Arthroprosthetic Cobaltism: Identification Of The At-Risk Patient

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The author was surprised to find in his practice two patients implanted with the same type of hip replacement with a similar syndrome of neurologic and cardiac symptoms and findings. The



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Metal-on-Metal (MoM) hip. Hip resurfacing arthroplasty (HRA) is a popular application of the MoM hip. These cases were reported by the State of Alaska Epidemiology Bulletin (SAEB).¹ Both patients were found to have remarkably high levels of serum cobalt ([Co]) and had gross metallosis of the periprosthetic tissues at revision surgery. The more severely affected patient's retrieved hip bearing (Figure 1, below) showed 400 microns of wear over the 43

patients were implanted with hip bear-

ings in which both articulating surfaces

were made of chrome cobalt steel with

an anatomically sized femoral head. This

type of hip replacement is known as a

months of implantation. This wear rate is 100 times the expected rate and his highest [Co] was greater than 100 times the average value found in patients with well functioning MoM hips.² The author could not find any prior case reports of systemic cobalt poisoning (cobaltism) in patients implanted with MoM hips.

The Articular Surface Replacement (ASR) bearings implanted in the Alaskan patients were recalled by its manufacturer



Photo by Stephen Tower, MD Figure 1: Retrieved hip bearing (chrome cobalt steel)

(Depuy, Johnson and Johnson) in August of this year because of a greater than 12 percent failure rate from periprosthetic metallosis during the first five years of implantation. Depuy estimates that 93,000 ASR hips have been implanted. It is recommended that ASR implantees be monitored with a [Co] if they have hip pain, if their shell is positioned at an angle of greater than 45 degrees, or if the femoral head is less than 50 mm diameter. The patients' and surgeons' recall information does not note that neuro-cardiac cobaltism might result from the systemic cobalt exposure associated with failed ASR bearings. ASR implantees with [Co] of greater than 7 have bearings that are wearing excessively and may require hip revision to prevent progressive periprosthetic tissue damage.³

The neurologic and cardiac symptoms and findings in the two Alaskan patients are consistent with prior reports of cobaltism related to hip arthroplasty (arthroprosthetic cobaltism), prescribed ingestion of cobalt chloride for anemia (iatrogenic cobaltism), industrial exposure to cobalt (industrial cobaltism), and ingestion of a cobalt laced beer by alcoholics (alcoholic cobaltism).4,5

Background

The common implantation of MoM hips over the past decade makes the recognition of arthroprosthetic cobaltism important. A Metal-on-Plastic (MoP) hip represents the gold standard hip replacement and has a 40-year history of success. Millions of MoP hips have been implanted, cobaltism has only been reported in three patients when their revision MoP bearings were contaminated with ceramic abrasive debris from their failed primary hip replacement.⁶⁻⁸ The MoM hip was developed and marketed as an option for younger or more active arthritics in the hope that the reconstruction might be more durable and less prone to dislocation. Presently about a third of hips implanted in the United States use a MoM bearing.9 Unfortunately, any benefit of a MoM bearing over a MoP bearing is unproven, MoM hips are failing at a greater rate than MoP hips due both the immune and cytotoxic effects of periprosthetic metallosis¹⁰.

Iatrogenic, alcoholic, and industrial cobaltism syndromes have been known for more than 30 years. Combinations of cardiomyopathy, neurologic impairments, goiter, and hypothyroidism have been noted in cobalt poisoned patients. Cobalt inhibits cellular respiration and has the potential to adversely affect multiple organ systems.4

The total body store of cobalt in an adult is about 1 mg. It is quite soluble and is primarily excreted in the urine. In minute amounts cobalt is essential for metabolism as an essential trace element, but typical of this class of nutrient, in excess it is toxic. Cobalt poisoning is known to result in cardiomyopathy, goiter, hypothyroidism, polycythemia, EEG changes, optic, olfactory, audio-vestibular and peripheral neuropathies. Cobalt poisoned patients can present with impairments of hearing, sight, taste, and touch. Other presenting symptoms and signs are breathlessness, irritability, headaches, weight loss, dysesthesias, tremor, seizures and weakness.^{4,5}

All prosthetic hip bearing generate wear debris. If the bearing couple is made of different materials the softer material usually wears the most. Accelerated wear can occur if fragments of a third material contaminate the bearing. Most MoM bearings produce microscopic metallosis. MoM bearings with too little or too great bearing clearance can result in gross metallosis as can a prosthetic malposition that results in edge loading of the bearing. If a MoP bearing is implanted at revision operation for a fractured ceramic implants small retained ceramic fragments can become embedded in the plastic liner resulting in gross metallosis due to abrasive wear of the steel femoral head.⁶⁻⁸ Mating of a ceramic liner with a steel femoral head due to surgeon error can also result in gross metallosis.¹¹ Metallosis can produce extreme levels of cobalt and chromium in blood and tissues.^{6-8,11} As neurologic and cardiac toxicity is the focus of this report we will focus on cobalt. Serum cobalt concentrations [Co] are one means of measuring systemic cobalt exposure and the unit of measure is typically microgram per liter (mcg/L).

A [Co] of 0.19 is average, and the 95th percentile in unexposed subjects is 0.42.12 A [Co] of greater than 1 represents maximal allowable industrial cobalt exposure and levels greater than 5 are thought to be toxic.^{13,14} A median [Co] of 1.0 with a maximal value of 2.0 was found in 27 patients with well functioning Metasul (Zimmer, Warsaw) bearings compared to a control group with MoP bearings that had a median of 0.3 with a maximum of 1.1. The Metasul bearing is 28 mm and usually generates half of the cobalt ion load of the larger MoM bearing sizes commonly used today.² Average [Co] in series of MoM implantees vary based on the bearing design, bearing diameter, duration of bearing implantation, and acetabular shell position. A mean [Co] of 2.4 (0.4-32) was found in 140 patients with well positioned Birmingham Hip Replacement (BHR, Smith-Nephew) hips, in the 72 patients in the same series with malpositioned implants the mean [Co] was 9.8 (0.6-111).¹⁵ The BHR is likely the most popular HRA.

Normal renal function is needed to excrete the excess cobalt produced by a well functioning MoM bearing. Cobalt levels of greater than 100 have been found in two MoM implantees with chronic renal failure.¹⁶

Published cases series of patients post Metasul, Sikomet (Sikov Medizintechnik), BHRs, and ASRs show a failure rate of about 1 to 3 percent per year due to excessive bearing wear that results in periprosthetic metallosis.¹⁷⁻²⁰ Patients with metallosis

often have serum cobalt levels of greater than 19.7

Due to concerns that untreated metallosis may result in progressive periprosthetic tissue damage the United Kingdom's Medical Products and Healthcare Devices Regulatory Agency (MHRA) has recommended that MoM implantees have [Co]s performed if they have hip pain or have malpositioned implants. Patients with [Co]s greater than 7 warrant further evaluation and consideration of revision surgery if they have pain or have evidence of periprosthetic fluid collections or masses.²⁰ Neither the MHRA's device alert or Depuy's ASR recall note concerns about potential systemic toxicity of the elevated [Co]s found in patients with failed MoMHAs.

Case Reports of Arthroprosthetic Cobaltism

Deafness and peripheral neuropathy from cobalt poisoning have been described in four patients, one with a ceramic-onmetal miscouple, and three when excessive wear of the chrome cobalt head of a metal-on-plastic couple resulted from debris from third body after revision arthroplasty for a fractured ceramic head. These patients improved once their worn hip bearings were removed or revised. These patients had neurologic impairments that progressed over several years before diagnosis was made.^{6-8,11} In three cases hypothyroidism was found⁶⁻⁸, in two cases blindness evolved^{7,11}, rashes were noted in two cases^{6,11}, heart failure, seizures and headaches were noted in one case⁶. Magnetic resonance imaging (MRI) of the brain in one patient was notable for changes of the optic nerves and tracts consistent with demyelination⁷, sural nerve biopsy in another also noted axonal loss and demyelination without inflammation⁸.

The symptoms and findings in the most detailed case report were first noted at six months' exposure with mental inefficiency, poor concentration, fatigue, and hypothyroidism. At seven months headaches, convulsions, peripheral paresthesias, weight loss, and slowed nerve conduction velocities were noted. At eight months the patient required admission for progressively severe hip pain and heart failure with tachycardia. Systolic dysfunction was noted on echocardiography and myocardial biopsy showed interstitial fibrosis. Nail changes, dysgeusia, and muscle atrophy were also noted. The diagnosis of cobaltism was suspected due to the presence of periprosthetic metallosis, a [Co] of 625 confirmed the diagnosis.⁶

The two Alaskan patients had milder arthroprosthetic neurocardiac cobaltism and [Co]s of 100 to 500 times normal.¹ Metallosis was found at revision surgery in all six patients and they improved as their [Co]s declined after bearing revision. Audiovestibular symptoms were common to all six patients. Only in one case history was hip pain not noted⁷.

All patients had normal renal function. [Co]s in these six patients at the time of revision surgery were 115 to 1990 times normal and were 23 to 398 times the level allowed in industry.^{12,13} In three^{1,7,11} of the five cases cerebral spinal fluid [Co] were obtained and were 20 to 100 times normal.²¹

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<u>Cobaltism</u>

Pathophysiology

The toxicity to the central and peripheral nervous systems in arthroprosthetic cobaltism is similar to that noted in patients with industrial cobaltism and iatrogenic cobaltism.²²⁻²⁵ Cobalt is directly neurotoxic and is epileptogenic.⁴ Optic nerve atrophy was noted in two cases of arthroprosthetic cobaltism^{1,7} and has been previously noted a case of industrial cobaltism²⁴ and in one case of iatrogenic coblatism²². The findings on brain MRI in one patient with arthroprosthetic cobaltism and on sural nerve biopsy in another suggests that the neurotoxicity occurs by demyelination and axonal loss of central and peripheral nervous systems.^{7,8} Cognitive symptoms were noted in half of the reported cases of arthroprosthetic cobaltism^{1,6}, subclinical memory impairments were noted in a controlled study of cobalt exposed workers without clinically apparent cobaltism.²⁶ CSF [Co] was elevated in the arthroprosthetic cobaltism cases in which it was measured and the degree of elevation seems to correlate with both the degree of neurologic impairment and the serum [Co].^{1,7,11}

Cardiac cobaltism has been reported in iatrogenic²⁷⁻²⁹, industrial^{30,31}, and in alcoholic cobaltism⁴. A controlled study of industrial workers exposed to cobalt has noted echocardiographic dysfunction similar that found in two of the reported arthroprosthetic cobaltism cases.^{1,32} The myocardial fibrosis found in another case of arthroprosthetic cobaltism⁶ may be a progression of the EDD noted in the less severely afflicted Alaskans¹. Accumulation of cobalt in the heart has been noted in industrial^{30,31}, alcoholic and iatrogenic cardiac cobaltism.^{4,33} Cobalt is thought to be causative of cardiomyopathy due to impairment of mitochondrial function, terminal cardiac cobaltism results a disordered myofibrillar and mitochondrial ultrastructure.⁴

MoM bearings are contraindicated in patients with abnormal renal function because [Co]s above 100 have been reported in two MoM bearing implantees with chronic renal failure.¹⁶ Many patients implanted for MoM bearings today will develop renal compromise in the future and may develop cobaltism without periprosthetic metallosis with its attendant hip pain. In the United States 43 percent of adults ages 40-59 have developed impaired renal function. By the age of 71, 74 percent of Americans have impaired developed impaired renal function.²⁸ The absence of hip pain in these patients might make the diagnosis of cobaltism elusive.

The early symptoms, signs, and findings of cobaltism are endemic within any aging population. There is no reported series of MoM bearing implantees that have had their [Co]s monitored over time and correlated with neurologic and cardiac impairments. A large cohort of MoM patients needs to be systematically followed for [Co]s and neurologic and cardiac impairments to define the latency, prevalence and spectrum of arthroprosthetic cobaltism.

[Co]s of greater than 20 are frequently reported in ASR bearing implantees related to component-position or to a femoral head size of less than 50 mm.³⁴ In a series of 214 patients with predominantly BHR HRAs a mean [Co] of 9.8 (0.6-111) was noted in 74 patients who had an acetabular inclination of greater than 55 degrees. Although [Co]s of greater than 20 were more likely found in patients with steep bearings they were also found in other patients. Ten of the 214 patients had [Co]s of greater than 20.¹⁵

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Epidemiology

Greater than 35 percent of the 273,000 elective hip replacements performed annually in the United States use a MoM bearing.^{9,35} It is likely that more than 200,000 Americans are implanted with MoM bearings and are at risk for arthroprosthetic cobaltism. MoM bearings have been widely implanted in wealthy Commonwealth counties and in Europe. It is likely that more than 1 million patients are at risk for arthroprosthetic cobaltism worldwide.

Summary

MoM hip bearings are being scrutinized due to high early failure rates and concerns that the results of the revision surgeries will be poor.^{29,30} However, orthopedic surgeons and the general medical community are unaware that patients with MoM bearings are also at risk for cobaltism.

Medical providers need to know that hip arthroplasty implantees that present with symptom complexes that include tinnitus, deafness, vertigo, visual changes, rashes, hypothyroidism, tremor, dyspnea on exertion, mood disorders, dementia, heart failure, and peripheral neuropathy may be presenting arthroprosthetic cobaltism. These patients need to be asked if they have had a hip replacement and if so what type. For those patients implanted with a MoM bearing or those with a history of hip revision for a failed ceramic bearing obtaining a [Co] is indicated. MoM implantees with renal failure are a particularly high risk for cobaltism. A [Co] can be measured by many reference laboratories from royal blue top trace elements tube of venous blood. Venipuncture with a standard needle is adequate as long as a red stoppered tube is drawn first.

The radiographic appearance of a MoM bearing is readily apparent to an orthopedic surgeon. The patient's operative report will usually specify the bearing type. Given that the publicity of the recent ASR bearing recall medical providers will be contacted by worried patients concerned about their hip implants. Most patients with hip replacements will not know the brand or material of their bearings. Providing patients with copies of their hip implant inventory might avoid worry by the majority of patients with hip arthroplasties that are not at risk.

Patients with a cobalt levels of greater than 7 mcg/l bear observation of neurologic and cardiac function.¹⁴ Those patients with levels greater than 20 should be advised to have revision of their hip arthroplasty to a bearing that eliminates cobalt.^{1,20} Most patients implanted with MoM bearings have cobalt levels greater than those allowed in industry and cobalt exposed workers may have an increased incidence of subclinical cognitive and cardiac impairments.^{26,32} This association merits further study.

Table 1 is a summation of the previously referenced data of this paper that might assist the clinician in interpreting a [Co].

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Table 1: [Co]s and Significance

[Co] (mcg/L)	Description	Possible Manifestations	Frequency in patients with MoM hips
0.19	Mean Normal		
0.4	95% Percentile of Normal		
> 1	Excessive Exposure	Subclinical myocardial and memory impairments	About half
> 5	Considered Toxic		Frequent
1 to 5		Subclinical myocardial and memory impairments	About half
> 7	British threshold for close observation for periprosthetic complications in patients with MoM bearings	Hip pain, periprosthetic tissue necrosis, periprosthetic pseudotumors	Frequent
19	Mean [Co] in patients requiring revision of MoM bearings for metallosis	Hip pain, periprosthetic tissue necrosis, periprosthetic pseudotumors	Common in patients with hip pain.
23	Case report of early arthroprosthetic cobaltism	Hip pain, cognitive decline, vertigo, high frequency deafness, DOE, EDD	Not rare in patients with hip pain
> 66	Case reports of severe cobalt poisoning	Hip pain, cognitive decline, tinnitus, deafness, blindness, depression, dysesthesias, tremor, seizures, weakness, heart failure, EDD, myocardial fibrosis, goiter, hypothyroidism, rashes, optic atrophy, abnormal VEPs, AEPs, NCVs, EMGs	Likely rare

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