

What is happening with hip replacement?

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Hard lessons for device manufacturers, regulators and surgeons in the wake of a market recall

Hip replacement is one of the most cost-effective surgical procedures undertaken today. It relieves pain and restores mobility and independence for almost 35 000 individuals each year in Australia. However, recent publicity in Australia and overseas about the recall of hip prostheses from the market has created uncertainty and anxiety in patients who have undergone or are about to undergo hip replacement or other types of joint replacement surgery. Medical practitioners need to have a clear understanding of the issues and their implications so they can assist and advise patients appropriately.

In December 2009, the ASR (articular surface replacement) hip system, manufactured by DePuy Orthopaedics (Warsaw, Ind, USA), a division of Johnson and Johnson, was withdrawn from the Australian market. The ASR system consisted of resurfacing (ASR Hip Resurfacing System) and conventional total hip replacement (ASR XL Acetabular Hip System) prostheses. The resurfacing prosthesis was introduced in Australia in 2003 and the conventional prosthesis in 2004. Both prostheses used a chromium-cobalt metal-on-metal articulation.

The Australian Orthopaedic Association National Joint Replacement Registry (AOA NJRR) first published concerns about the outcome of the ASR resurfacing prosthesis in its 2006 annual report.¹ In its 2007 report, it identified the ASR resurfacing prosthesis as an outlier,² meaning that its revision rate was greater than twice the rate for all other resurfacing prostheses combined and that this difference was statistically significant. In 2008 and 2009, the Registry identified both the ASR resurfacing and conventional prostheses as outliers.^{3,4} DePuy voluntarily recalled both prostheses from the Australian market at the end of 2009. At that time, more than 5500 patients in Australia had received these devices (4410 conventional ASR and 1167 resurfacing ASR). After receiving further information from the National Joint Registry of England and Wales, DePuy undertook a worldwide recall of both prostheses in August 2010. It is estimated that 93 000 patients globally had received these devices.⁵ The most recent (unpublished) data from the AOA NJRR show that, at 6 years, the ASR conventional prosthesis has a 13.6% cumulative percentage revision rate (after 1.5 years: hazard ratio, 4.92 [95% CI, 4.25–5.70], $P < 0.001$) and the ASR resurfacing prosthesis has an 11.1% cumulative percentage revision rate (hazard ratio, 2.24 [95% CI, 1.81–2.77], $P < 0.001$). It is not currently possible to know how many patients with an ASR prosthesis will eventually require revision, but this number could potentially be high.

It remains unclear why the ASR system has a high revision rate. It is known that these prostheses can wear at an accelerated rate, but the mechanisms causing this have yet to be established. Such wearing results in high local concentrations of both metal particles and metal ions, which cause an inflammatory response that can be quite marked and associated with significant bone and soft tissue damage.⁶ Revision surgery is usually required, but the outcome is

often less than satisfactory. Very high serum levels of chromium and cobalt have also been detected in some patients,⁷ raising concerns about the potential for serious systemic toxic effects.

In this issue of the Journal, Mao and colleagues report the first Australian patients with ASR prostheses to show a potential association between high serum metal ion levels and systemic toxicity.⁸ Their report also highlights the difficulties in understanding the relevance and significance of these high metal ion levels. To date, there have only been anecdotal case reports of potential toxicity,⁷ and this is another such publication. The authors have been clear in stating that it is not possible to draw conclusions because there is not enough evidence to determine if the problems these patients have experienced are coincidental rather than causal. What this and other reports have done, however, is highlight the urgent need to undertake comprehensive research to examine the relationship between high serum metal ion levels after total hip replacement and the risk of toxicity. It is critical to determine at what concentration elevated cobalt and chromium serum levels may cause toxicity, and how the extent and severity of toxicity varies with the level. This is important because surgeons currently have no information on whether a hip should be revised based simply on the patient's serum metal ion levels. Revision surgery has significant morbidity and mortality risks and should not be undertaken without good indications to do so.

The high revision rate of the ASR system raises the question of whether this is a prosthesis-specific problem or a wider issue with all metal-on-metal prostheses. The ASR system certainly has a higher rate of revision than other metal-on-metal prostheses, but there is increasing evidence that some metal-on-metal hip prostheses are not performing as well as those that use other articulations, particularly where larger femoral head sizes are used.^{4,9} The AOA has recently advised its members to use metal-on-metal prostheses with caution.

There has been discussion within the orthopaedic and wider community regarding the role of surgeons in the design, development and subsequent use of new prostheses. Surgeon involvement can be a very good thing as it may ensure that not only the design, but also the approach to implanting the device, is optimised. However, it is clear that transparency and accountability are needed around any relationship a surgeon may have with a device manufacturer. In 2010, the AOA developed a code of conduct for its members, which incorporates a position statement on interaction with the medical industry.¹⁰ This clearly defines surgeons' responsibilities when dealing with companies.

The global experience with the ASR system, and potentially all metal-on-metal devices, has important ramifications for arthroplasty device regulation. How is it that the ASR was approved for use? Could this situation occur again? Currently, it is not mandatory in Australia for a new hip or knee prosthesis to have clinical evidence specific to the device that indicates it is either safe or effective. The regulatory requirements for medical devices are stratified according to perceived risk. This situation is not unique to Australia. Some years ago, the AOA recommended to the



Therapeutic Goods Administration (TGA) that clinical evidence requirements for joint replacement prostheses should be increased. In particular, it requested that these devices be reclassified from Class 2B to Class 3. Class 3 requires greater scrutiny of clinical evidence before a device is approved. The TGA is currently considering the reclassification of these devices and it is hoped that the experience with the ASR system will ensure it happens soon, as this would significantly reduce the likelihood of another similar occurrence.

The good news story out of all this is that Australia clearly has a very effective post-market surveillance system for joint replacement prostheses. The early identification by the AOA NJRR that the ASR system had a higher than anticipated rate of revision significantly reduced the local use of these prostheses and eventually resulted in Australia being the first country to have the ASR system recalled. The AOA NJRR has been supported by the Australian Government since its inception, and Commonwealth legislation passed in 2009 has ensured the ongoing funding of the Registry.

The most recent data from the Registry indicate that 95% of people undergoing hip replacement still have a functioning joint 10 years after surgery. Despite the experience with the ASR system, the risk of revision is declining. These results will be further enhanced if device manufacturers, regulators and surgeons take heed of the lessons learned from the ASR system recall.

Competing interests

I am paid by the Australian Orthopaedic Association as Director of the AOA NJRR.

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See pages 649 and 661.

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