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A Review on Total Hip Joint Arthroplasty: Prosthesis Design and Clinical Trials

Elnaz Tamjid[1,*], Masoud Rezaei[2], Yasin Akhtari[2], Afsaneh Ehsandoost[1], Behnoush Samavati[2]

1-Department of Nanobiotechnology, Faculty of Biological Sciences, Tarbiat Modares University, PO Box, 14115-175, Tehran, Iran.

2-Department of Biomaterials, Faculty of Interdisciplinary Science and Technology, Tarbiat Modares University, PO Box, 14115-175, Tehran, Iran

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Abstract:

Advanced osteoarthritis, rheumatoid arthritis, reconstruction of dysplastic hip joints or following bone defects caused by accidents or diseases, and avascular necrosis, are the main surgical indications of total hip joint arthroplasty (THA) operations. THA is increasing due to the aging population, while the average age at the first operation and the life span of hip prosthesis is reduced. Such an increasing interest was the motivation of this review article which gives a brief introduction to design and components of THA prosthesis. In the meantime, this study is focused on various fixation methods of THA implants, in addition to the biocompatibility issues of the commercial biomaterial components. Advantages and disadvantages of each component, design, and method are given to facilitate the comparison. Furthermore, the main clinical concerns, including metallosis symptom, pseudotumor formation, local tissue reactions, toxicity, and noise are pointed out. Finally, the most recent clinical trials have been reported, in order to give a general overview on the state of the art. This mini-review is potentially useful for researches in the field of biomedical engineering, total hip joint arthroplasty, and toxicology studies.

Keywords: Total Hip Joint Arthroplasty; Fixation Methods; Prosthesis Design; Biomaterials; Clinical Trials**.**

1. Introduction

Total Hip joint Arthroplasty (THA) surgeries are performed about one million/year worldwide [1]. The high rate of success (~95%), and safety introduced this surgery as “the operation of the century”. Moreover, THA is relatively inexpensive; regains pain-free mobility, restores functionality of the hip join, and relive the patient from sever joint disease or trauma. The number of people who need a primary or revision THA is increasing due to the aging population, while the average age at the first operation and the life span of hip prosthesis is reduced. According to a recent report [2] based on Nationwide Inpatient Sample (NIS) historical database, by the end of 2030, the number of THA surgery will increase by 174%. The history of total hip replacement (THA) goes back to the 19th century. However, the practical operations were not successful until middle 20th century when Charnley as the pioneer surgeon started to practice some clinical trials

*Corresponding Authors: Elnaz Tamjid,
Email: tamjid@modares.ac.ir

[1] during 1970s and early 1980s, the first generation of hip resurfacing with metal on polymer (MOP) bearing surface emerged but with poor outcome [3,4]. In 1951 metal on metal (MOM) hip resurfacing was used by Haboush and others until mid-1970s. MOM resurfacing began to be used again in 1988 because of improving in metallurgical technologies. In 2006, Food and Drug Administration approved the MOM resurfacing [5] the hip prosthesis is typically designed to endure about 20 years. Nowadays, there are a lot of research and study performed worldwide to increase the life span, and reduce revision surgery. The large variety of the prosthesis in the market and rapid innovation in the field is an indication of such an interest [6] Although, it is prospected that better diagnostics and strong tissue engineering, will significantly reduce the necessity of total joints operations in the distant future [7,8], the significant rise in the global population aging highlights the importance of such an essential orthopedic implants. This review briefly introduces the main surgical indications, design and components, biomaterials classifications, fabrication and fixation methods, recent biocompatibility studies, and clinical trials.

2. THA Surgical Indications

The most common medical indication for THA are advanced osteoarthritis, rheumatoid arthritis, reconstruction of dysplastic hip joints or following bone defects caused by accidents or diseases, and avascular necrosis [9,6]. In general, the replacement of both articulating surfaces of a degenerated hip joint called as total hip arthroplasty, relies on trimming the spherical part or substitution of the spherical part (modular hip prosthesis) with metallic cap (resurfacing). However, the counterpart of the joint in both cases is a semi-spherical shell. The former strategy includes the replacement of femoral stem, acetabular cup, outer shell and inner line. To ensure fixation of the prosthesis, a good integration of the shell and stem should occurred between the iliac bone of pelvis and femur, respectively. Femoral head and the liner rolling as the articulating surfaces. the latter strategy is based on the femoral head reshaping and replacement with a metallic articulating surface. It is claimed that the advantage of this method is the low amount of femoral neck and femoral bone mass discharge, good wear resistance during service, matching with human anatomy, and enhanced stability due to larger articulation diameter [10]. The disadvantage of hip resurfacing is the large amount of debris and metal ions released. Studies have shown that level of cobalt and chromium in patients' blood serum increases in comparison with the patient using conventional total hip [11,12].

3. Design and Components of Hip Prosthesis

Undoubtedly, design of the components plays a critical role in the functionality of prosthesis. A typical multi-component hip prosthesis is shown in Figure 1. In order to reduce the stress concentration on weak cemented mantle in cemented prosthesis, a round-off design with no sharp edges should be considered in designation. In contrast cement-less implants should be composed of sharp design, ribs, fins or self- tapping threads. Specific surface treatments are required to be performed on the stem to enhance the osseointegration properties [13].

Stem as an important part in prosthesis which should have the ability of transferring load uniformly from the prosthesis to the lower part of the stem, bears the majority of the applied loads. In the mean time, the femoral head is coupled to the neck of the stem by means of a taper junction. The space between the stem and head is known as taper junction and it improves the prosthesis functionality. It was reported that this space induces significant increase in titanium and cobalt concentration in patient serum [14]. It is noteworthy that the range of motion and stability of the head against the dislocation is achieved by the means of femoral head diameter. Liner is half spherical cavity to reduce friction and simplify motion of femoral head and is mechanically locked in the shell. Minimum thickness of the shell is limiting factor for the choice of liner material. The shell is the outer side of the acetabular cup which is fixed into the pelvis by cemented or uncemented techniques. In the massive pelvis bone for more fixation screws can be used [6].

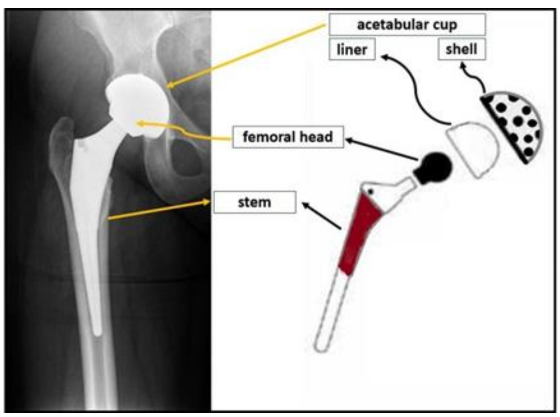

Figure 1. A typical multi-component hip prosthesis

4. Fixation Methods

4.1 Cementless Method

Cementless hip prosthesis have porous coated surface and they have been performed since 1977 at Anderosn clinic [15]. To achieve the aim of long term osteointegration of cementless prosthesis, porous surface finishing or porous coatings are utilized to generate de-novo bone tissue. Frequent coating methods include plasma-spray deposited hydroxyapatite [16,17], Ti sintered beads, or plasma-sprayed Ti that facilitate integration into hosting bone tissue [18]. Cementless hip prosthesis contains edges and grooves to enhance the primary mechanical fixation. Some effective factors limiting the application of cementless prosthesis are age, pathological condition and patient health states, which reduce the capability of bone growth. It is worthy to note that in case of older patients, the cemented method is preferred due to the lower metabolism and less active bone tissue, while cementless method is preferably used for younger patients [19]. Moreover the limited life span of the prosthesis is the main restriction for the young patients who are potentially candidates for further replacement surgeries. Therefore, employment of cemented method would be problematical due to the removal of the hard cement and cement debris [18]. In comparison between cemented and uncemented methods, the latter has more sophisticated surface finishing which makes it difficult to build and more expensive [20]. Cobalt –chromium and titanium alloys are the materials used in cementless hip prosthesis [21,22]. Moreover, Cementless prosthesis is fixed without or with pressing (press fitting). An investigation on porous-coated cobalt-chromium femoral implants evaluated in 307 patients after two years and in 89 patients after five years indicated that bone ingrowth was achieved in 9 out of 11 retrieved specimens, while the fibrous tissue fixation occurred in the remaining two [15]. Fixation by bone ingrowth occurred in 93% of the cases in which a press fit of the stem at the isthmus was achieved. (only 69% of those without a press fit). Pain and limp was much lower when there was either a press fit of the stem or radiographic evidence of bone ingrowth. Factors such as age, sex, and the disease process did not influence the clinical results. Although the fixation by the ingrowth of bone or of fibrous tissue appeared to be stable, the former gave better clinical outcomes. It is worthy to note that the attractiveness of biological fixation lies on its potential for direct attachment of the implant to bone without any fibrous tissue layer [15].

4.2 Cemented Method

Mainly in case of arthroplasty for older patients, THA stems are fixed with acrylic bone cement and polymethylmetahacrylate (PMMA). PMMA is a standard material as the bone cement [6]. It is intended to attach the bone and implant and to transfer the load uniformly to the joint between bone and implant. Notably, cement serves as filler and does not adhere neither to the implant nor to the bone, but relying instead on close mechanical interlock between the irregular bone surface and the prosthesis [2, 19, 23]. As the stiffness of the prosthesis increases, the level stress concentration in cement is reduced. Additionally, it is shown that increasing the young modulus of the cement leads to an increment in the stress concentration of the cement resulting in cracks propagation in the cement. Notably, the majority of the cement stresses is proximally, and may lead cracks to propagate in a distal direction through the stem [24].

In a study on improving the adhesion between implant and the cement, the grit –blasting process was utilized on titanium surfaces. The results exhibited higher aspetic loosening on grit –blasted surfaces in comparison with the polished ones [25]. Meanwhile, the cemented method encounters some disadvantages including shrinkage during the polymerization and insufficient osseointegration, exothermal reaction during polymerization, and monomer release leading to necrosis of surrounding bone tissue [26], and also the significant effect of surgical skills to uniformly fill the gap between bone and implant [6]. Besides, some hybrid methods based on cemented stem and none cemented socket are also used [27].

5. Biomaterials used for hip prosthesis

Mechanical characteristics, which control the implant life span, play an important role in the design and selection of biomaterials for THA. Non-mechanical characteristics include biocompatibility, osseointegration, non-allergen and non-toxic nature are also of essential significance. The biomedical components commercially utilized by the manufacturers are listed in Table 1. It should be mentioned that materials selection and fabrication have not been altered to great degree after 1990s [28]. As a rule, in POM implants femoral stem is made of metals and cup liner is made of polymer like UHMWPE [29]. In MOM, stem and cup liner of the hip implants are made of metals (cobalt chromium alloy, titanium alloy or sometimes stainless steel) and in ceramic on metal (COM) implants, femoral head and cup liner are made of ceramics such as alumina and zirconia. It is noteworthy that MOMs are not recommended for all patient such as the ones with poor functional kidneys or pregnant woman and woman in childbearing ages. Evaluation of metal ions crossing placenta are still under study, but the main concern relies on the particle size and rate of debris release in the joint surfaces. It was shown that the majority of the particles are in the range of 51-116 nm, with an average of 81 nm. It is also estimated that the number of released particles per year is about 6.7×10^{12} to 2.5×10^{14} [30].

The effect of dimensional parameters on metallic hip joints is still controversial. For example, Clarke et al.(2003) demonstrated an increase in the level of cobalt and chromium in patients' blood serum, using metal on metal hip resurfacing with the main size of 48mm rather than with 28 mm implants. On the other hand [31], reported no significant relation between diameter and Co-Cr levels in patients. This comparison was done between hip resurfacing of large diameters and that of smaller diameters [10] In general, the dissimilarity roots from the different samples and methods used. It is noteworthy that the larger femoral head diameter leads to less chance of dislocation which results in elevated wear resistance. In polyethylene on metal joints, the bearing surfaces are produced in smaller diameter in order to reduce the wear. Highly cross linked polyethylene acetabular components are available for larger diameters. However, simultaneously increasing the strength and toughness in highly cross-linked polyethylene is an important issue. While the aim of high cross linking is reducing wear rates, it make the material more brittle.

6. Biocompatibility

The biocompatibility of total hip joint as a long-term implant is defined as optimizing the rate and quality of bone apposition to the material, minimizing the release rate of corrosion and the wear debris, the tissue response to the released particles and optimizing the biomechanical environment, minimize disturbance to homeostasis in the bone and surrounding soft tissue [32]. Biocompatibility of implants and particulate debris in THA has been a historical concern and has been considered since 1890s [28,33,34,35,36]. Biocompatibility is mainly determined by the implant surface through the contact with the biological tissue. Principally, the implant is covered with proteins from the body fluids followed by the cell attachment according to the implant surface properties. Thus, the body will either tolerate a biocompatible implant or a foreign body reaction will occur. For metals, this reaction is mainly depends on the surface properties of the implant, such as surface chemistry and roughness. It is noteworthy that proteins and cells interact differently on surfaces with different properties, leading to chronic inflammation in case of non-biocompatible materials [28]. Consequently, the list of commercially used combination of materials in THA (Table 1) has been remained almost unchanged over the past decades. This section is a brief introduction to the most common combination of biomaterials used as components of the hip prosthesis.

6.1 Stainless steel

Singh & Dahotre [37]. indicated that stainless steel THA implants are often degraded due to pitting, crevice, corrosion fatigue, fretting corrosion, stress corrosion cracking, and galvanic corrosion in the body. Their corrosion resistance can be modified by lowering the nickel content and alloying them with Mn or N. Austenitic stainless steel has a weak wear resistance and because of the large number of wear debris, rapid loosening occurred. Worse corrosion resistance as well as the danger of allergic reaction which appears in a big number of patients restricts their application in orthopedic joint prosthesis. Moreover, the modulus of stainless steel is about 200 GPa which is much higher than that of bone [38,39].

6.2 Cobalt-Chromium

Wrought Co-Ni-Cr-Mo alloy is now used for making the hip stems. Because of spontaneous formation of passive oxide layer within the human body environment, they are highly resistant to corrosion even in chloride environments. They have superior mechanical properties such as high resistance to fatigue and cracking caused by corrosion with a good wear resistance. They are not recognized as brittle alloys regarding to the minimum of 8% elongation. Their high elastic modulus (220–230 GPa) are similar to that of stainless steel (approx. 200 GPa) which is higher than that of cortical bone (20–30 GPa) [40,41]. Elements such as Ni, Cr and Co are indicated to be released from the stainless steel and cobalt chromium alloys due to the corrosion in the human body [42].

6.3 Ti and its alloys

Their excellent characteristics such as high strength, low density (approx. 4700 Kgm^{-3}), high specific strength, good resistance to corrosion (by the formation of an adhesive TiO_2 oxide layer at the surface), complete inertness to body environment, enhanced biocompatibility, moderate elastic modulus of approximately 110 GPa are a suitable choice for implantation. Ti and its alloy also have this ability to become tightly integrated into bone. This high capacity to join with bone and other tissues considerably improves the long-term behavior of the implanted devices, decreasing the risks of loosening and failure. Commercially pure Ti (CP Ti) and Ti–6Al–4V ELI (Ti64, Extra Low interstitial) are most commonly used titanium materials for implant applications. Ti-6Al-V4 is slowly replacing CP Ti due to the greater mechanical strength but it has raised some concern because of releasing aluminum and vanadium. Both Al and V ions are associated with long-term health problems like Alzheimer disease and neuropathy [43]. Ti–6Al–4V can be modified by replacing V with Nb, Zr or Ta in order to make it more biocompatible and corrosion resistant. The poor wear resistance of titanium alloys restricts their application as femoral head components in typical hip implants, although the femoral stem is often made of Ti-based alloys. A variety of surface treatment methods, such as ion implantation, titanium nitride (TiN) coatings, and thermal oxidation have been proposed to enhance the wear resistance. Two recently developed promising biomedical alloys, Ti-35Nb-7Zr-5Ta (TNZT) [43], and Ti-29Mo-13Ta-4.6Zr (TNTZ) [44], show significant improvement because of their high yield strength and low modulus, in comparison with the previous generation alloys such as Ti-6Al-4V, stainless-steel and cobalt–chromium-based alloys.

Table 1 Commercial biomaterials used as components of the hip prosthesis [2]

component	Femoral stem	Femoral head	Acetabular cup liner	Acetabular cup shell
Material class	metal	Metal/ceramic	Polymer/metal/ceramic	Metal
Commercial Materials	CoCrMo-wrought/Ti-alloys/stainless steel	CoCrMo-cast/ stainless steel/Alumina (pure or zirconia-toughened)/zirconia	UHMWPW/XLPE/ CoCrMo-cast/ Alumina(pure or zirconia-toughened)/zirconia	Commercially pure titanium/ stainless steel

Table 2. Different combinations of biomaterials used as components of hip prosthesis [2]

Combination	MoP(UHMWPE)	MoP(crosslinked UHMWPE)	MoM	MoM HRS	CoM
Pros	Most commonly used/longest experience and flow up(more than 40 years in some cases)/most economic device	Expectation of drastically reduced wear rate and reduced risk of aseptic loosening	Low volumetric wear rate/improved joint stability due to larger femoral head diameters(28-60mm)/low rate of aseptic loosening	Femoral bone conserved/facilitates revision surgery/improved joint stability and range of motion due to larger femoral head size/low volumetric wear rate	Improved joint stability and range of motion due to larger femoral head size of up to 38-40 mm possible/low volumetric wear rates
Cons	High polyethylene wear volumes/late aseptic loosening possible in response to exposure to polyethylene wear debris/insufficient longevity for patients younger 60-65 years	Introduced 1998/follow-up period still limited less than 10-15 years	Risk of metallosis, metal allergy and hypersensitivity/unknown long-term effects of exposure to metal ions	Surgically more delicate/elevated risk of femoral neck fracture/risk of excessive wear/pseudotumours observed/increased blood metal-ion concentrations/possibly enhanced toxicity due to nanotoxic effects of nanosized wear debris	Catastrophic fragile fracture of ceramic components/no experience with metal-ion release/debris even smaller than with MoM(6-7nm)
Remarks	Wear rate = 0.1mm/year	0.01-0.02mm/year	0.005mm/year Used since the 1950s Reintroduced 1988 FDA approval in 1999 NiW used in about 1/3 of all THA procedures in the US	0.005mm/year Not recommended in case of renal insufficiency or in women in childbearing age Hip resurfacing requires large femoral head diameters and this is only possible with MoM	Reduced in vitro wear rates CoCrMo acetabular cup components provide stability for larger ceramic femoral heads

7. Clinical Concerns

The greatest concern after metal-on-metal hip resurfacing may be the development of metallosis. Metallosis is an adverse tissue reaction to the metal debris generated by the prosthesis and can be seen with implants and joint prostheses. The reasons that patients develop metallosis are multifactorial, involving patient, surgical, and implant factors [45]. "Metallosis" comprises local damage and changes in tissue characteristics provoked by a metallic foreign body in the host with (1) direct (by pressure, destruction or displacement of tissues), (2) collateral through chemical reactions with body fluids, electrolytic processes with direct galvanic impairment of cellular activity and impregnation of host tissue with ionizing metallic particulate matter, and (3) biologic reactions of the adjacent tissues" [46]. Metallosis has been found with stainless steel, titanium, and cobalt-chromium alloy, femoral prostheses articulating either with a similar metal or (rarely) with a polymer acetabula component. Titanium and stainless steel femoral head prostheses are no longer used, so today metallosis usually refers to tissue changes observed after the use of cobalt chromium-on-cobalt-chromium (metal-on-metal) implants [47]. The term ‘‘metallosis’’ also has been defined as aseptic fibrosis and local tissue necrosis with or without implant loosening [48].

The symptoms of metallosis include pain, a sense of instability, and increasing noise coming from the hip. Metallosis has not been proven to occur earlier than 9 months postoperatively but symptoms always pre-sent within the first 4 years after surgery. Up to 18% of patients with hip resurfacing experience groin pain after surgery but only 2--5% have metallosis. There is no medical, physical, or non-operative treatment for progressive metallosis. It is not possible to chelate the excess cobalt from either the joint or serum. Usually, once metallosis occurs, the tissue response continues and thus surgery would be necessary. In some cases, a small amount of metallosis does not progress, and surgery may not be necessary [49].

MOM hip replacements specifically have the advantage of increased toughness and decreased wear. Additionally, metal on metal implants allow the use of large sized femoral heads, which wear better than smaller ones and significantly decrease the chance of the hip dislocating. Continuous motion at the MOM surfaces is the main reason for wear of the implant. This causes release of micro-particles of metal debris into the surrounding tissue, sometimes referred to as metallosis. These metalic micro-particles can be corroded resulting in the release of metal ions into the circulation. The condition that causes adverse effects related to sensitivity to the metal or due to wear of the metal surfaces is called adverse reaction to metal debris [50]. A. B. Pedersen, Total Hip Replacement Surgery: Occurrence and Prognosis: Health, Aarhus University, 2016.

Pseudotumor Formation is another important concern which has been described by Liu et al. as ‘‘a soft-tissue mass associated with the implant, which is neither malignant nor infective in nature.’’ Most authors associate pseudotumor with an effusion that can be very large [49]. It is reported that patients with a pseudotumor had up to 6 times the median cobalt serum concentrations and up to 7 times the median chromium serum concentrations compared to patients without pseudotumors. They found that evaluation of enhanced lymphocyte reaction to MOM was highly variable and possibly more related to nickel sensitivity than actual MoM wear. Reports of ‘‘pseudotumours’’ occurring after metal-on-metal resurfacing began appearing in the literature since 2008, but now are reported regularly [51].

There is conflicting information about the incidence and predisposing factors. Implant manufacturers and some surgeons report that women or smaller size patients, with or without steep abduction angles, are more likely to develop metallosis [52,53]. Pseudotumors regress when the local cobalt level is reduced either by removal or revision of the prosthesis, hence, there is no need to resection the involved tissues aggressively. Osteolysis and further tissue necrosis, however, will follow if treatment is not provided. There is no non-operative treatment for pseudotumors or progressive metallosis. In some patients, the tissue reaction is mixed; with pseudotumor formation, the tissues are overgrown but in other instances the tissues become avascular and necrotic. Thickened fibrotic soft tissues can be found immediately adjacent to the necrotic tissue. The underlying bone can be avascular with a dead-appearing surface [49]. Meanwhile, increased wear from the MOM bearing surfaces was associated with an increased failure rate [49].

In addition to the design and the diameter of the MOM bearings, the position of the implant—which is influenced by the technical skill of the surgeon inserting the prosthesis—also plays a role in the degree of metal ion release [54]. There is evidence from a recent animal study to suggest that Cr ions can accumulate in the liver [55]. Marker et al. (2007) investigated potential long-term effects on kidney function resulting from Co and Cr wear in MOM THA by measuring serum metal ion levels and creatinine clearance at 10-year follow-up in 75 patients [54].

Another crucial concern about all artificial joints is that they make noise. Most often, the frequency of the noise generated is above the human audible range. Thinner acetabular shells produce lower frequency noise and when two very thin shells are used, such as with resurfacing, noise within the audible range is possible. Resurfaced hips with metallosis reliably produce an audible or palpable sense of noise or vibration. Noise that becomes more prominent is suggestive of metallosis. Clunking rather than squeaking is the important noise for a MOM hip. Two or three injections (16 mg each week) generally have been successful in substantially reducing or eliminating squeaking. Although there are no published reports of injecting hyaluronic acid into a resurfaced joint [49]. The initial press fit limits the amount of initial pain. Within a few months, pain from poor osseointegration may occur. The onset of this pain generally is earlier than the onset of pain from metallosis [49].

Toxicity is another big issue. Elevated chromium and cobalt concentrations may indicate implant wear, but they are not indications of toxicity. $Chromium^{3+}$ compounds are not considered a health hazard, while the toxicity and carcinogenic properties of chromium 6^{+} are well known. Chromium 6^{+} that is exposed to tissues is instantly converted to chromium 3^{+} by cellular¬reducing enzymes, and this reduction releases electrons that are destructive to surrounding tissues, initiating the carcinogenic process. A key point to note is that chromium 3^{+} is not toxic, and that only chromium 3^{+} is released from orthopedic implants [56]. Cobalt Levels are also of great importance. All patients with metal-on-metal hip prostheses have elevated levels of cobalt detected in their hair, blood, urine, vital organs and, if present, placenta. Evans et al. in 1974, described metal ‘‘sensitivity’’ as the cause of bone necrosis and prosthetic loosening in a small cohort of patients with hip and knee total joint replacements using cobalt-chrome alloy [49]. Cobalt is an essential element that is integral to vitamin B12 and required for carbonic anhydrase activity. Cobalt toxicity, known as cobaltism, can occur after ingestion of large amounts of cobalt. Symptoms associated with cobaltism include myocardial damage, renal failure, and hypothyroidism. Interstitial lung disease develops if cobalt-laden dust is inhaled. Several case reports of patients with MOM implants suggest a relationship between high serum cobalt and nonspecific neurologic manifestations (fatigue, ataxia, cognitive function decline). However, no case control studies confirm such relationships. There is no definitive proof that high serum cobalt associated with MOM wear either causes toxicity or is benign. Large population studies are underway; More definitive information will evolve over the next few years.

Different metals are present in different organs, for example chromium, titanium and nickel are mainly found in the lung, whereas cobalt is often detected in the kidney, heart, pseudocapsule, liver and spleen [47,37,38]. Binding of metal ions to proteins allows them to be systemically transported and either stored or excreted [47,57].

Accumulation of a high concentration of metal ions beyond the metabolic ability of the liver and kidneys resulted in a type IV T-cell mediated hypersensitivity [58]. Willert et al. in 1977, described the tissue reactions of the articular capsule to wear products of artificial joint prostheses [59, 60]. In their landmark article, they reported the development of a foreign-body reaction (consisting of macrophages and foreign-body giant cells) to wear debris. This foreign-body reaction takes place in the neo capsule and depending on its magnitude, may lead to the formation of granulation tissue, which may subsequently cause scarring and decrease joint mobility. They went on to discuss the concept of an “equilibrium state”, which is achieved when the periprosthetic lymph vessels are effectively clearing the wear debris at the rate of debris production [60].

Joint fluid helps to transport wear particles to new sites, resulting in activation of osteoclasts and inhibition of osteoblasts via molecular signaling pathways involving a host of inflammatory mediators [61]. This phenomenon has also been called “particle disease” [58, 62]. The “threshold” of the periprosthetic lymphatic to effectively clear wear debris is subject to interindividual variability as well as on the volume of wear. This phenomenon may partially explain why some people develop adverse tissue reactions and early osteolysis in response to metal debris whilst others seem to have a mild or no reaction, assuming all other factors being equal [63].

Head size may be another factor which drives the predominant type of tissue response in one direction or another. It has been described that the MOM hip replacements with large heads have higher rates of pseudotumour development [63] Gill et al. reported corrosion at the neck-stem junction as an important source of debris leading to pseudotumour formation [39]. Cook et al. have reported pseudotumour formation due to tribocorrosion at the taper interface of large diameter metal-on-polyethylene modular total hip replacements [53]. Cooper’s group reported the occurrence of adverse local tissue reactions (ALTR) similar to those seen in MOM THAs. Corrosion at the head-neck junction in ten patients with metal-on-polyethylene total hip prostheses, from three different manufacturers

MOM articulations generate approximately 6.7×10^{12} to 2.5×10^{14} particles every year, which is 13 500 times the number of polyethylene particles produced from a typical metal-on-polyethylene bearing [64]. Despite this, the actual volumetric wear of a MOM articulation is lower because of the nano-scale size of the particles (generally < 50 nm), when compared with polyethylene particles, which are rarely less than 0.1 μm [65]. They showed that Co ions at a concentration of 0.1 mg/L (equivalent to 1.6 μmol/L) induced the death of osteoclast precursors after 2 weeks of co-culture [54]. Furthermore, there was a decrease in the area of resorbed dentine after 3 weeks, indicating a toxic effect of Co on bone marrow osteoclast precursors [66]. Toxicity of iron is also a significant issue. Large amounts of iron released from metallic implants can cause excessive levels of iron in the blood. High blood levels of free ferrous iron react with peroxides to produce free radicals, which are highly reactive and can damage DNA, proteins, lipids, and other cellular components. Iron typically damages cells in the heart and liver, which can cause significant adverse effects, including coma, metabolic acidosis, shock, liver failure, coagulopathy, adult respiratory distress syndrome, longterm organ damage, and even death if left untreated [61,62,67]. Nickel is known as a trace element in the body [68]. The biological role of nickel as an essential trace element was not recognized until the 1970s [29]. Nickel exists in urease, an enzyme that assists in the hydrolysis of urea. In blood, nickel is mainly bound to the albumin fraction, but also to some other proteins of serum [69].

Molybdenum is also known as a trace element in the body. Molybdenum is an essential trace element for a number of enzymes important to cellular metabolism. The most important enzymes that require molybdenum are sulphite oxidase, xanthine oxidase, and aldehyde oxidase. Sulphite oxidases catalyze the oxidation of sulphite to sulphate, which is involved in the metabolism of sulphur-based amino acids. Sulphite oxidase deficiency or absence leads to neurological symptoms and early death. Xanthine oxidase catalyses oxidative hydroxylation of purines and pyridines including conversion of hypoxanthine to uric acid. Aldehyde oxidase is responsible for oxidizing purines, pyrimidines and pteridines, and is also involved in nicotinic acid metabolism. Low dietary molybdenum leads to low urinary and serum uric acid concentrations and excessive xanthine excretion [68]. Molybdenum is also present within human tooth enamel and may help prevent its decay [68], associated with increased rates of esophageal cancer in a geographical band from China to Iran [70], possibly due to low soil levels that end up in crops. Compared to the United States. Toxicity of molybdenum. Molybdenum is much less toxic than many other metals (e.g. Co, Cr and Ni) of industrial importance. Molybdenum does not constitute a hazard to human beings either in trace concentrations occurring in environmental pollution, or from exposure to higher concentrations encountered in industrial processes and applications [71,72].

Studies on the concentrations of chromium, cobalt and molybdenum in patients with MOM total hip replacement and hip resurfacing arthroplasty have shown that the level of molybdenum in serum is generally low, compared with Cr and Ni. So far, no data are reported on systemic toxicity of molybdenum in connection to metallic implants [49,73].

Local tissue reactions are also of great importance. In patients with MOP bearings aseptic loosening is thought to be due to the response of macrophages to particulate wear debris. By contrast, particles from MOM bearings have a limited capacity to activate macrophages and may cause osteolysis by some immunological reaction involving hypersensitivity [38,74]. The pattern of inflammation in the peri-prosthetic tissue of loose MOM articulations is significantly different to that of metal-on-polyethylene articulations, and is characterised by perivascular infiltration of lymphocytes and the accumulation of plasma cells [75]. Experimental data suggest that orthopaedic metals induce immunological effects which support a cell-mediated hypersensitivity response [75]. It has been documented that the size, shape, number and nature of the particles released from the articular surfaces of prostheses are responsible for the type and extent of the biological response [76]. For the MOP prostheses, most of the particles are in the micrometer range with few in the submicron size, which corresponds to the size of bacteria [77]. Polyethylene particles have been shown to elicit a foreign-body, granulomatous response simulating infection, which is non-specific and consists mainly of macrophages and fibroblasts with occasional lymphocytes [54]. Co-Cr particles have an effect on cells that is different to that of poly-ethylene and most other biomaterial. Particles are commonly phagocytosed by macrophages. Once phagocytosed, Co-Cr particles can be toxic and rapidly kill the cells. This is probably because they corrode quickly within the cells, owing to the acidic environment in the phago-lysosome—and release ions in high concentrations within the cells, leading to toxicity. The cells will then lyse, releas-ing the particles and cell contents to cause further damage [78].

8. Clinical Trials

Clinical results of cementless total hip arthroplasty with shortening osteotomy have shown that for preventing both prosthetic micro motion and fibrous tissue around the stem in cementless implants, initial fixation of the femoral part is essential and mechanical strength of the cancellous bone causes a suitable cortical rim fit of the components. To achieve a secure fixation of the cups, additional fixation with screws should be performed. When the porous surface in HA coated stem is kept in the metaphyseal and upper metaphyseal of the femur more cortical bone interface have been achieved and this design allows distal loading. It has been reported [70] that 40% aseptic loosening for femoral stems at an average of 16 years follow-up and some reports regarding the increase in stress shielding with increased stem diameters [41] which may lead to stem loosening. However in some controversial studies [79] severe stress shielding with larger distal was not observed. On the contrary, in some studies [39, 68], delayed union of the osteotomy site has been reported. However, osseointegration process of the osteotomy site generally takes less than six months [63]. It takes longer with cemented stems due to the presence of the cement in the medullary cavity which degenerates endosteum and decreases number of bone marrow cells. In a recent study [79], cementless hip arthroplasty components showed suitable performance and patients had satisfactory clinical and radiographic results. When Femoral stem structure can fit to larger canals, cortical contact at the distal femoral stem-cortical bone interface will appeared and may lead less osteolysis distally without causing significant delay of union at the osteotomy site. Meanwhile, meta-analysis for comparing clinical and radiographic outcomes of ceramic on ceramic (COC) and MOP hip implants have shown that COC decreases the risks of revision, osteolysis, aseptic loosening and dislocation, but also increases the risks of squeaking and intraoperative ceramic fracture comparing with MOP. In the end COC bearing surface has been suggested [80]. Because of the increasing popularity of dual-mobility cups in total hip arthroplasty, it is necessary to know that which of implant-specific features or tissue response may increase the risk of intra-prosthetic dislocation that is the major importance for reduced revision rates by using optimized surgical techniques and implant designs. A kind of wear pattern in the capture area of the femoral stem and a frequent impingement between the neck and the retentive rim has been reported [63, 67]. Another wear pattern seen on retrievals is an asymmetric degradation of the retentive rim due to liner tipping under gravity or various tilting, respectively [43]. In some cases, dislocated polyethylene liners showed eccentric wear at the inner sliding surface [62, 63]. These various intra-operative findings clearly indicate that more than one mechanism can lead to intra-prosthetic dislocation. Peri-operative findings indicate extensive fibrosis at the large articulation as well as cup loosening as potential causes for the intra-prosthetic dislocation. In addition, the failure mechanism is affected by the surface topography of the femoral neck and in particular by the design of the dual-mobility system [81].

Studies showed that in the first decade of use, patient selection, techniques of surgery, the way of fixation and metal bearing parameters had an important effect on failure rates. In all studies, the best survivorships were in patients with larger femoral component sizes that they were interestingly males. In all studies it was shown that activity levels in patients were as good as a total hip arthroplasty. The effect of component size in hip resurfacing on area of fixation as well as the wear characteristics of the bearing was significant. smaller component failed sooner because of their smaller area of fixation that undermined more rapidly by the osteolytic process and it can has the risk of fracture and loosening and it’s the cause of maintenance of a proper fluid film lubricant for achieving optimal wear properties which is referred to as arc of cover or contact patch rim distance. Lucency [82] studies also showed that neck narrowing was occurred about 3% and 4.7% and it’s not clear if they are because of osteolytic response to metal wear debris or to stress-shielding. Loosening of the acetabular component was the most frequent reason for revision in patients. Mismatch of elasticity modulus between the monoblock cobalt–chromium socket and the host bone make the high prevalence of acetabular component failure but another reason may be the lack of initial fixation and osteoinegration of the porous beaded cobalt chromium interface. Studies [82] also showed that the Birmingham Hip Resurfacing (BHR) acetabular component with hydroxyapatite coating has a very good long-term survivorship by both the designer surgeons and other independent centers. The risk of vascularity to the femoral head with the approach of cutting the deep branch of the medial circumflex femoral artery is unavoidable. This puts the femoral neck at risk of femoral neck fracture due to osteonecrosis and subsequent weakening of the bone. In conclusion, early clinical experience with the Conserve Plus hip resurfacing has showed that it to be a safe and reliable implant with low risk of adverse tissue reaction. Also, intra-operative radiographs could help in showing a useful adjunct to minimize poor placement of the acetabular component.

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