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## Potential Cobalt Toxicity from Corrosion of Fractured Cobalt Spinal Rods

### Background

Cobalt-based alloys have been used as a common biomaterial for implant instrumentation (e.g., orthopedic, dentistry, and cardiovascular) due their favorable characteristics.<sup>1</sup> Cobalt is an essential trace element that is required for vitamin B12 synthesis and for numerous metabolic reactions. Blood cobalt concentrations ([Co]) are homeostatically controlled at typical exposure levels. The 95% percentile for [Co] in the general U.S. population is 0.430 (0.380–0.480) µg/L in blood and 1.61 (1.37–1.88) µg/L in urine.<sup>2</sup> Cobalt-based alloys from instrumentation can leach cobalt ions, resulting in elevated blood and urine [Co] and the potential for cobalt toxicity.<sup>3–5</sup>

There is considerable variability on what [Co] can cause toxicity-related adverse health effects, which may be influenced by duration of exposure, nutritional status, genetic variability, renal function, hypoalbuminemia, or individual health factors or complications. Moreover, some people might develop a hypersensitivity to cobalt – even at low exposure levels.<sup>3</sup> There are currently no established [Co] thresholds that are reliably associated with systemic toxicity. Cobalt toxicity can cause a range of effects, including soft tissue damage, peripheral neuropathy, hearing and vision loss, impaired renal function, hypothyroidism, cardiac and hematologic problems, and hypometabolism of the temporal lobes and posterior cingulate cortex of the brain.<sup>5</sup> Additionally, neurologic symptoms may precede sentinel symptoms at the location of the implant.<sup>6,7</sup>

There are numerous case reports documenting elevated blood and urine [Co] and associated toxicity in patients with cobalt-based hip arthroplasties, including an Alaska case report.<sup>8</sup> The case report below highlights the potential for cobalt toxicity to occur in patients with cobalt-based spinal instrumentation, as has been reported elsewhere.<sup>4</sup>

### Case Report

A 56-year-old woman with a complex medical history involving Ehlers-Danlos syndrome, hypothyroidism, a metal-on-plastic Zimmer total knee replacement (cobalt/chromium and titanium/aluminum) in 2015, and a cobalt spinal fusion from T11 to the pelvis in March 2018. Eight months post spinal instrumentation, she developed a new fine intention tremor, cognitive degeneration, insomnia, and visual impairment. Her blood [Co] was 3.1 µg/L and urine [Co] was 11 µg/L. Joint fluid [Co] of the replaced knee was <1.0 µg/L. She was started on 600 mg N-acetyl cysteine, administered thrice daily to increase the excretion of cobalt through urination with the goal to decrease blood [Co] and apparent cobalt encephalopathy.

At 20 months post spinal instrumentation, the patient had a quantitative FDG-PET-CT scan that showed hypometabolism in the midbrain, right inferior lateral posterior temporal cortex, and right posterior cingulate cortex -- a pattern consistent with cobalt encephalopathy.<sup>7,9</sup>

At 27 months post-op, she reported improvements in her tremor, cognitive function, and vision; however, at 48 months post-op, she required a walker to ambulate. On physical exam, she developed pitting edema and bibasilar rales. At 55 months post-op, her urine [Co] was 18 µg/L. At this point, the decision was made to explant the spinal rod. At 56 months post-op, the revision surgery was performed. A periprosthetic fluid sample was collected and had a [Co] of 4,800 µg/L. During explant, there were multiple spots of corrosion between the pedicle screws and the rods, and bilateral breakage of the rods between S1 and the iliac crest. There was also evidence of metallosis surrounding the implant at all levels.

At 3-months post-revision to a cobalt-free construct, spinal pain and deformity were resolved and an assistive ambulatory device was no longer required. Her blood [Co] was 1.1 µg/L, and urine [Co] was 2.9 µg/L. At 10-months post-revision, the patient's encephalopathic symptoms resolved and she was able to stop taking benazepril.

### Discussion

This Alaska case report involves a patient who experienced a range of symptoms consistent with cobalt toxicity that developed 8 months after implantation of cobalt-based spinal rods and resolved shortly after their removal. While it is not known definitively if Co toxicity or hypersensitivity caused this patient's symptoms, the clinical and radiologic findings combined with resolution of symptoms shortly after rod removal are highly suggestive. This report underscores the importance of monitoring patients with cobalt-based alloy instrumentation for possible signs or symptoms of toxicity or hypersensitivity.

There is substantial patient-to-patient variability regarding if or when adverse symptoms might occur in persons with elevated [Co]. There are currently no known restrictions or warnings for cobalt instrumentation beyond metal-on-metal (MoM) hip arthroplasties. However, individual case reports demonstrate that implant biocorrosion can result in cobalt ions entering the bloodstream, accompanied by potential toxicity or hypersensitivity.<sup>3,4,6,8</sup> There is no clear national guidance on toxicity thresholds or recommendations for revision or explant surgery; therefore, determining an appropriate course of action must be made on a case-by-case basis.

### Recommendations

- Clinicians should be aware that patients with cobalt-based instrumentation might be at risk for cobalt toxicity or hypersensitivity and monitor patients accordingly.
- There are currently no established [Co] toxicity thresholds pertaining to cobalt-based arthroplasties or implants; clinicians should assess patients' symptoms in conjunction with blood or urine [Co].
- Elevated blood [Co] should not be used alone to diagnose Co hypersensitivity or toxicity.<sup>3</sup>
- Clinicians who suspect Co toxicity or hypersensitivity in a patient with a cobalt implant should consult with the patient's orthopedic surgeon or neurosurgeon.

### References

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