so it is imperative to assess hip range of motion. Nerve palsies are uncommon, but assessing the neurovascular status of the limb is essential in any musculoskeletal examination.

Physicians treating patients who have a symptomatic metal-on-metal implant must perform a thorough history and physical examination and obtain anteroposterior and lateral radiographs of the hip. Infection should be considered, and appropriate laboratory markers must be evaluated. Because serum erythrocyte sedimentation rate, C-reactive protein level, and synovial white blood cell count can be falsely elevated in patients with metal-on-metal bearings, these tests have poor predictive value. In these cases, a synovial neutrophil percentage is recommend, and a level greater than 80% is highly accurate in the diagnosis of infection.

Serum ion concentrations of cobalt and chromium are used for screening and diagnosis, although research has shown mixed results. A retrospective study evaluated the relationship of serum cobalt and chromium ion levels and their sensitivity and specificity in predicting failure of metal-on-metal articulations. A cutoff value of 7 parts per billion (ppb), set by the Medicines and Healthcare Products Regulatory Agency in 2010, had specificity of 89% and sensitivity of 52% in detecting preoperative unexplained failed metal-on-metal articulation in patients with normal imaging results. However, the optimal cutoff value for serum cobalt and chromium levels was 5 ppb, with specificity of 63% and sensitivity of 85%. High serum cobalt and chromium ion levels correlate with poor implant positioning, specifically, abduction/inclination angle greater than 55° and anteversion less than 5° or greater than 25°. These data support the association of implant malposition, wear, and failure. Hence, implant malposition or an elevated serum cobalt or chromium ion level necessitates revision because implant failure is occurring in the symptomatic patient and implant failure is impending in the asymptomatic patient. Langton et al showed that cobalt and chromium concentrations were indicators of the performance of metal-on-metal implants. Sidaginamale et al also found cobalt to be more reliable compared with chromium and whole blood testing to be a quicker, more accurate representation of systemic exposure compared with serum levels.

If serum metal ion levels are elevated, radiographs should be evaluated for osteolysis and inappropriate component position. If either is found, then revision THA should be strongly considered. If the patient does not have osteolysis and the components are appropriately oriented, careful monitoring of serum metal ion levels every 6 months is recommended. In the asymptomatic patient, the track record of the implant also should be considered.

Data conflict regarding head size in relation to metal ion production. Some studies found no relationship between femoral head size and serum metal ion levels in metal-on-metal THA, although others showed increased serum metal ion levels with 28-mm femoral heads compared with 36-mm femoral heads in metal-on-metal THA. Registry data from Australia showed an increased failure rate for metal-on-metal THA implants with a femoral head size greater than 32 mm. Modular metal-on-polyethylene THA implants with 36-mm heads have greater corrosion damage to the trunnion compared with 28-mm heads. Metal ion production is increased in metal-on-metal THA implants with large femoral heads and short taper lengths.

The finding of fluid or a soft tissue mass is a strong indication for revision THA. Although measurement of serum metal ion levels is an important part of the standard diagnostic algorithm, as discussed earlier, serum metal ion levels are poor predictors of soft tissue damage. In the setting of adverse reactions to metal debris or adverse local tissue reactions and pseudotumor formation, magnetic resonance imaging (MRI) has emerged as a powerful diagnostic tool. The amount of artifact from the implant on a traditional MRI scan is significant. Adjusting the matrix and receiver bandwidth of a clinical MRI scan can reduce 90% of the metal artifact from


THA.97 These alterations to a traditional MRI scan produce metal artifact reduction sequence MRI.

With the use of metal artifact reduction sequence MRI, prospective evaluation of 31 patients with painful metal-on-metal implants found that fluid collections and severe muscle atrophy were the most likely findings, in addition to muscle edema. Metal artifact reduction sequence MRI is useful in diagnosing and monitoring at-risk metal-on-metal THA implants.98 A case-control study showed that although fluid collection, or pseudotumors, could readily be found in patients with metal-on-metal implants, no difference was noted in those with a well-functioning implant vs those with a painful implant. This result called into question the importance of the finding on metal artifact reduction sequence MRI.99 Similar results have been reported in the radiology literature, where conventional sequences with 1.5-Tesla clinical imaging showed no correlation between pseudotumor and patient pain.99

A Japanese study on the benefit of ultrasound as a cost-effective means of detecting soft tissue changes surrounding metal-on-metal implants showed promise.100 Hence, a complex cyst or mass (large, heterogeneous, and irregularly shaped) on metal artifact reduction sequence MRI or ultrasound necessitates revision. This finding indicates that implant failure is occurring in the symptomatic patient and that implant failure is impending in the asymptomatic patient.

Observation should be considered only in asymptomatic patients with serum cobalt and chromium ion levels less than 5 ppb, with or without a simple cyst on metal artifact reduction sequence MRI or ultrasound. Yearly observation is suggested because cyst progression has not been observed earlier than 6 months with metal artifact reduction sequence MRI or ultrasound studies.

**Conclusion**

Metal-on-metal bearings are a prime example of how a new technology and its potential benefits must be weighed against the possibility of new mechanisms of failure. Metal particles have the potential for genotoxicity, cytotoxicity, and hypersensitivity, but more importantly, they produce adverse reactions to metal debris or adverse local tissue reactions. Patients with metal-on-metal bearings must be monitored closely with physical examination, serum ion measurement, and imaging for pain and complications specific to metal-on-metal implants, specifically, osteolysis and pseudotumor formation.

**REFERENCES**


