MEDICAL DEVICES

Ongoing problems with metal-on-metal hip implants

Carl Heneghan, David Langton, and M Thompson examine what has gone wrong with hip implants

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Problems with hip devices emerged in July 2008 when the Zimmer Durom acetabular component was voluntarily recalled because of much higher failure rate than expected. And in 2010 DePuy had to voluntarily recall its ASR hip prostheses (one for resurfacing and one for total hip replacement) because of failure rates of about one in eight. A year later the UK regulator, the Medicines and Healthcare Products Regulatory Agency (MHRA), had to send letters to surgeons to notify them “that some of the 40 000 patients who received the metal-on-metal DePuy ASR hip implants never received the recall notice.” At the British Orthopaedic Association’s 2011 conference, further concern was expressed that large diameter metal-on-metal devices from other manufacturers were also showing higher than expected failure rates, especially in women. To add to all this, complaints of “metal poisoning” are growing among patients with DePuy Pinnacle metal-on-metal hip implants.

Metal erosion

Metal on metal hip components are constructed from a cobalt-chromium alloy. The levels of these ions increase in the body after implantation and seem to persist in some patients, particularly those whose implants suffer wear and tear. The potential health hazards of these metals are well known and particularly those whose implants suffer wear and tear. The body after implantation and seem to persist in some patients, particularly those whose implants suffer wear and tear. The potential health hazards of these metals are well known and particularly those whose implants suffer wear and tear.

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However, over a decade later, evidence on safety is still lacking. A 2011 systematic review of 29 studies of hip resurfacing found no studies fulfilled the NICE 10 year benchmark of 10%.

Indeed, a 2007 technology assessment of hip resurfacing concluded “the peer-reviewed literature had not kept pace with changes in hip resurfacing technology.”
Concerns over levels of cobalt and chromium found in patients with metallic hip replacements were first raised over 40 years ago. Large diameter metal on metal bearings result in a greater systemic exposure of cobalt and chromium ions. In addition, chromosomal aberration rates in blood and bone marrow samples are higher in cells adjacent to the prosthesis at the time of revision. Although several cohort studies have found no increased risk of cancer after total hip replacement, a recent retrospective study of causes of death found patients with metal-on-metal hips had higher cancer mortality than patients with metal-on-polyethylene during the first 20 years after implantation but not thereafter. Temporary increases in haematopoietic cancers at different follow-up periods have also been observed, as well as small increases in prostate cancer and malignant melanoma. However, mean follow-up in studies tends to be short and the exposure level is shifting, pointing to the need for continued vigilance. A safe level for metal ions has yet to be defined for patients with hip implants. Side effects of cobalt toxicity were also noted 40 years ago and include nausea, vomiting, nerve damage, and thyroid and cardiovascular disorders. Epidemiological studies of workers have established that inhaled chromium increases the risk of lung cancer. Chromium can also cause problems with the reproductive system; indeed, the US Food and Drug Administration states metal-on-metal prostheses should not be implanted in women of child bearing age. Raised cobalt levels have been found in newborns of mothers with such hips.

**Design flaws**

The ASR total hip implant has now been shown to have a failure rate of up to 50% within six years. There are two main reasons for this. The first, which is ASR specific, is that the design of the cup is too shallow. Metal on metal joints are designed to harness naturally occurring lubricating fluids from the native hip. In a shallow joint the prothetic head has a greater tendency to rub against the edges of the cup. This starves the joint of lubrication and greatly accelerates wear. As wear debris is generated, hip joints become filled with high concentrations of metallic ions then diffuse into the blood stream and are excreted renally. Unfortunately, the ASR also has a second major problem that may be common to all metal-on-metal implants with large diameter heads. The heads are creating too much stress in the area where they attach to the stems (the "taper junction") and cause release of debris. It is likely that design modifications to stems over the past decade are responsible.

**Oversight**

Hip replacement or resurfacing are common procedures; however, the evidence highlights that regulators, industry, and the surgical community are not equipped to deal with and prevent further problems. The European Commission’s solution is to oblige all EU countries to use a central European Data Bank for Medical Devices (Eudamed). The aim is to strengthen surveillance of devices after approval (in current use) by providing regulators with fast access to information. Yet the central repository is not publicly accessible, even to researchers, and the burden of responsibility for submitting data lies with relevant authorities in individual countries rather than manufacturers. Many problems exist with this approach, and there is uncertainty about whether it will improve safety.

But a far bigger problem is the process for regulatory approval of new devices. Guidelines from the EU for manufacturers state: “The depth and extent of clinical evaluations should be flexible and not unduly burdensome.” This seems curious given the potential risks associated with some medical devices. Even more concerning, the current CE regulatory framework allows clinical evaluations of hip replacements to be based on existing technologies rather than the actual device and the clinical data submitted to be based on a literature review alone. Hip replacement systems were considered class II devices until February 2007, when they were reclassified as highest risk, class III (the same as other invasive devices such as defibrillators). Class II devices have substantially lower evidence requirements that do not include an assessment of patient safety. Because of transition arrangements it was not until 2010 that all hip implants on the market had to meet the stricter standards. Failings continue after approval. The MHRA received evidence that the ASR was a danger to health as early as 2008, yet it took two years before it issued a medical device alert (MDA/2010/033) requiring systems to be in place for the follow-up of patients with metal-on-metal hip replacements including, where appropriate, measuring blood metal ion concentrations and cross sectional imaging. The MHRA somewhat played down the problems, stating, “The majority of patients implanted with MoM hip replacements have well-functioning hips and are thought to be at a low risk of developing serious problems.” During this time the MHRA was using information from the National Joint Registry (NJR) for England and Wales, to inform its decision making. The problem with using the NJR is that it records revisions. Thus the patient has to develop symptoms and present them to an orthopaedic surgeon, who has to investigate these symptoms and then consider revision. Only when that joint is removed will the information reach the registry offices. There is a further considerable time lag before data are analysed and finally presented. In fact, in some cases there is confusion about how “revision surgery” is defined.

Similar problems occur in the US, where most hip implants are evaluated through the FDA’s 510(k) programme, under which manufacturers have only to prove that they are “substantially similar” to other devices already on the market. As of 31 December 2010, the FDA had cleared for marketing 175 submissions for metal-on-metal hips through this route, including the the DePuy ASR implants. Several others are also now failing. The Institute of Medicine has recently advised the FDA that the system for approving medical devices is not fit for purpose, recommending the elimination of the 510(k) process. In response, a US bill currently before the Senate would allow the FDA to compel manufacturers to track implant performance after approval and would also increase scrutiny on recalls. Yet at the same time, manufacturers are lobbying for a faster route to market. The institute’s report concluded that “the FDA’s finite resources would be better invested in developing an integrated premarket and post-market regulatory framework.” No premarket system can ensure all devices are safe, but they can certainly make it more likely. At a minimum there should be an elimination of the use of multiple predicates in 510(k) and CE approval. Creating an independent system for post-marketing analysis for implantable medical devices that is robust and increasing international coordination around device
alerts and withdrawals should go some way to sorting out the current mess.

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Figure

Metal debris that has been removed from the tissue surrounding a metal-on-metal hip implant; DePuy's ASR-XL device (centre); Tony Nargol and team.