The Delicate Balancing Act of Metallic Biomaterials
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Ever since metals have been used within the human body, there has been controversy over whether they do harm as well as good. There is now another dimension to this issue provided by experiences with recent metal-on-metal hip replacements.

Early innovations in hip replacement materials
I can remember in the late 1960s, when the world of orthopedic surgery had been turned upside down by the invention of total hip replacement; a powerful argument erupted over which was the best combination of bearing surfaces to use in these devices. On one side was the late Professor Sir John Charnley, working in the northwest of the United Kingdom (UK), who considered that the only effective combination of materials was that of a polymer articulating against metal. On the other side, working in the east of the UK, were, separately, Peter Ring and Graham McKee, who both thought that metal bearing on metal would be better. Both arguments had their advantages and disadvantages. As Charnley soon found out, the polymer in the polymer-metal combination was prone to wear, the extent and consequences of which would depend on the polymer and the design. To this day, the minimization of the rate of release of wear debris and of the osteolysis that can ensue is still one of the major concerns in the use of these devices. The rate of wear of metal-on-metal should have been, and in general was, much lower because of the intrinsically higher hardness of the surfaces. However, the consequences of the release of metal could be so great, with massive bone loss and tissue reactions (termed by some as metalloses), that the procedure was considered too risky. Gradually, the metal-on- metal devices fell out of favor and polymers, especially ultrahigh molecular weight, high density polyethylene reigned supreme for a while. Osteolysis, of course, did not go away. Although there have been significant developments in materials science and especially in the processing conditions associated with polyethylene, osteolysis is still an issue and probably the greatest cause of premature failure of the devices.

The metal-on-metal concept did not really disappear. Normal tribological considerations in the engineering of bearing surfaces preclude using two exactly similar metals, or more correctly, alloys. Depending on the lubrication regime, one of the major factors that determine the tendency towards high friction and high wear rates is the affinity that the two surfaces have for each other. Two identical metals, in contact and under pressure, will have greater affinity; the force of attraction requires greater forces to produce sliding movement (that is, higher friction) and there is a greater tendency to generate wear particles. First principles in tribology state that substantially different alloys should be used and before the 1960s often one surface was chosen as a relatively soft material bearing against a much harder one. This led to the development of families of alloys designed specifically to be bearing surfaces, for example, a range of bronzes was developed. However, this solution was not available to the orthopedic bioengineer, because of the problems of corrosion that would occur when dissimilar metals were in contact within the fluids of the human body. The only alternative was to use similar metals, but to select the hardest and the most corrosion resistant of them. The usual choice was a cobalt-chromium-nickel alloy. It was at this point that the biological arguments started to arise. Cobalt, chromium and nickel were not deemed to be the most appropriate. Although they could be considered to be essential minor trace elements with specific biological functions, they could also induce adverse effects, locally or systemically, especially in view of their potential proinflammatory and prohypersensitivity character. Although clinical follow up showed that many hip replacements worked extremely well and without any problems whatsoever (indeed many surgeons considered them to be superior to the Charnley prosthesis), the number of patients who experienced significant tissue reactions meant that the devices fell into disrepute.

Twenty-first century metal-on-metal experiences

The matter may well have ended there, but for the introduction of a new concept in hip replacement. Approximately 15 years ago, it was becoming obvious that there could be a significant difference between the performance of total hip replacements in older, less active patients compared with those in younger counterparts, and that the more rapid wear rate in the latter group was leaving large numbers of relatively young patients with their first or even second revision, and a poor prognosis. Alongside improvements to the polyethylene in the metal-polymer prostheses and the development of alumina-on-alumina products, some surgeons decided to revert to the metal-on-metal concept. Two things were different. In the majority of designs, the metal-on-metal devices were used for resurfacing hips where only the surface of the femoral head and the acetabulum were replaced rather than the whole joint. Also, far more sophisticated engineering processes were available for optimizing sphericity and accurate matching of components. It was assumed that the wear of previous metal-on-metal devices had been largely caused by poor engineering tolerances and less than optimal surfaces. In the last decade, many manufacturers have introduced their own versions of the modern metal-on-metal hips.

I recall talking about metal ion toxicology at a clinical orthopedic meeting in California, USA, in 2004. During the course of this meeting three surgeons from different parts of the world and using different products, separately and quietly told me that, although the general performance was good, a small but finite number of their patients had experienced a profound reaction to their prosthesis. Correction required early removal (within a few years) that was usually accompanied by the collection of large amounts of sterile fluid from the joint space. Sure enough, after several studies showed good early clinical performance, papers started to appear questioning the safety of the metal-on-metal products, with observations of pain, oedema and histological evidence of persistent cells of an immune response.[1]The orthopedic world was once again thrown into controversy and many papers and editorials took strident views for or against.[2] This has not been helped by more than one paper suggesting evidence of carcinogenesis.[3]

The general consensus today is that this is a real problem.[4] It is clear that in a significant number of patients there is a type of delayed hypersensitivity (Type IV) response, with T lymphocytes reacting against the metal modified self proteins and diffuse perivascular lymphocytic infiltration. During the summer of 2008, one company took its principal product off the market in the US following some adverse reports and litigation is already taking place. It has argued that the use of these devices requires rather more clinical skill than conventional devices and that this is the cause of some early failures, rather than any problem with the design or materials.

Lessons to learn

The purpose of this discussion is not to castigate any surgeon or manufacturer who has promoted this reinvention of metal-on-metal devices. Far from it, this is another good example of balancing innovation with risk. The real issue is whether we have learned any lessons from the past about metal biocompatibility. I continue to argue that with all long term implantable devices, we should do all we can to make the materials as chemically and biologically inert as possible, consistent with their mechanical or physical function.[5] The alloys that are used in these newer metal-on-metal products are as good in terms of corrosion and mechanical properties as any used elsewhere in the body. So why is there a problem? It probably arises because the individual elements in the alloy do have innate immunogenic character, even with a dose-response relationship. Although the volumetric amount of wear debris is much less than that generated with metal-on-polymer devices (where the wear particles are almost wholly microscopic particles of polyethylene), the particles generated in metal-on-metal are largely nanoscale in character, giving far more surface area for interaction with the tissue. Metals will always be the capricious, potentially extremely good and potentially highly dangerous. We should not forget that.

References

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