Back in Focus: Biologic Reactions to Wear Debris and Corrosion Products

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It is my pleasure to introduce this special issue of CeraNews, which is dedicated to the latest clinically relevant findings about particle release from orthopedic implants. This is a time-honored topic! Since the invention of THA by **Charnley**, there has been clinical concern about the potential for a biologic reaction to implant debris. After the introduction of modularity in the 1970s, there has also been increasing concern about fretting and corrosion products from the interfaces of modular components. The worry about wear and corrosion reignited after the recall of the ASR metal-on-metal hip in 2010. As a result, there has been an explosion of interest in biologic reactions to metal release in the recent literature. However, there is still much to be done. This special issue of CeraNews highlights three frontier topics in clinical research for wear debris and corrosion products, including: genetic susceptibility of tissue reactions to wear debris and corrosion products; metal release in TKA; and potential systemic complications for cobalt release. Finally, although much of the focus has been on adverse tissue reactions from cobalt-chromium alloy, some implications are emerging from wear and corrosion research for ceramic components as well.

Genetic Susceptibility to Wear and Corrosion Products

Although wear and corrosion are common with orthopedic implants used in millions of patients each year, relatively few patients develop clinically significant adverse local tissue reactions, such as pseudotumors [1], which is suggestive of an underlying genetic susceptibility. What is clear is that currently the reasons underlying a patient's specific response to metal ions and corrosion products are not yet possible to predict using a generally accepted diagnostic test. Two independent systematic reviews have identified biomarkers that may be utilized as diagnosing ALTR in this setting [1, 2]. Sumner and colleagues' systematic review [2] found that the most studied markers were tumor necrosis factor-α and interleukin-1β. Genetic susceptibility to innate foreign body responses to excess polyethylene debris has been well recognized, although susceptibility appears to result from a combination of a multitude of genetic polymorphisms [3]. Recently, Kilb and colleagues [4] has identified an "at-risk" genotype in patients for developing pseudotumors around metal-on-metal THAs, which likely would include an adaptive, metal hypersensitivity type immune response. This small case-control study with 26 MOM patients provides clinical evidence supporting the hypothesis of a genetic association with developing a specific type of ALTR. Certain periprosthetic tissue responses, including lymphocyte infiltration and aseptic lymphocytic vasculitis-associated lesions (ALVAL), which can be more severe in those with lower wear and blood metal levels, suggest that a genetic predisposition to metal hypersensitivity may also exist [5, 6]. Taken together, it is clear that a better understanding of the pre-emptive diagnosis of metal hypersensitivity and susceptibility to ALTRs is under development for orthopaedic surgeons to potentially avoid these serious complications for their patients in the future.

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Metal Release in TKA

Most of the research on metal reactions of wear debris and corrosion products has been completed for THA patients, but comparatively little is known about metal release and their consequences in other total joints, such as TKA. Previous retrieval studies have reported that in vivo metallic debris release mechanisms for TKA may include bearing surface wear (including third-body wear), mechanically-assisted corrosion at the cement-implant interface, and mechanically-assisted taper corrosion in modular junctions [7]. **Arnholt** and colleagues have recently found metallosis and elevated Co, Cr, and Ti concentrations in periprosthetic tissue from necropsy retrieved TKA [8]. Since these patients died with their TKAs intact, this study adds to the current understanding of metal concentrations in clinically successful TKAs. As research continues to focus on metal reactions in the hip, it will continue to be important to understand the impact of metal release in other joints, like the knee, where CoCr alloys are the dominant bearing surface against polyethylene.

Potential Systemic Complications for Metal Release

Just as research on the local effects of wear and corrosion products continues, both in the hip and knee, so too does research into the potential for systemic effects of metal release from medical implants. The FDA has recently issued a statement and paper about the Agency's continued efforts to evaluate the safety of implantable metallic medical devices, based upon information learned from devices including metal-on-metal **https://www.fda.gov/news-events/press-announcements/statement-continued-efforts-evaluate-materials-medical-devices-address-potential-safety-questions** and **https://www.fda.gov/media/131150/download**. The FDA recently convened an advisory panel meeting to discuss the concerns about immune responses to metal in medical devices in certain patients that might result in exaggerated immune or inflammatory reactions, including those resulting in systemic effects.

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Implications for Ceramics?

Of interest to readers of Ceranews is how the increased scrutiny of adverse reactions to wear and corrosion products with metal components is being translated to ceramic implants. For example, when ceramic-on-polyethylene has been used as a control group to compare with MOM hips in the literature, periprosthetic fluid collections have also been observed [9]. However, the fluid collections around ceramic components are generally asymptomatic, except when there is a secondary source of metal release, such as from a modular neck [10]. There are also case reports in the literature of a pseudotumor after fracture of a ceramic component, when the revision involves the use of a CoCr head that articulates with residual ceramic fragments and abrades the metal [11].

Retrieval analyses have demonstrated that the use of a ceramic head is associated with 90% reduction in metal release compared with the use of CoCr head [12]. However, these findings were based on heads and stems that were from the same manufacturer (no "mixing and matching") and none of the heads in the retrieval study were associated with an ALTR. It is clear, as well, that fretting at the head taper interface is increased when the taper is suboptimally assembled [13]. Thus, to minimize fretting, corrosion, and metal release with a ceramic head, proper assembly under clean and dry conditions is still recommended.

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