Evaluation of Metal-on-Metal Wear of Orthopedic Implants — Role of Serum Chromium and Cobalt Analysis

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Total hip replacement is a successful treatment for advanced joint disease; more than 1 million total hip replacements are surgically inserted world-wide each year. Wear of the plastic in hip replacement has traditionally been the limitation in the durability of these implants, especially in young patients. Improved bearing surfaces such as ceramic-on-ceramic and metal-on-metal were therefore brought into the market with the expectation that these could be used in younger more active individuals and wear would no longer be an issue. Metal-on-metal (MoM) hip replacements specifically have the advantage of increased toughness, decreased wear, and larger head sizes could be used, which wear better than smaller heads, and in turn lower the risk of dislocation. While these patients benefit from joint replacement with improved mobility and quality of life, implant-specific local and systemic adverse effects due to either a hypersensitivity to the metal or hyperreactivity due to the wear of MoM surfaces affect a small number of implant recipients. Metal implants wear due to continuous motion at the MoM surfaces, resulting in release of micro-particles into the surrounding tissues. These micro-particles can corrode, resulting in the release of metal ions into the systemic circulation.

Patients experiencing joint pain after an MoM hip replacement should be evaluated appropriately. The majority of failures associated with MoM implants are not necessarily due to the bearing surface itself, and therefore an evaluation should be carried out to rule out implant loosening and infection. Pain is a characteristic symptom. Patients can experience groin or buttock pain, and in select patients with pseudotumors, a fluid-filled collection can be present around the lateral aspect of the hip. Flexion around the hip from activities such as going up stairs or sliding into a car are particularly painful and may point towards iliopsoas irritation or impingement, which is commonly seen with these implants. Patients with pain should undergo evaluation with an anteroposterior pelvis and a lateral radiograph and should get screening blood work including a complete blood cell count with differential, sedimentation rate, and C-reactive protein level as a baseline to rule out infection. If these tests are elevated the hip should be aspirated. Once infection is ruled out and adverse reaction to metal debris is suspected, then cobalt and chromium serum concentrations and an ultrasound or magnetic resonance imaging of the hip with metal suppression is performed to rule out the presence of pseudotumor. The term most accepted today for this phenomenon around MoM hip arthroplasty is ARMD (adverse reaction to metal debris).

Orthopedic implants are created from various metal alloys. Porous titanium (Ti) is frequently employed in the acetabular cup or stem to facilitate osteointegration; a porous titanium surface allows bone to grow into the implant, creating a strong bond between bone and the implant. The articular interface, the ball and socket joint where motion occurs, is usually made from very hard alloys comprised of various combinations of aluminum (Al), chromium (Cr), cobalt (Co), iron (Fe), magnesium (Mg), molybdenum (Mo), nickel (Ni), and/or vanadium (V); the most commonly used alloy is comprised of Co and Cr. These hard alloys allow for smooth motion and facilitate great weight bearing required of a successful joint.
A number of abstracts, peer-reviewed articles, and reviews (4-9) report that the degree of MoM wear can be assessed by evaluation of serum chromium and cobalt concentration. Chao (4) reported increased Al, Co, Cr, Mo, Ti, and V in serum proportional to the surface area of the implant in human subjects. Jacobs (5) was first to report in a peer reviewed paper that serum Co and Cr increased with the duration of implant. Lhotka (6) reported on a long-term evaluation of a large number of subjects, demonstrating in a large population that whole blood Co and Cr concentration increased with duration of MoM implant in all patients examined. Liu (7) reported a correlation between blood concentration of Co and Cr and implant loosening. Keegan (8) provided a lengthy review comparing the clinical findings associated with metal exposure in steel workers and implant patients, observing that: 1) the inflammatory response observed in deteriorating implants is caused by macrophage accumulation and the usual release of inflammatory regulators in tissues surrounding the implant in response to accumulating debris; 2) this inflammatory response results in ulceration and tissue necrosis; 3) these findings are similar in steel industry-related lung exposure and orthopedic implant-related exposure to Co-Cr particles. Keegan also observed that: 4) Co-Cr particle size and Cr species (Cr+6 vs Cr+3) differentiates the exposure observed in steel industry-related exposure from orthopedic implant-related exposure; and 5) steel industry-related exposure involves higher level acute exposure while orthopedic implant-related exposure is associated with low level, continuous exposure. Keegan concluded that health care providers could not associate clinical findings in steel industry-related exposure to orthopedic implant-related exposure. Steel industry-related exposure involves exposure to highly toxic Cr+6, whereas orthopedic implant-related exposure is to the essential element Cr+3. Madathil (9) reported similar findings, and De Hann (10) has shown the relationship between abduction cup angle and metal ion concentrations. Patients who experienced edge loading, with smaller sized cups placed at greater than 55 degrees of abduction, had higher metal ion concentration than those who did not.

DeSmet (11) provided well-founded data relating serum and joint synovial fluid concentrations to orthopedic implant status. Joint fluid concentrations of metal ions were at least an order of magnitude higher than those measured in the serum. The median ratio of the joint fluid Cr concentration to the serum Cr concentration was 47.4 (range, 10.5 to 394.4) and the median ratio of the joint fluid Co concentration to the serum Co concentration was 36.5 (range, 8.3 to 699.1). Relating measurements of MoM wear, the median serum Cr and Co concentrations in the patients with MoM wear were approximately ten times higher than those in the patients without MoM wear (p < 0.001). The median joint fluid Cr concentration was 28 times higher and the median joint fluid Co concentration was 20 times higher in the patients with MoM wear (p = 0.001). Femoral component wear in the patients with positive indices of MoM wear was approximately five times greater than in the patients without measureable MoM wear (p = 0.002). Joint fluid Co and Cr concentrations correlated with serum Co and Cr concentrations,
although when compared to serum Co and Cr concentrations, there was greater overlap in joint fluid Co and Cr concentration between patients with MoM wear and those without. These findings are summarized graphically below.

Figure 1. Differences in serum and joint fluid metal-ion concentrations and femoral component wear between the patients with and those without metallosis found at revision. The interquartile range is shown as a box, containing a horizontal line indicating the median. The error bars indicate the extreme values within 1.5 times the interquartile range, and the plus symbols indicate outliers. Used with permission from De Smet K et al. Metal ion measurement as a diagnostic tool to identify problems with metal-on-metal hip resurfacing. J Bone Joint Surg Am. 2008;90:202-208. [jbjs.org]

Kwon and colleagues (12) have extensively studied the relationship between metal-on-metal bearings and pseudotumor, a periprosthetic tissue mass with histologic findings also referred to as an aseptic lymphocyte dominated vasculitis-associated lesion (ALVAL)(13), finding that evaluation of enhanced lymphocyte reaction to MoM was highly variable and possibly more related to Ni sensitivity than actual MoM wear. They also found that elevated serum Co and Cr were most closely associated with pseudotumor.
Tower (14) provided a case report of two patients (one of the patients was the author himself) requiring joint replacement. Serum Co and Cr correlated with the degree of tissue degradation observed during replacement surgery, but joint fluid Co and Cr varied by an order of magnitude between patients.

Collation of data from the above reports provides some guidance regarding what serum Co and Cr concentrations indicate in the context of an orthopedic implant evaluation.
Serum Co and Cr are recommended as the optimal tests for evaluation of implant wear; the majority of peer reviewed clinical correlation studies report serum values. All patients with an orthopedic implant will have Co and Cr concentration higher than unexposed (ie, no implant) individuals. Patients symptomatic for implant wear with serum Co >10 ng/mL and serum Cr >15 ng/mL are likely to have significant implant deterioration. Some laboratories offer whole blood testing for Co and Cr. Unfortunately, all peer reviewed work relating ARMD to Co and Cr concentrations was performed using serum for evaluation. The only evaluation relating blood Co and Cr to implant deterioration (7) correlated Co and Cr with implant loosening. So far, only De Smet (11) has documented a relationship between MoM-related wear, tissue damage, and elevated synovial fluid Co and Cr. While this work is well founded, until it is corroborated by others, synovial fluid analysis remains a research tool.

Based on personal experience, and corroborated by observations of others (6,7), serum Co and Cr are highest in the first year after implant. In subsequent years, and with run-in wear, Co and Cr decline, then reach steady state around 3 years after implant. This is important when evaluating patients, especially those who are asymptomatic. It would be advisable to repeat serum Co and Cr serum at 6 months to a year later and see if Co and Cr have dropped before recommending revision.

Collection of uncompromised specimens for Co and Cr testing is difficult (15,16). Most specimen collection products contain Co and Cr in the rubber stopper or O-rings to add plasticity to the rubber. Special rubber was created to manufacture evacuated blood collection tubes suitable for use in trace metal testing. Also, our environment contains high Cr concentrations; airborne dust contains Cr as concentrations 10,000 times more than the Cr concentration in blood. Plastic syringes with black rubber plunger seals commonly used in specimen collection are particularly problematic because the black rubber contains high concentrations of Co and Cr. Attention to detail during specimen collection is essential to achieve successful and clinically valid testing. Avoid use of syringes with black rubber plunger seals, and only use blood collection tubes that are FDA approved for trace metal testing.
References


