OPEN

Hip Metallosis and Corrosion—A Million Harmed Due to FDA Inaction

Stephen Tower, MD

On February 18, 2016, FDA rule 78FR4094 became "effective," which requires the arthroprosthetic industry to file a premarket approval (PMA) application for all metal-on-metal hip replacements (MoMHR), which are currently on the market. These implants had bypassed comprehensive testing required by PMA and were expedited to market a decade ago using the FDA'S premarket notification process (510(k)), a process which only requires an implant to have "substantial equivalence" to a current or previously approved medical device, regardless of whether the antecedent device underwent premarket trials.

The new rule is too little too late. Industry has already removed the MoMHR from the market through formal and silent recalls by 2014. It has no incentive to fund the now required clinical trials, which were avoided by the 510(k) approval process because it is known, from unfortunate clinical experience, to be largely a failed technology.[1]

Rule 78FR4094 is emblematic of dysfunctional FDA medical device approval processes. This rule does not obligate industry to monitor patients already implanted with nonrecalled MoMHR for adverse reactions to metallic (chrome-cobalt) debris (ARMD). Periprosthetic ARMD results in inflammation, with severity ranging from minor pain to irreparable tissue loss and hip tissue necrosis.[2] Systemic ARMD consists of multiple organ cobalt poisoning (cobaltism) most commonly manifesting as encephalopathy or cardiomyopathy, with morbidity ranging from moodiness and cognitive decline to death from heart failure.[3]

The MoMHR (Fig. 1) uses a chrome-cobalt femoral ball articulating on a chrome-cobalt acetabular socket. Its predicate device used a metal-on-metal articulation that was voluntarily withdrawn from the market in the 1980s. A million of the reintroduced MoMHR were implanted in Americans between 2003 and 2013. By 2010, it became apparent that some of these newer MoMHR had rates of failure that were 10 to 20 times greater than that of metal-on-plastic hip replacement (MoPHR) models from the 1970s, like the Charnley low-friction arthroplasty.[1,2,4] One particularly poorly performing MoMHR, the DePuy ASR, was formally recalled in 2010. The Australian Total Joint Registry (ATJR) rather than the FDA or the manufacturer, Johnson & Johnson, was the first to sound the alarm regarding the high failure rate of the ASR. The ATJR later found that the high failure rate generalized to all MoMHR.[1]

Unfortunately, problems with 510(k) extend well beyond the approval of the MoMHR. The original MoPHR has been modified and now uses a modular chrome-cobalt head that articulates on a plastic socket. The Stryker Rejuvenate MoPHR was designed with a second junction, allowing the chrome-cobalt neck to be a separate component. This was thought to be advantageous, allowing the surgeon additional intraoperative flexibility to maximize the stability of the arthroplasty.

The taper junctions between chrome-cobalt components, such as those involved in the Rejuvenate MoPHR, are prone to mechanically assisted crevice corrosion (MACC). Chrome-cobalt metallosis produced by corrosion seems to be an order of magnitude more toxic than the metal debris generated by the wear of chrome-cobalt articular surfaces that plagued MoMHR. The Rejuvenate MoPHR became the "canary in the mine" for MACC. Some Rejuvenate implanted patients developed ARMD within months because the supernumerary distal neck taper is particularly prone to corrosion.[5] The design change that birthed the Rejuvenate hip was deemed substantially equivalent by the FDA and was approved without testing. Subsequently, MACC has been identified at the proximal head-neck taper used in most of the 4 million MoPHR, which have been implanted in the United States over the past 20 years (Fig. 2).[6]

The more rigorous PMA is not a guarantee of safe medical devices, despite favorable premarket clinical studies. Trials may have inadequate follow-up periods or be insufficiently controlled or powered to ensure that a new device is as safe as a market standard. Several brands of metal-on-metal hip surface replacements (MoMHSR) have PMA status and yet are failing at 10 to 20 times the annual rate of the Charnley MoPHR.[1,4]

From the University of Alaska Anchorage, Anchorage, AK.
Correspondence: Stephen Tower, MD, University of Alaska, Health Watch USA, Suite 300, 4100 Lake Otis Parkway, Anchorage, AK 99508 (e-mail: Tower@tjrclinic.com).
The author discloses no conflict of interest.

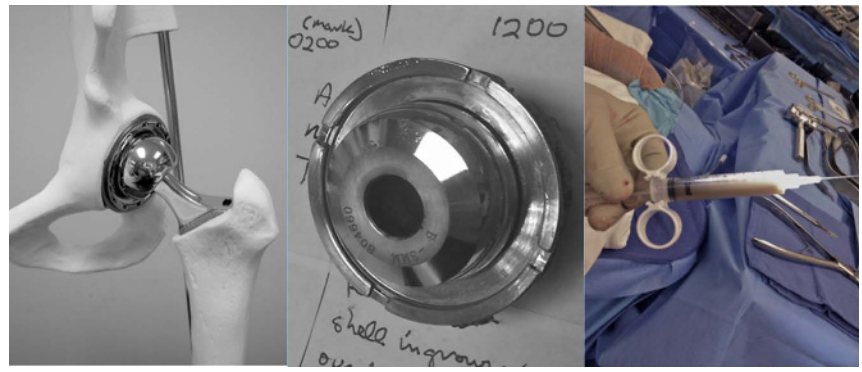

FIGURE 1. Metal-on-Metal hip replacement. Left—MoMHR consists of an articulating chrome-cobalt ball and socket. Center—A nonrecalled MoMHR revised for periprosthetic pseudotumor and neurocobaltism. Right—Periprosthetic fluid collected at revision surgery is colored by metallosis. After revision, the patient's severe hypercobaltemia and Parkinsonism resolved.

The FDA tasks industry with compiling and reporting medical device complications and failures. However, the current postmarket surveillance system has not been able to detect a disturbing number of device failures. For example:

- The ATJR was the first to recognize the excessive revision rate of metal-on-metal hip replacements and is primarily responsible for the withdrawal of MoMHR from the global market and for the diminished popularity of MoMHSR.[1]
- The delayed recognition of upstaging of uterine cancers with "minimally invasive" morcellators.
- The spread of carbapenem-resistant Enterobacteriaceae (CRE) due to design-related problems rendering fiberoptic duodenal endoscopes difficult to sterilize.

The above points to the need for rigorous premarket testing and postmarket follow-up on high-risk medical devices.

To be effective, medical device adverse event reporting must be transparent, universal, and not dependent on industry. In the U.S. Healthcare System, reporting of medical device–related complications has been sporadic and confounded by conflict of interest. Little useful information from the FDA's medical device reports survives redaction, substantially limiting the usefulness of the publically assessable Manufacturer and User Facility Device Experience database (MAUDE). The MAUDE has been unable to achieve its intended function as a leading indicator of an underperforming or otherwise dangerous medical device.

The lack of effective FDA regulatory oversight has fueled litigation, which by default seems to be the only, albeit inefficient, force promoting safe medical device development in the United States.

The tort system is unjust, inefficient, and ineffective. In recent litigation, Johnson and Johnson paid a $500 million dollar verdict to just 5 plaintiffs who were injured with the Pinnacle metal-on-metal hip implant.[7] Approximately 350 million was awarded in punitive damages. DePuy's cost to settle 12,000 ASR claims is estimated to be in excess of $4 billion.[8] Only 1 in 5 patients with ASR hips are within this litigation cohort, yet 4 of 5 are likely to require costly, complication prone, premature revision surgery related to metallosis.

Between MoMHR, MoMHSR, and the hips prone to MACC, it is likely a million Americans will undergo premature revision surgery because of metallosis complications. Assuming a medical cost of $50,000 per revised hip and a 30% surplus 10-year revision rate, the American medical cost of remediation of hip metallosis complications will be on the order of $50 billion dollars. Given the present rate of litigation, its expense, and assuming that a third of the awards will be dedicated to medical expense, $45 billion of the medical remediation cost will be borne by the public. The lion's share will fall to Medicare, given the age of patients by the time that revision surgery is indicated.

The 21st Century Cures Act is currently being debated in the legislature. Many patient advocates had hoped it would fix the 510 K "loophole" but instead it further weakens safeguards for

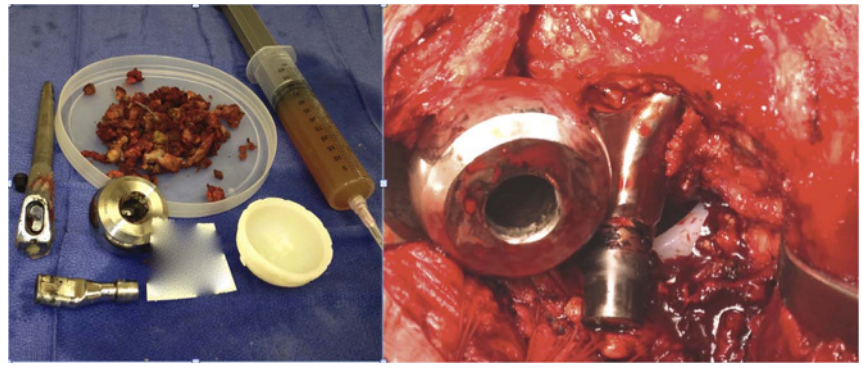

FIGURE 2. Adverse reactions to metallic debris from mechanically assisted crevice corrosion. Left—A recalled Stryker Rejuvenate, note corrosion of the female bores for the chrome-cobalt head and the titanium alloy stem and at the male ends of the chrome-cobalt neck. Right—A nonrecalled Zimmer ML Taper stem with a chrome-cobalt ball revised for symptomatic hip pseudotumor, hypercobaltemia, and neurocobaltism.

patient safety by reducing the level of evidence necessary for a device to obtain a PMA designation. It also fails to reform the 510 (k) process.[9] Premarket approval status also grants devices near immunity to civil litigation. However, litigation can proceed on issues surrounding the integrity of the underlying research, which was presented to the FDA.

The FDA's premarket approval processes and postmarket surveillance mechanisms are systematically flawed and have resulted in incalculable suffering at great public expense. The 21st Century Cures Act places the fox in the coop, and it needs to be amended to strengthen patient protection or be discarded.

REFERENCES

1. Graves SE, Rothwell A, Tucker K, et al. A multinational assessment of metal-on-metal bearings in hip replacement. *J Bone Joint Surg Am*. 2011; 93:43–47.
2. Bolland BJ, Culliford DJ, Langton DJ, et al. High failure with a large-diameter hybrid metal-on-metal total hip replacement clinical, radiological and retrieval analysis. *J Bone Joint Surg Br*. 2011;93:608–615.
3. Gessner BD, Steck T, Woelber E, et al. A systematic review of systemic cobaltism after wear or corrosion of chrome-cobalt hip implants. *J Patient Saf*. 2019;15:97–104.
4. Berry DJ, Harmsen WS, Cabanela ME, et al. Twenty-five-year survivorship of two thousand consecutive primary Charnley total hip replacements: factors affecting survivorship of acetabular and femoral components. *J Bone Joint Surg Am*. 2002;84:171–177.
5. Meftah M, Haleem AM, Burn MB, et al. Early corrosion-related failure of the rejuvenate modular total hip replacement. *J Bone Joint Surg Am*. 2014;96:481–487.
6. Matsen Ko L, Coleman JJ, Stas V, et al. Iliopsoas irritation as presentation of head-neck corrosion after total hip arthroplasty: a case series. *Orthop Clin North Am*. 2015;46:461–468.
7. Dye J. Johnson & Johnson hit with $500 million verdict in hip implant trial. *Reuters Mar* 16, 2016. Available at: http://www.reuters.com/article/us-johnson-johnson-lawsuit-verdict-idUSKCN0WJ2I2. Accessed June 29, 2016.
8. Feeley J.J&J to Pay as Much as $420 Million More in ASR Hip Accord. Bloomberg. Available at: http://www.bloomberg.com/news/articles/2015-02-23/j-j-to-pay-as-much-as-420-million-more-in-asr-hip-accord. Accessed March 8, 2016.
9. Avorn J, Kesselheim AS. The 21st Century Cures Act—will it take us back in time? *N Engl J Med*. 2015;372:2473–2475.