Wear Particles in Bone Marrow of Humerus, Spine and Sternum in Patients Hosting a Hip or Knee Replacement <u>Urban RM</u>, Hall DJ, Dahlmeier EL, Wright JL and Jacobs JJ Dept. of Orthopedic Surgery, Rush University Medical Center, Chicago, IL

Purpose: Systemic dissemination of particulate wear debris generated by joint replacement prostheses has been described for the liver, spleen and lymph nodes, but data are lacking on the distribution of wear particles in many other distant tissues. Bone marrow, which is one of the largest organs of the body, is of particular interest because of its highly active production of red and white cells as well as other important functions. In this study, biopsies of red bone marrow at sites distant from hip or knee replacements were analyzed to determine the presence and nature of metallic wear particles in this tissue. We hypothesized that prosthetic wear particles disseminate widely from their local site of generation to bone marrow throughout the body.

Methods: Multiple bone marrow trephine biopsies were obtained postmortem from sites of red marrow in the proximal humeri, sternum and lumbar vertebrae of 3 females and 4 males after a mean of 15.6 yrs (range 8 to 25 yrs) following total joint arthroplasty. One subject had hosted bilateral knee replacements, 1 had bilateral revised knee replacements, 1 had a primary hip replacement, and 4 had one or more revised total hip replacements. The hip and knee devices had been fabricated from c.p. Ti, Ti6Al4V and CoCrMo alloys and had polyethylene modular inserts. The revised hip replacements also employed FeCrNi alloy plates and screws and CoCrWNi cable grip systems.

The marrow specimens were fixed in neutral-buffered formalin and decalcified. Standard paraffin sections were stained with hematoxylin and eosin for study using light microscopy. Adjacent serial sections were mounted unstained on high-purity carbon planchettes and examined in a scanning electron microscope (JSM 6490LV) at 1,000 to 20,000X. Individual particles were imaged in the back-scattered electron mode, and their elemental composition was determined using energy dispersive x-ray analysis. Sections of liver, spleen and abdominal lymph nodes from every subject were examined in a similar manner.

Results: Intracellular metal alloy particles generated by wear of the prosthetic devices were detected in the red bone marrow of the humerus, sternum and lumbar vertebrae. Particles of c.p. titanium, Ti6Al4V, CoCrMo, CoCrWNi and FeCrNi alloys were identified. The histological appearance of wear debris in the marrow was similar for all 3 sites examined. The particles were detected in the cytoplasm of single or clustered macrophages often lining the sinusoidal channels of the marrow (Fig. 1). A few particles were resolvable, but manv macrophages had gray-colored cytoplasm suggesting abundant particles at or below the resolution of the light microscope. In the scanning electron microscope, the majority of the metal alloy particles proved to be submicron in size, ranging from 0.1 to 3 micrometers.



Figure 1. Cluster of wear particle laden macrophages (arrows) in bone marrow of humerus of patient with bilateral revised knee replacements for 18 years. H&E, 600X.

In these subjects, no pathological changes were evident in the marrow that could be attributed to the presence of the metal wear debris. Histological sections of liver, spleen and para-aortic lymph nodes also showed concentrations of metal alloy particles. Intracellular particles of apparent environmental sources were also detected in bone marrow macrophages. The particles consisted of 0.2 to 5 micrometer sized silicates, some containing traces of aluminum and titanium. Intracellular iron was detected in most samples.

Conclusions: This study demonstrates that prosthetic wear debris can disseminate widely from its local site of generation to bone marrow throughout the body. Bone marrow, in addition to its hematopoietic functions, contains resident macrophages that serve to recognize and phagocytize senescent or defective blood cells, bacteria, and other circulating particles in the blood. Wear particles are known to disseminate through the lymphatic drainage. The presence of wear particles in phagocytic cells of bone marrow provides convincing evidence that wear particles are also transported via the blood circulation.

These findings also stress the importance of reducing particle generation and release of metal ions at both bearing and non-bearing surfaces of joint replacement devices. Adverse reactions to wear particles in distant organs can include histiocytosis, necrosis, fibrosis, and rarely a systemic granulomatous response. The deposition of wear debris in distant tissues is cumulative, and the debris can be retained for the life time of the patient. The tissue response to wear particles depends on the concentration and rate of particle deposition as well as the physical and chemical nature of the debris. Assessing the potential long-term pathological effects of disseminated wear products in bone marrow will require further studies, including those of patients with alternative bearings.