Metal-On-Metal Hip Arthroplasty – A Brief History

Total hip replacement (THR) has been classed as the Orthopedic operation of the century; improving a patient’s quality of life by drastically reducing the pain and mobility issues associated with arthritis. As of 2017 890,681 primary hip replacements were recorded in the National Joint Registry. Of these, < 1% were comprised of metal-on-metal (MoM) bearings, a sharp decline from the peak of MoM implants reaching 20% in 2005.

The first metal total hip replacement was both designed and conducted by Philip Wiles in 1938 using matched femoral heads and acetabular cups of stainless steel bolted to bone. McKee advanced the prototype designs of MoM bearings. Throughout the 1940’s and 1950’s he introduced the idea of resecting the femoral head, and using dental acrylic cement to fix the stem into the femur. In 1953 Haboush proposed the idea of using polymethylmethacrylate (PMMA) as bone cement.

Professor Sir John Charnley, determined to find a self-lubricating bearing, conducted his first hip replacement in the 1950’s using polytetrafluoroethylene (PTFE), however, failure was observed after two years, due to the accelerated wear of the polymer and adverse tissue reactions. Charnley tried again with High Density Polyethylene however, this too was unsuccessful. In 1961, on his third attempt, Charnley invented what is known today as the low friction arthroplasty, using Ultra High Molecular Weight Polyethylene, one of the most successful techniques in the world.

During this time Mc Kee continued to develop and modify the acetabular cup in his cemented MoM THA, and Watson-Farrar designed a stem with smaller neck geometry. The size of the femoral head was also revised, to incorporate a polar bearing, allowing a slight clearance between the two articulating surfaces. These alterations significantly reduced the wear and with only minor alterations, led to the conclusive McKee – Farrar implant as is known today.

Peter Ring, in collaboration with the Russians, pioneered cementless MoM bearings. The final Mark III Ring design consisted of a polar bearing and modified, thicker screw threads. It showed unexpectedly good success rates, but was phased out in the early 1970’s, due to the effects of the metal particles released.

As early as the 1970’s literature investigating the tissue from retrieved MoM hip replacements documented necrosis resulting from the CoCr particles found in the acetabular collagen and phagocytic
cells[8]. Evans et al[7] proposed the idea of metal sensitivity to Co and Cr ions produced from MoM hip replacements in-vivo, suggesting this was the reason behind the bone and capsular tissue necrosis observed at revision. This was later confirmed by Jones et al[10] in 1975 who suggested the toxic hypersensitivity reaction caused by the Co and Cr ions lead to an avascular phenomenon. A larger study examining 20 failed McKee-Farrar implants was then conducted by Brown et al[11] in 1977. Brown reported similar bone and tissue necrosis, in a few cases extensively so, as both Evans and Jones noting a macrophage response to the metallic debris in all specimens, combined with a lymphocytic infiltrate in some specimens.

Despite the literature’s reports of these adverse reactions to metal debris (ARMDs), the occurrence of osteolysis in metal-on-polyethylene bearing couples, a direct consequence of the polyethylene wear debris produced, meant that MoM implants were revisited in the 1990’s. This second generation of MoM implants designed by Webber incorporated a cobalt-chromium-molybdenum alloy (CoCrMo) metal alloy, which was shown to be more resistant to wear than stainless steel 316L. CoCrMo demonstrates a good wear profile with a linear wear rate of approximately 0.1 micron per year, which is half that of 316L stainless steel[12]; it has excellent biocompatibility and is highly resistant to corrosion. It is for these reasons that MoM bearing couples gained popularity in the early 1990s[13]. However, geometrical factors such as head diameter, radial clearance and edge loading were found to have a greater impact on the wear of MoM implants with an increase of 22-27 fold in wear for MoM when subject to edge loading[12,13].

Finally, the third generation MoM, similar to the second generation just uncemented, was introduced in the 1990’s, with the first MoM resurfacing in 1991. A few years later in 1997 the Birmingham Hip Resurfacing (BHR) designed by Derek McMinn was brought to the European market. This was just shortly after Visuri et al[14] in 1996 reported a link between patients with MoM hips being at an increased risk of cancer and by Doorn et al[15] who noted necrosis and extensive tissue degeneration, necrobiosis, in peri-implant tissues and both first and second generation MoM hip implants. This was further supported by Haynes et al[16] who, in 1998 demonstrated that Co and Cr particles were toxic to monocytes in-vitro. Following this, in the millennium NICE published a benchmark revision rate of ≤ 10% at 10 years for bearing couples. Despite this, as positive results were starting to emerge for the BHR in 2003, there was an increase in the implantation of larger sized MoM femoral heads.

In 2005, as the adverse reactions to metal wear debris was increasingly being observed clinically, DePuy released a statement voicing their concerns that the metal wear debris released may be carcinogenic. In spite of these concerns, and a recommendation by MHRA committee in 2006 that all patients should sign a consent form informing them of the metal ion risks prior to surgery, MoM resurfacing reached its peak in 2007, with 20% of implants being of this bearing combination[17].

The decline in MoM hips then began in 2008 when 20% of patients with DePuy’s Pinnacle hip were found to have blood metal ions above the upper limits accepted (7 µg/L). This lead to a recall of all DePuy ASR implants in 2010 combined with the release of a medical device alert (MDA/2010/033)[18].

Today, the adverse reactions to Co-Cr debris combined with the local adverse tissue response to the deposition of Co-Cr particles in periprosthetic tissues is well documented[8,11,12,13], including studies on the later third generation MoM implants. It is due to these adverse effects that the use of MoM bearings are now restricted to active males with large hip sizes, with hip resurfacing performed by high volume surgeons working in specialist centres, where the results in this high demand group continue to be good[19]. The studies above reported in the 1970’s illustrate the value of histopathology in the assessment of implant failure and should not be taken lightly. It could be argued that insufficient attention was given to the significance of the pathological findings in these studies before MoM hip implants were re-introduced.

**PROBLEMS WITH CURRENT METAL-ON-METAL DESIGNS**

Approximately 25% of MoM total hip replacements and 13% of MoM resurfacing operations will require a revision at 10-13 years. Furthermore, approximately 13% of hip resurfacing operations will require revision 10 years after the primary surgery. This is compared with MoP implants, which are revised in less than 4% of cases 10 years after insertion[15].

MoM bearings have initial wear rates 10-20 times that of other bearing couples during the first 1-2 years but this subsequently reaches a plateau. MoM bearings possess the ability to ‘self-heal’, with movement at the interface of components polishing out any imperfections on the surface of the alloy reducing friction. The volumetric wear of MoM bearings has been documented as ranging...
between 0.2 mm$^3$/million cycles to 2.5 mm$^3$/million cycles\cite{39}. This is notably less than wear rates for metal-on-ultra high molecular weight polyethylene or cross linked polyethylene, documented at 32.8 mm$^3$/million cycles and 9 mm$^3$/million cycles respectively\cite{26,27}, albeit greater than that of ceramic-on-ceramic (CoC), which ranges between 0.02 and 0.1 mm$^3$/million cycles\cite{39}. However, it is not only the volume of wear that is important but also the number, size and shape (aspect ratio) of the wear particles\cite{19}.

The number of wear particles produced by MoM bearings can be some 500 times greater than that of the average MoP bearing, even if the total volumetric wear is less\cite{49}. The particles tend to be much smaller, with the majority in the nanometer size range, resulting in a greater surface area of metal debris coming into contact with the corrosive body environment. This increases the propensity of releasing metal ions in vivo\cite{39}. Today, there remains concern with the corrosion, ion release and toxicity of the metal debris.

Polyethylene wear particles range from 0.1-10 µm, with those between 0.1-1 µm classed as biologically active in terms of osteolytic cytokine response\cite{41}. These relatively large particles tend to remain localized where they are phagocytosed by macrophages. This subsequently leads to activation of the innate immune system with local release of inflammatory mediators, including IL-1, IL-6, IFN, TNF-alpha and RANKL, which can lead osteoclast activation, osteolysis and aseptic implant loosening\cite{47}.

MoM bearing implants have relatively few incidences of osteolysis and aseptic loosening although this can occur in those with metal hypersensitivity\cite{16,43}. Metal-on-metal wear debris are comparatively smaller ranging from 25 nm to 100 nm, with the mean diameter of in-vivo particles identified to be < 80 nm\cite{44,45}. Whereas, larger particles will be internalized by macrophages with localized activation of the innate immune system, smaller particles can be disseminated throughout the body, by way of the vascular and lymphatic systems, risking disease at distant sites. It is their small size and high number that allow metal debris it induce immunological responses at distant sites including the liver, spleen, nervous system, kidney, lymph nodes and bone marrow\cite{21,28,31,40}.

Metal debris have been linked to activation of CD4+ T-lymphocytes by way of antigen presenting cells\cite{47}. Activation of the adaptive immune system and a type IV delayed hypersensitivity reaction may result in the presentations of Aseptic Lymphocyte Vasculitis Associated Lesions (ALV AL) and metallosis\cite{24}. Metal wear debris are also described as toxic. Intracellular accumulation of charged ions and free radicals can damage DNA and intracellular organelles, which can lead to cell death or mutation\cite{22,23,32}. It is by this mechanism that metal wear debris can result in pseudotumour formation and carcinogenesis.

Higher metal ions levels have been shown to reflect a poorly functioning implant and increased risk of complication\cite{20,44}, with a correlation observed for wear rates, larger femoral heads (> 36 mm)\cite{49} and failure, where 2 ppb can be expected with wear rates of 2 cubic mm per year\cite{20,80}. This effect is more pronounced in the female cohort\cite{81}. Furthermore, asymptomatic pseudotumours have been identified by way of MRI or ultrasound scan in as many as 32 % of patients\cite{82} yet not all of these will require intervention\cite{77}.

In comparison to this, ceramics are the hardest of all bearing surfaces with minimal production of wear particles. The particles produced tend to have a bimodal size distribution: 5-25 nm and 14-70 µm\cite{15,54}. Some of these particles may be of similar size as MoP or MoM wear debris, however, as the rate of wear and number of wear particles produced is so low, the dissemination of these particles and immune system activation is to a much lesser extent.

### The immune response to metal wear debris – a closer look

The host’s response to metal wear debris is initially innate and non-specific. Metallosis involves phagocytosis of metal wear debris by macrophages and multinucleated giant cells. This subsequently leads to macrophage activation and release of inflammatory mediators including tumour necrosis factor-alpha (TNF-α), Interleukin-1 (IL-1), IL-6 and IL-23\cite{35-37}. The effect is to recruit further inflammatory cells to the site of wear particle ingestion, in attempt to clear the foreign material. These inflammatory mediators may also activate osteoclasts in adjacent bone causing bone absorption and osteolysis, as well as damaging soft tissues, with resultant fibrosis and necrosis.

ALVAL is a histological diagnosis resulting from excessive and chronic activation of immune cells in susceptible patients. When cells are exposed to Co and Cr ions they can induce a CD4+ lymphocyte mediated delayed type IV hypersensitivity reaction\cite{48}. Metal wear
debris are ingested, processed and presented on the surface of antigen presenting cells (APCs), bound to class 2 major histocompatibility complex (MHC) molecules. When CD4+ Th1 helper T cells recognise these complexes they release various mediators, including IL-12, IL-2 and INF-gamma[50, 61].

This cooperation between APCs and lymphocytes results in activation of the adaptive immune system[61]. IL-2 stimulates the proliferation of further CD4+ cells capable of recognising the metal debris bound to class 2 MHC molecules. This results in further sensitisation of the patient to metal wear debris. IL-2 promotes differentiation of T cells into effector T cells[62]. INF-gamma increases natural killer cell activity, increases macrophage activity, activates inducible nitric oxide synthase and promotes adhesion and binding required for leukocyte migration. Vasodilation, increased blood vessel permeability and leukocyte chemotaxis allows for perivascular invasion and accumulation of lymphocytic infiltrates, which induces a state of chronic inflammation. This in turn causes vasculitis and tissue damage.

Pseudotumour is the term given to the aseptic mass that can present in the periprosthetic tissues of some patients with MoM bearing couples. They can be either solid or cystic and are the consequence of chronic inflammation. Pseudotumors are likely to be on the same pathological spectrum of disease as metallosis and ALVAL, with progression of these disease states resulting in pseudotumor formation[21, 28, 31, 46, 65]. Pseudotumors can be highly destructive, damaging soft tissue and bone. If large enough they will stretch soft tissues, possibly compress neurovascular structures and lead to necrosis. They can cause pain, reduced mobility, implant loosening and failure. Lymphocytic infiltration into the soft tissues, soft tissue and bone destruction by pseudotumors is thought to link to the poor outcomes following revision surgery in this patient cohort[64].

Further to these localised complications, the toxic effects of metal wear debris can be disseminated around the body, by way of the vascular and lymphatic systems, and have been linked to disease processes at distant sites, including the lymph nodes, spleen, liver, kidney, heart, nervous system and bone marrow[21, 28, 31, 46, 65].

CURRENT GUIDANCE ON MONITORING

In 2010 the Medicines and Healthcare products Regulatory Agency (MHRA) published guidance to healthcare professionals on what action should be taken in respect of those patients who had been fitted with MoM hip bearing couple articulations[18]. At the time the advice was that all symptomatic patients but only some asymptomatic patients (those with DePuy ASR hip replacements and stemmed MoM total hip replacements with a femoral head size of > 36 mm) should have annual review. This review is to include symptomatic MoM total hip replacements with a femoral head size of > 36 mm, all females and all males with a femoral head of < 48 mm. For asymptomatic patients with a femoral head diameter of < 36 mm or male patients with a head diameter of > 48 mm and implant without a 10A ODEP rating the recommendation is annual review for the first five years followed by three yearly thereafter. For those with an implant of 10A ODEP rating, assessment should be at one year, at seven years and then three yearly thereafter. The ODEP 10A rating is awarded to those implants that have the highest quality data on outcomes, with followed up for a minimum of 10 years, which supports their safe use[64].

DISCUSSION

The principle behind the redevelopment of the MoM bearing couple in the 1990s was to reduce the wear rate and ultimately improve the longevity of the bearing couples. At this point little was understood regarding the nature and biological impact of metal wear debris. However, patients soon presented with complications. These included soft tissue inflammatory reactions, such as metallosis, aseptic lymphocytic vasculitis associated lesion (ALVAL) and pseudotumour, which together are grouped under the umbrella term – adverse reactions to metal debris (ARMDs)[79]. These complications occur in combination with the toxic effects of reactive metal ions. They can have disastrous consequences for the patient. Therefore, a sound understanding of the underlying biological mechanisms and natural progression of these disease states should be well understood. ARMDs are destructive and can demonstrate a very gradual progression. They have been demonstrated to develop in patients that appear asymptomatic[64, 69, 70]. The link identified between elevated blood metal ion concentration, a poorly functioning implant, metallosis, ALVAL and pseudotumor formation[21, 28, 31, 71, 72] supports blood sampling, as a simple method of patient screening. MARS is an effective and non-invasive method of identifying these soft tissue reactions[73, 74].

With close monitoring, these complications can be identified and managed early, avoiding further deterioration that can complicate treatment. Research has demonstrated that females with femoral heads > 36 mm are at increased risk[49], as are those without IDEF 10A rated implants. By dividing patients into high and low risk the MHRA guidelines not only encourage monitoring of the whole patient cohort but also encourage surgeons to maintain a high index of suspicion for those patients most at risk[13].

Initially, studies investigating the outcomes following revision surgery, owing to the complications of MoM THR, reported poor outcomes[49, 75, 76]. However, a systematic review completed by Matharu et al[71] in 2014, reported that research into outcomes following revision for ARMDs was of poor quality, comprising studies of limited sample size and missing data. Further to this they identified a lack of robust thresholds for performing ARMd revision surgery. This prompted further investigation with a later paper published in 2018[78] concluding that outcomes of revision surgery for ARMDs are improving with time. They postulated that this was facilitated by regular patient monitoring in accordance with the MHRA guidelines, coupled with a lower threshold for performing revision surgery. This means that patients with ARMDs are being identified and operated on earlier and that this is having a positive impact upon outcomes.

REFERENCES


Hughes LD et al. Metal-on-Metal Total Hip Replacement, Development and Demise


