Hip implants—metal wear impairs bone-forming cells' function

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In metal-on-metal pairings, both the shell and head of an implant consist of a cobalt-chromium-molybdenum alloy. The release of metal ions into the body has been reported as a result of implant wear. Bone loss (osteolysis) was observed in many cases. Some implant manufacturers have withdrawn devices of this type from the market. Recently, physicians and researchers from Charité - Universitätsmedizin Berlin and DRK Klinikum Westend have been able to show that cobalt and chromium release contributes to bone loss. Their findings, which show that metal ions impair the progenitors of bone-forming cells, have been published in the current edition of the journal *Biomaterials*.

Total hip replacement has been hailed as the 'operation of the century', and approximately 220,000 such procedures are performed in Germany every year. Most hip replacement operations produce satisfactory results, allowing patients to regain their mobility and pain-free status. Most of the procedures performed today use metal-on-polyethylene or ceramic-on-ceramic implants. Metal-on-metal pairings have been shown to be associated with additional bone loss, leading to premature revision surgery.

The Berlin-based team of researchers tested adjacent tissues, joint fluids and bone marrow, looking for changes that might be triggered by exposure to chromium and cobalt. The research revealed that both, metal wear particles and also dissolved metals, play a crucial role in the patient's overall level of exposure. Dissolved metal ions were shown to reach the bone marrow, where they impair mesenchymal stromal cells

(MSCs), the progenitors of osteoblasts, a type of cell that is responsible for bone mineralization. The study revealed that MSCs isolated from the bone marrow of patients with elevated bone marrow metal concentrations had lost the ability to differentiate into bone-forming osteoblasts. The researchers were then able to replicate this effect by exposing cell cultures derived from non-exposed patients to a relevant level of dissolved chromium and cobalt - with identical results.

"Local exposure assessment represents a significant contribution in our quest to better understand the biological responses to metal wear, and helps to identify causations of implant failure," says Anastasia Rakow, a physician and researcher at Charité's Center for Musculoskeletal Surgery. Janosch Schoon, researcher at the Julius Wolff Institute and member of the German Society of Toxicology (GT), adds: "According to our research, the products of corrosion and wear are caused by multiple factors. The properties of the materials involved play a central role, as do biomechanical and anatomical factors specific to the individual patient. We need a systematic approach if we intend to be able to adequately estimate actual exposure levels arising from the various metals used in hip implants." Artificial hip joints are becoming increasingly more durable, and there has been a significant drop in the incidence of complications such as aseptic loosening. "In order to ensure long-term success and an implant lifespan of more than 15 years, we need to further improve our understanding of the biological effects of the materials used, in particular those of the implanted metals" explains Prof. Dr. Carsten Perka, Medical Director of the Center for Musculoskeletal Surgery. "This is why we will further encourage and promote interdisciplinary collaborations between physicians, toxicologists and biologists at the Berlin-Brandenburg Center for Regenerative Therapies." The researchers conclude the findings of their study as follows: the risks associated with metal-on-metal pairings clearly exceed their benefits. The researchers' long-term aim is to optimize patient safety by using their findings to improve the design and

composition of future implants.

More information: Anastasia Rakow et al, Influence of particulate and dissociated metal-on-metal hip endoprosthesis wear on mesenchymal stromal cells in vivo and in vitro, *Biomaterials* (2016). DOI: 10.1016/j.biomaterials.2016.04.023

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