Cobalt and Chromium Measurement in Patients with Metal Hip Prostheses

Moderators: Mathew P. Estey1 and Eleftherios P. Diamandis1*
Experts: Catherine Van Der Straeten,2 Stephen S. Tower,3 Alister J. Hart,4 and Thomas P. Moyer5

Approximately 1 million metal-on-metal (MoM)6 hip prostheses have been implanted worldwide to alleviate pain, restore hip function, and improve overall quality of life. These implants contain femoral and acetabular bearing surfaces that are typically composed predominantly of cobalt (Co) and chromium (Cr). Although the majority of MoM hip replacements have been successful, multiple recent reports have documented markedly increased Co and Cr concentrations in the joint synovial fluid, periprosthetic tissue, blood, and even peripheral tissues of some patients with MoM hip prostheses. Consequently, concerns have been raised about the physiological consequences of metal release from MoM hip prostheses into the periprosthetic tissue and systemic circulation.

Co and Cr concentrations in the serum and hip joint fluid correlate with the degree of MoM implant wear and are increased in individuals with an accumulation of metal debris in the periprosthetic tissue. Therefore, some scientists have suggested that Co and Cr concentrations be routinely measured during the management of patients with MoM hip prostheses. In this Q&A article, 4 experts provide their opinions on the use of MoM hip prostheses, the adverse biological consequences of metal release, and the clinical utility of Co and Cr measurements. They also discuss the methodology used to assess the concentration of these metal ions and provide insight into the many challenges associated with Co and Cr measurement.

What are the advantages of MoM hip prostheses over other types of implants?

Catherine Van Der Straeten: MoM was reintroduced as a bearing surface for hip arthroplasty to solve the problem of particle-induced osteolysis secondary to polyethylene wear. In vitro hip-simulator studies demonstrated much less volumetric wear and much smaller particles with MoM compared to metal-on-polyethylene (MoP). This finding was confirmed in vivo with high-carbon alloy MoM 28-mm and 32-mm total hip arthroplasty (THA). The use of larger-diameter femoral heads (≥36 mm) as a solution to postoperative dislocation became possible with alternative bearings [MoM, ceramic-on-ceramic (CoC)] with less apparent wear compared to MoP. Larger heads have effectively reduced the dislocation rate.

MoM hip-resurfacing arthroplasty (HRA) was reintroduced to address the inferior survivorship and unsatisfactory clinical results with THA in young and active patients. The anatomical reconstruction of the joint has proved to lead to a better function and higher activity levels compared to THA. Despite the bad results with certain HRA designs, independent series and arthroplasty registries have demonstrated a better survivorship of good hip-resurfacing designs, such as the Birmingham Hip Resurfacing System (BHR) (Smith & Nephew), compared to THA, especially in young and active males.

1 Mount Sinai Hospital, Toronto, Ontario, Canada; 2 St.-Martens-Latem, Belgium; 3 Anchorage Fracture and Orthopedic Clinic, Anchorage, AK; 4 Imperial College London, London, UK; 5 Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN.* Address correspondence to this author at: Mount Sinai Hospital, 60 Murray St., 6th Floor, Toronto, Ontario, MSG 1X5 Canada. Fax 416-586-8628; e-mail ediamandis@mtsinai.on.ca.
Received August 19, 2012; accepted August 23, 2012.

6 Nonstandard abbreviations: MoM, metal-on-metal (prosthesis); Co, cobalt; Cr, chromium; MoP, metal-on-polyethylene (prosthesis); THA, total hip arthroplasty; CoC, ceramic-on-ceramic (prosthesis); HRA, hip-resurfacing arthroplasty; ARMD, adverse reaction to metal debris; ICP-MS, inductively coupled plasma mass spectrometry; GFAAS, graphite furnace atomic absorption spectrometry; BEI, biological exposure index; FDA, US Food and Drug Administration; ImPACT, Immediate Post-Concussion Assessment and Cognitive Testing.
Stephen S. Tower: Unfortunately, we know of no advantages. The concept was repopularized a decade ago on the basis of theoretical advantages over the MoP hips of that time.

First, there was less wear. Plastic wear was known to drive loosening, and there is a threshold of volumetric wear per year that is associated with loosening. Laboratory MoM experiments and evaluation of MoM explants suggested that MoMs could have low volumetric wear. This could be true, but we have learned that with Co and Cr the number of wear particles might be more important than the volume. Since MoMs produce nanometer or ionic debris, they produce many more particles than MoP hips. Some patients have immediate problems with periprosthetic tissue sensitivity due to minimal debris produced by a well-functioning bearing. Others will have an indolent response to gross metallosis that becomes a problem about 5 years postimplantation and is similar histologically to what we see with MoPs that have been in >10 years. The plastic wear issues are now moot due to the development of cross-linked oxidatively stable polyethylenes that show no or minimal wear at 10 years. Total-joint registries are now showing that the MoM hips of either modular or resurfacing types are underperforming MoPs.

The second advantage was that MoM allowed for hip resurfacing. The hip-resurfacing concept has never performed on par with contemporary MoP technology. Retaining bone on the femoral side was thought to be advantageous for eventual likely revision in younger, active patients. However, present femoral stems rarely fail. Clinicians are finding that hip resurfacings require revision more frequently and more rapidly in almost all patient groups. Revision of MoMs of both modular and resurfacing designs has been more problematic than timely revision of a MoP hip, likely due to the periprosthetic tissue problems that the Co and Cr debris can provoke and because the bearing size will likely be reduced. This combination sets up the revised patient for instability.

The third allowed for use of an “anatomically sized head.” Use of a head about the same size as the original was thought to enhance performance and stability. Level 1 data have not confirmed enhanced performance, and stability is a relative advantage likely matched now by present MoP technology.

Alister J. Hart: The main advantage is their ability to be used as hip resurfacing. Other advantages, such as large-diameter bearings with low volumetric-wear rates that are available by using CoC, are now outdated.

Thomas P. Moyer: MoM hip prostheses replaced plastic-bearing hip implants because plastic bearings did not stand up to vigorous activity and were prone to dislocation. Improved bearing surfaces, such as CoC and MoM, were brought into the market with the expectation of use in younger, more active individuals and the anticipation that wear would no longer be a major concern. MoM hip prostheses have the advantage of increased toughness and decreased wear, and because larger head sizes can be incorporated, there is reduced risk of dislocation, improved mobility, and improved quality of life.

What is the mechanism by which metal is released from MoM hip prostheses? Are there factors that increase the likelihood of metal release?

Catherine Van Der Straeten: Tribological and clinical studies have described a characteristic wear pattern of MoM HRA initially characterized by a running-in period of increased wear with metal debris formation (particles and ions), followed by a lower-wear steady state. The duration of the running-in period varies but is thought to be up to 1 million cycles and is usually over by 9–12 months in younger, more active resurfacing patients. The so-called “patch,” the surface area where the wear and friction occurs in the running-in phase, is likely to increase with time. However, as long as it is contained in the cup, fluid film lubrication can occur with a nonwearing and ideal articulation over time. The steady state is followed by a “bedding-in” phase with minimized wear and decreasing systemic metal ion concentrations. However, in cases of impingement or edge loading caused by malpositioning of the acetabular component (mainly too much inclination), the wear patch will extend outside the cup coverage area (“runaway” wear) with continuous or in-
increasing generation of a large amount of metal debris (particles and ions).

Metal ions are also generated by corrosion of metal surfaces and particles. Tribocorrosion studies have shown the formation of a passive protective film on the articulating surfaces after the initial wear-in, preventing further corrosion during the bedding-in phase. From that point on, ions are mainly formed by corrosion of the particulate debris generated during the run-in phase.

Recently, increased wear of taper and trunnion surfaces has been demonstrated with large-diameter (≥36 mm) MoM THA, leading to large amounts of metal debris and so-called metallosis.

Stephen S. Tower: One factor is the in vivo wear of the articular surfaces. In vitro, this wear was thought to be minimal due to hydrodynamic lubrication and “self-polishing” of any surface damage. Explant analysis has found that that neither exists in vivo. All explants show at least some minimal dimensional wear to surfaces from direct contact or asperities. Some explants show notable wear, usually in one section of the shell, consistent with a “breakaway or runaway wear” edge-loading phenomenon. Some brands and models of MoM implants are more prone to this than others. Some patients may be at a higher risk due to anatomy, gender, and activity levels.

A second factor is surface corrosion of articular surfaces, and a third is fretting wear and crevice corrosion of modular junctions. The wear debris produced by this mechanism may be biologically more active than bearing-surface wear. The ions produced can be substantial. Several studies of modular and resurfacing MoMs of the same design show that metal concentrations tend to be higher in the modular group.

Alister J. Hart: The mechanism is a result of implant design (e.g., cup articular arc angle, clearance), surgical positioning (e.g., cup inclination angle, cup version angle, horizontal femoral offset), and patient factors (e.g., unusual anatomy, activity level).

Thomas P. Moyer: The junction of the acetabular cup and femoral head is exposed to tremendous pressure during motion; this joint bears the total body weight. Metal implants wear due to continuous motion at the MoM surface, impingement, edge loading, and improper acetabular abduction angle. These events cause release of microparticles of metal, which can become integrated into the soft tissue surrounding the implant. The metal particles also undergo corrosion, resulting in metal ions entering and circulating in blood.

What are the local and systemic adverse biological effects of metal debris from MoM hip prosthesis?

How common are these adverse effects?

Catherine Van Der Straeten: Immunological reactions to metal debris and metal ions are now well recognized. These reactions are manifested either as inflammatory fluid collections or as cystic or solid noninfectious soft-tissue masses around the hip or osteolytic lesions. Immunological reactions can be subdivided into 2 categories. One category, which we call “metal reactivity,” is an innate immunity response manifested as a nonspecific foreign-body reaction. This is a normal immunologic response to a large amount of metal debris, is the most common local adverse reaction, and invariably occurs with increased wear. With well-positioned, well-functioning HRAs, they are rare but do occur more frequently with large-diameter MoM THAs as a result of enhanced taper/trunnion wear.

A second category, which we call “metal allergy,” is an adaptive immunity response manifested as a delayed type IV hypersensitivity, a rare abnormal response to a small amount of metal debris that occurs in people with a genetic allergic predisposition.

Recently, several cases of systemic manifestations of Co toxicity from MoM have been termed “arthroprosthetic cobaltism.” This syndrome may include various peripheral and central neurological manifestations, headaches, visual impairment, optic nerve atrophy, hearing loss, vertigo, tasting disorders, hypothyroidism, and cardiomyopathy. To our knowledge, cobaltism from MoM hip implants is rare.

Genotoxicity and carcinogenesis are other concerns, but these have not been supported by epidemiological studies. In fact, the National Joint Registry of England and Wales demonstrated a significantly lower mortality with MoM HRA, compared to any other type of THA, even after adjustment for age and other factors.

Stephen S. Tower: Excessive systemic Co exposure (arthroprosthetic cobaltism) may have adverse mental, neurologic, cardiovascular, and endocrine effects. I believe these problems in subtile form are likely epidemic in patients with failed MoM hips and endemic in patients with apparently well-functioning arthroplasty. MoM implants are apparently at no greater risk for cancer in general but may be at a 2- to 3-fold higher risk for hematopoietic malignancy, particularly lymphoma. Combined Co and Cr concentrations correlate with genotoxicity in lymphocytes. Blood Cr concentrations increase in lockstep with Co, and it appears that some ions will be in the more worrisome +6 valence state.

The response to metallosis varies between individuals. The worst reactions in my experience occur early, they
are intense, and patients may not have increased metal concentrations. In studying the histopathology of a series of failed MoM hips, we see individual variability with combinations of necrosis, chronic inflammation, and histiocytic response. Those patients with gross metallosis may exhibit any of these features with different patterns. Those patients with indolent local symptoms seem to have a histiocytic response with some necrosis, similar to patients with failures of MoP hips with the “old” plastic. The metal-sensitive patients with an acute picture of chronic inflammation (aseptic lymphocytic vasculitis–associated lesions, ALVALs) seem to be most common. Most patients with a large metal burden show a mixed histopathology pattern with all elements. The rate of occurrence is a matter of controversy. On histopathology, most patients show some form of tissue reaction, and on imaging, many will have masses of fluid collections, though not symptoms. I believe that the present revision rates underestimate the problem. I have followed revised patients with indolent symptoms who had significant local tissue loss (bone in particular) that made revision surgery challenging. As far as the incidence of true acute-hypersensitivity reactions, I fear they are not as rare as believed.

**Alister J. Hart:** The local effect is most likely a Co-induced synovitis. The systemic effects are uncertain and will require long-term studies for potential cancer effects and studies of detailed examination of vulnerable tissues (thyroid, peripheral nerves, cranial nerves, and myocardium).

**Thomas P. Moyer:** If MoM surface wear generates microparticles, these particles become integrated into tissues surrounding the implant, resulting in tissue necrosis. Degraded tissue and metal debris become encapsulated to form a fluid-filled sac called a pseudotumor; these events present with symptoms of pain, spontaneous dislocation, nerve palsy, and a palpable lump. These findings define an adverse reaction to metal debris (ARMD). Several large population studies suggest the incidence of ARMD is 1%–2%. Systemic adverse events reported in a small number of patients include neurologic symptoms such as dyspnea, fatigue, headache, vertigo, and decreased cognition. These systemic observations have not been confirmed as associated with ARMD in large-scale case-controlled studies, and there are no data describing the incidence of systemic events.

In what biological fluid(s) would you recommend measuring Co and Cr concentrations?

**Catherine Van Der Straeten:** For assessing metal ion concentrations in patients with a MoM hip prosthesis, various matrices, such as whole blood, serum, urine, and hip fluid, may be used. Analyses in whole blood or serum are preferable, since the metal ion concentration in urine samples is variable and depends on the hydration of the patient. Twenty-four–hour urine concentrations are more reliable, but a 24-h urine collection is cumbersome and often incomplete. Although there is a good correlation between blood and 24-h urine values, blood is definitely the specimen of choice for routine use, either whole blood or serum. There is no consensus on which matrix (whole blood or serum) is superior, and both matrices are used in routine clinical practice.

Hip fluid concentrations may also be informative when serum or whole blood concentrations are not conclusive.

**Stephen S. Tower:** It is critical to understand that ion concentrations in different fluids provide both general and specific information. For screening and monitoring, I believe that whole-blood Co might be the best. It is best to consistently use one type of fluid for monitoring a patient. Although the Co and Cr concentrations in various fluids and blood fractions generally correlate with each other, there exists substantial intra- and interindividual variability. Co or Cr in blood and urine correlate somewhat, and I do not think that both metals need to be checked for monitoring purposes. Co tends to be cleared quickly, about a 5-fold reduction within 2 months of revision of a failed MoM. Therefore, Co might be the best indicator of bearing function at a fixed time. Cr tends to get bound periprosthetically, so it clears more slowly. For general screening and monitoring purposes, I favor whole-blood Co as a standard test. Serum Co might be the best measure of present bearing function, and the red cell fraction is a good measure of both bearing function over time and individual susceptibility to cobaltism. Symptomatic cobaltism is likely related to intracellular Co concentrations.

Measuring 24-h urine concentrations of these metals in patients with normal renal function may be a good measure of how well the articulation is wearing. If there is homeostasis, then the amount of metal in a 24-h urine sample should approximate the wear of the bearing over a day. Spot urine values tend to be 2–3 times serum values, so that in patients with normal renal function, a less expensive means of determination [graphite furnace or chemical rather than inductively coupled plasma mass spectrometry (ICP-MS)] might be applicable. The problem is that if the patient has poor renal function, ion concentrations in the urine might be low compared to blood. There has been some concern that patients with high metal concentrations might be at increased risk for bladder cancer. If this is borne out, then urine cytology might be appropriate in patients with known high metal concentrations in
blood and urine. In patients with symptomatic neuroco- 
cobaltism, I think it is reasonable to check cerebrospinal 
the time of revision surgery, because a 
fluid Co at the time of revision surgery, because a 
spinal anesthetic is advantageous for hip surgery, and 
result might be helpful to the patient and physician.

**Alister J. Hart:** I would analyze whole blood and only 
in patients with symptoms of hip dysfunction/pain.

**Thomas P. Moyer:** Most studies correlating Co and Cr 
concentrations with MoM implant deterioration were 
performed in serum or aspirated joint synovial fluid. A 
strong association between serum and synovial fluid 
Co and Cr concentrations and MoM wear has been 
clearly demonstrated. Typically, patients with measurable 
MoM wear have serum Co and Cr concentrations 
more than 20 times higher than patients with no 
evidence of ARMD. Since synovial fluid requires an 
ultrasound-guided needle biopsy and since most phy- 
sicians performing such biopsies are not aware of the 
potential to contaminate the sample, serum is the pre- 
ferred specimen for evaluation.

**Are there accepted thresholds that define high Cr 
and Co concentrations in patients with MoM hip 
prostheses? What actions should be considered when 
a patient has increased metal ion concentrations?**

**Catherine Van Der Straeten:** We conducted a study to 
define acceptable upper limits of serum Co and Cr. 
Patients with well-functioning MoM HRAs had low 
metal ion concentrations, with acceptable upper Co 
and Cr limits of 4.6 μg/L and 4.0 μg/L, respectively, for 
unilateral MoM HRAs and 7.4 μg/L and 5.0 μg/L, re- 
spectively, for bilateral MoM HRAs. The established 
safe upper limits have a high diagnostic specificity but a 
low diagnostic sensitivity. Although low concentra- 
tions may be found with symptomatic HRA, the find- 
ing of increased concentrations allows the early detec- 
tion of increased wear and, if necessary, a timely 
revision before extensive destruction has occurred. The 
correct interpretation of systemic metal ion concentra- 
tions implies the exclusion of other sources of metal 
ions.

To provide practical guidelines for the follow-up 
of MoM HRAs, we developed an algorithm. A patient is 
first classified as symptomatic or asymptomatic on the 
basis of subjective and objective clinical symptoms. Ra- 
diographic assessment further characterizes the risk 
status of the HRA, followed by the interpretation of 
metal ion concentrations. After exclusion of other pos- 
sible sources of metal ions (other metal implants, med- 
ication, or food supplements) or renal insufficiency 
(with decreased excretion of metal ions) and once the 
run-in phase of initial surface wear (up to 12 months) is 
over, serum Cr and Co concentrations from patients 
with a MoM HRA can be subdivided into 4 categories. 
Concentrations <4 μg/L are normal steady-state val- 
ues. In the absence of clinical and radiographic symp- 
toms, a routine follow-up regimen is also followed (1, 
2, 3, 5, 7, and 10 years postoperatively). Concentrations 
between 4 and 10 μg/L are moderately increased, and 
adDITIONAL INVESTIGATIONS, including cross-sectional imaging (ultrasound, magnetic resonance imaging, 
and/or computed tomography scan), are advocated. If 
no abnormalities are found and the patient is asym- 
tomatic, a close clinical follow-up and remeasurement 
of metal ion concentrations are advisable. In the case of 
bilateral HRA, the acceptable upper limits are some- 
what higher (Cr and Co, 7.4 μg/L and 5.0 μg/L, re- 
spectively). Concentrations between 10 and 20 μg/L are a 
definite sign of increased wear. Thorough diagnostic 
investigations including cross-sectional imaging are 
avocated and must be repeated until the cause of the 
increased concentrations is found. Metal ion measure- 
ments should be repeated even when no abnormalities 
are found. Concentrations >20 μg/L are concerning, 
because they are a sign of high wear, even in the absence 
of clinical or radiographic symptoms around the hip, 
and warrant additional investigation. Co concentra- 
tions >20 μg/L may be associated with systemic toxic- 
ity. Revision must be considered even in the absence 
of clinical problems.

**Alister J. Hart:** The data for the Medicines and Health- 
care Products Regulatory Agency threshold of 7 μg/L 
for whole-blood Co or Cr in a patient with a unilateral 
MoM hip, no other orthopedic implants, and normal 
renal function come from the London Implant Re- 
trieval Centre. However, this threshold is probably 
only useful as a means of stratifying the risk of local hip 
problems attributable to a MoM hip, rather than as a 
screening tool or as a level for action. The low diagnost- 
ic sensitivity of the 7-μg/L value is the main reason for 
its inadequacy as a screening tool. This diagnostic sen- 
sitivity can be improved by lowering the threshold con- 
centration, but this would reduce the diagnostic 
specificity.

**Thomas P. Moyer:** Unexposed humans, individuals 
with no metal implants or exposures, have serum Co 
and Cr values <1.0 μg/L. Patients with hip implants in 
good working order, no articulation-induced pain, and 
no pseudotumor typically have Co values <5 μg/L and 
a Cr value <10 μg/L. Increasing serum Co and Cr con- 
centrations after implantation are common, reaching a 
steady state approximately 3 years after implantation. 
Patients with ARMD will have Co value >10 μg/L and 
a Cr value >15 μg/L, and the Co:Cr ratio is typically 1:1.
Patients experiencing joint pain after a MoM hip should be evaluated for implant loosening and infection. Patients with pain should undergo radiographic evaluation with anterior-posterior pelvis and lateral radiographs, a complete blood count with differential, sedimentation rate, and C-reactive protein as a baseline to identify infection. Once infection is ruled out and ARMD is suspected, Co and Cr serum concentrations should be measured, and an ultrasound or magnetic resonance imaging of the hip with metal suppression should be performed to identify pseudotumor. The only active treatment option for ARMD is resurfacing or replacement of the implant. Some physicians have treated patients with chelation therapy, but there is no evidence in the peer-reviewed medical literature that chelation therapy is indicated or effective.

**What methodology does your institution use to measure Co and Cr? What precautions are taken to prevent sample contamination?**

**Catherine Van Der Straeten:** Co and Cr concentrations are measured with ICP-MS. Other measuring analytical methods, such as graphite furnace atomic absorption spectrometry (GFAAS), can be used, but ICP-MS is known to have lower detection limits and the possibility for simultaneous multielement determination. One of the major technical challenges of biological metal ion testing is the risk for contamination from needles, collection tubes, or containers, and thus rigorous protocols are advocated for every step of the process. At our institution, blood samples are always collected with an intravenous catheter (Becton Dickinson Insyte-W™). After the catheter is introduced, the metal needle is withdrawn, and the first 5 mL of blood are discarded to avoid possible metal contamination from the needle. A subsequent second 5 mL of blood is collected with Terumo Venosafe® 6-mL tubes (catalog no. VF-106SAHL) for serum or plasma (store the tube at 4 °C before analysis) and with Becton Dickinson Diagnostics trace-element tubes (BD Vacutainer® K2EDTA) 6-mL tubes (catalog no. 368381) for whole blood. For urine, 24-h specimens are collected in 3-L Sarstedt containers (catalog no. 77.578); a 5-mL urine fraction is removed for analysis and backup storage. For each blood or urine sample, 1 analysis is performed on a 400-μL aliquot. The remaining fraction is stored in the freezer at −15 °C.

**Stephen S. Tower:** I have not had any difficulty in obtaining helpful Co and Cr concentrations on serum, whole blood, urine, cerebrospinal fluid, periprosthetic fluid, and periprosthetic tissue. I have yet to have a value return that appeared spurious. My hospital and the other laboratories in Anchorage send specimens to a reference laboratory. It usually takes a couple of weeks to receive the results. The phlebotomists seem to know the procedure and how to use the correct evacuated collection tube (trace-element tube) and to draw several blanks first to flush the needle. Monitoring trace elements in blood and urine has been done for reasons of industrial hygiene for decades. For industry and surgeons associated with industry to continue to insist that the tests are hard to organize, potentially spurious, and difficult to interpret seems to be disingenuous. When I first started checking concentrations years ago, the method was often GFAAS; now it is almost always ICP-MS. Though ICP-MS has lower detection limits, the graphite furnace values were analytically sensitive enough usually for my purposes, because the patients I was monitoring had such notably high concentrations. Some of the urine determinations still come back with measurement done with the graphite furnace technique. It would be best for laboratories to standardize their methodology and standard values. In terms of normal values, I believe that the mean normal for nonexposed subjects ± 2 SDs should be referenced, as well as the biological exposure index (BEI) with an explanation of what the BEI is.

**Alister J. Hart:** We use high-resolution ICP-MS using methods that follow the most robust interlaboratory quality control system (the Trace Element Quality Assurance Service) in the world. We use the first 10 mL of blood—collected with a stainless steel needle—for insurance Service) in the world. We use high-resolution ICP-MS using other tests, such as C-reactive protein. We also use trace-element blood-collection tubes.

**Thomas P. Moyer:** ICP-MS is the most suitable method for high volume Co and Cr analysis. GFAAS has adequate analytical sensitivity, but is labor-intensive and slow. Preanalytical issues are of major importance in achieving an accurate result. Co and Cr are present as stabilizers and coloring agents in many rubber products, including the colored stoppers on some evacuated blood-collection tubes. Co and Cr are present in the black rubber plunger seals found in most disposable syringes. The Monoject® Royal Blue Stopper Tube (Coviden) is the only US Food and Drug Administration (FDA)-approved evacuated blood tube suitable for Co and Cr analysis. Synovial fluid collected with a plastic syringe with a black rubber plunger seal will be contaminated with Co and Cr. HSW is the only manufacturer of syringes approved by FDA for use in humans that do not incorporate black rubber plunger seals. Call your local radiologist, and ask what syringe is used for synovial fluid collection. Invariably, the answer will be a syringe with a black rubber plunger.
seal; these collections will produce misleading Co and Cr values.

In your opinion, should Co and Cr be routinely measured during the management of patients with MoM hip prostheses?

Catherine Van Der Straeten: Yes, as outlined above, metal ion measurements are part of the routine follow-up of MoM THA and HRA. However, metal ion concentrations cannot be used as the sole parameter and must be interpreted as an adjunct to clinical and radiographic evaluation and, if necessary, cross-sectional imaging.

Stephen S. Tower: In all patients with MoM hips, whole-blood Co should be measured at baseline (pre-implantation) and at 6 months and annually postimplantation. A baseline audiogram, an Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT) battery, blood pressure, resting heart rate, and echocardiogram should also be performed. These measures of mental, neurologic, and cardiovascular function should be repeated annually in all cobaltemic patients and semiannually in those patients with a whole-blood Co >10 μg/L.

Alister J. Hart: No, because it is not suitable as a screening tool. It may be warranted for some cohorts of patients at high risk of problems (such as females with large-diameter DePuy ASR™ XL hips or those with cup inclination angles >70 degrees).

Thomas P. Moyer: Assessment of serum Co and Cr concentration is recommended annually during the first 3 years postimplantation and earlier in any symptomatic patient as indicated.

Given the issues associated with metal debris, do you think there will be a decline in the use of MoM hip prostheses in favor of nonmetal implants?

Catherine Van Der Straeten: The large-diameter MoM THAs are associated with a significantly worse outcome and a high number of adverse reactions secondary to taper/trunnion wear, and their use will probably be discontinued in the near future. Unfortunately, however, some countries (Sweden, Denmark, the Netherlands) have decided to ban all MoM hips, including HRA, despite better clinical functional results and survivorship of good HRA designs compared to THA in the group of young and active patients.

Stephen S. Tower: This decline has already occurred. At its peak, MoM represented about a third of the hips implanted in the US. Now, it is likely <5%, and that is largely as resurfacing. I believe that resurfacing may go away as well, since surgeons and patients understand that there is no level I evidence to support resurfacing over MoP with a head size of 32 or 36 mm.

Alister J. Hart: Yes, this decline has already happened with dramatic effect, according to the UK National Joint Registry.

Thomas P. Moyer: This is outside my area of expertise, but it is clear from our practice that use of MoM hip prostheses is decreasing. Many orthopedic surgeons have stopped using certain MoM implant devices in favor of ceramic or MoM hips that are not associated with ARMD for the younger, more active patient. In the more senior, less active patient, prostheses with plastic bearings may be a good choice.

Author Contributions: All authors confirmed they have contributed to the intellectual content of this paper and have met the following 3 requirements: (a) significant contributions to the conception and design, acquisition of data, or analysis and interpretation of data; (b) drafting or revising the article for intellectual content; and (c) final approval of the published article.

Authors’ Disclosures or Potential Conflicts of Interest: Upon manuscript submission, all authors completed the author disclosure form. Disclosures and/or potential conflicts of interest:

Employment or Leadership: E.P. Diamandis, Clinical Chemistry, AACC; T.P. Moyer, Mayo Clinic.

Consultant or Advisory Role: A.J. Hart, Joint Replacement Institute and DePuy.

Stock Ownership: None declared.

Honoraria: None declared.


Expert Testimony: None declared.

Patents: None declared.

Previously published online at DOI: 10.1373/clinchem.2012.193037