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SEPPO SANTAVIRTA

Compatibility of the Totally Replaced Hip

Reduction of Wear by Amorphous Diamond Coating

Doctoral dissertation

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ABSTRACT

During the more than four decades since introduction of the original low-friction arthroplasty of the hip by John Charnley, the fixation, loosening, wear, and longevity of the artificial hip have been subject to extensive studies. The present thesis shows that particulate wear debris in totally replaced hips causes adverse local host reactions. Further, the extreme form of such a reaction, aggressive granulomatosis, was found to be a distinct condition and different from simple aseptic loosening. Reactive and adaptive tissues around the totally replaced hip were made of proliferation of local fibroblast like cells and activated macrophages. Methylmethacrylate and high-molecular-weight polyethylene were shown to be essentially immunologically inert implant materials, but in small particulate form functioned as cellular irritants initiating local biological reactions leading to loosening of the implants. Chromium-cobalt-molybdenum is the most popular metallic implant material; it is hard and tough, and the bearings of this metal are partially self-polishing. In total hip implants, the two key issues which are prerequisites for longevity of the replaced hip are good biocompatibility of the materials and sufficient tribological properties of the bearings. The third key issue is that the bearing must minimize frictional shear at the prosthetic bone-implant interface to be compatible with long-term survival. Some of the most recent approaches to meet these demands are alumina-on-alumina and metal-on-metal designs, as well as the use of highly crosslinked polyethylene for the acetabular component. In order to avoid the wear-based deleterious properties of the conventional total hip prosthesis materials or coatings, the present work included biological and tribological testing of amorphous diamond. Amorphous diamond was found to be biologically inert, and simulator testing indicated excellent wear properties for conventional total hip prostheses, in which either the ball or both bearing surfaces were coated with hydrogen-free tetrahedral amorphous diamond films. Simulator testing with such total hip prostheses showed no measurable wear or detectable delamination after 15,000,000 test cycles corresponding to 15 years of clinical use. The present work clearly shows that wear is one of the basic problems with totally replaced hips. Diamond coating of the bearing surfaces appears to be an attractive solution to improve longevity of the totally replaced hip.

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To Nina

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Helsinki 3.3.03
Seppo Santavirta

List of original publications

This thesis is based on the following original articles, referred to by Roman numerals I-X in the text.

I Santavirta S, Konttinen YT, Bergroth V, Eskola A, Tallroth K, Lindholm TS: Aggressive granulomatous lesions associated with hip arthroplasty. Immunopathological studies. J Bone Joint Surg 72-A:252-258,1990

II Santavirta S, Xu JW, Hietanen J, Ceponis A, Sorsa T, Konttinen YT: Activation of periprosthetic connective tissue in loosening of total hip replacement. Clin Orthop 352:16-24,1998

III Santavirta S, Konttinen YT, Bergroth V, Grönblad M: Lack of immune response to methylmethacrylate. Acta Orthop Scand 62:29-32,1991

IV Santavirta S, Konttinen YT, Lappalainen R, Anttila A, Goodman SB, Lind M, Smith L, Takagi M, Gómez-Barrena E, Nordsletten L, Xu JW: Materials in total joint replacement. Curr Orthop 12:51-57,1998

V Santavirta S, Takagi M, Gómez-Barrena E, Nevalainen J, Lassus J, Salo J, Konttinen YT: Studies of host response to orthopaedic implants and biomaterials. J Long-term Effects of Medical Implants 91:67-76,1999

VI Santavirta S, Böhler M, Harris WH, Konttinen YT, Lappalainen R, Muratoglu O, Rieker C, Salzer M: Alternative materials to improve THR tribology. Acta Orthop Scand, in press

VII Nordsletten L, Högåsen AKM, Konttinen YT, Aspenberg P, Aasen A, Santavirta S: Human monocytes are stimulated by particles of hydroxyapatite and silicon carbide, but not by diamond. In vitro studies of new prosthesis coatings. Biomaterials 17:1521-1527,1996

VIII Aspenberg P, Anttila A, Konttinen YT, Lappalainen R, Goodman SB, Nordsletten L, Santavirta S: Benign response to particles of diamond and SiC. Bone chamber studies of new joint replacement materials in rabbits. Biomaterials 17:807-812,1996

IX Santavirta S, Lappalainen R, Pekko P, Anttila A, Konttinen YT: The counterface, surface smoothness, and coatings in total joint prostheses. Clin Orthop 369:92-102,1999 (Also included in Dr. Panu Pekko´s PhD-thesis)

X Lappalainen R, Selenius M, Anttila A, Konttinen YT, Santavirta S: Reduction of wear in total hip replacement prostheses by amorphous diamond coatings. Applied Biomaterials, in press

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1 Introduction

More than four decades have passed since Charnley reported his clinical experience with total hip replacement in 1961. The system of Charnley´s original low-friction arthroplasty was based on polyethylene acetabular and metallic femoral components attached to bone with the use of methylmethacrylate. Today the number of total hip replacements done worldwide each year is over 800,000. From the beginning, this procedure was clearly more successful than several previous trials that failed because of poor design and often disastrous biocompatibility. The reported survivorship of Charnley low-friction arthroplasties ranged from 65% to 84% at 20 to 30 years (Callaghan et al 2000, Brown et al 2002). Early metal-on-metal McKee-Farrar total hip replacements have shown survivorship ranging from 53% to 89% at 10 to 15 years (Brown et al 2002). However, eventually it became clear that even in the best series, total hip components gradually tend to become loose, with aseptic loosening still the single most important complication of total hip replacement (Harris 1994). Close association seems to exist between wear rate and osteolysis in total hip replacement (Dumbleton et al 2002). The adverse effects of continuous mechanical loading in the loosening process have been emphasized, and for many years it was thought that methylmethacrylate and polyethylene debris were of a benign nature (Editorial, Lancet 1990). When periprosthetic osteolysis was first recognized, it was hypothesized that it was caused by a chronic low-grade infection. More recently it has become clear that extensive lysis also may appear around mechanically well-fixed total hip components in the clear absence of infection (Goldring et al 1983). With time, methylmethacrylate and especially its wear products were found to be the cause of local adverse host reactions toward the total hip replacement complex (Jones and Hungerford 1987). The wear-products also cause third body wear in the bearings (McKellop 1998). However, periprosthetic lysis soon was noticable also in the uncemented total hip replacements where the production of polethylene wear particles is similar to that in cemented total hip replacements (Santavirta et al 1991). It became clear that not only the periprosthetic synovial-like membrane but also the pseudocapsule contains biologically multipotent and active cells that produce chemical substances contributing to prosthetic loosening (Takagi 1996).

To date, many different materials have been tested to reduce wear and the generation of submicron-sized particles. Corrosion and ionic-type wear products are also important factors in the longevity of total joint replacement. At the same time, the implant materials have to undergo examination for their biocompatibility. For example, titanium, which commonly is used in uncemented total hip replacements, is very biocompatible in bulk form, but is at the same time soft and wears extensively, causing massive metallosis (Wright and Goodman 1995). Chromium-cobalt-molybdenum, although hard and

showing minimal wear, produces wear particles more toxic locally than those of Ti. Trials to improve methylmethacrylate cement have not been very successful, and many experiments with new polyethylenes and innovative designs have failed (Huiskes 1993).

Currently, several research groups study the material properties and tribology of total hip designs and materials. Simulator testing of new bearings (McKellop 1998), artificial aging of polyethylenes (Li and Burstein 1994), and Scandinavian hip registers (Herberts and Malchau 1997; Puolakka et al 1999) are examples of effective approaches to study materials and the function of total hip replacements. Predicting and evaluating the long-term performance of new or modified designs is a challenging subject at the forefront of orthopedic research today (Walker 2000). Clearly, metal-on-metal designs have become popular again (Schmalzried et al 1996), new highly cross-linked polyethylenes seem promising (Muratoglu et al 1999), and various coatings or surface treatments are undergoing experimentation (Lappalainen et al 1998). Regarding new materials, diamond coating of metallic components to reduce wear and to provide more biocompatible prosthetic surfaces has been shown to succeed.

Concurrently, the large Scandinavian national hip registers reveal that Charnley low-friction arthroplasty still has one of the best 10-year records in large populations. Great effort is required to improve a component that already is very good. Regarding the huge and still increasing numbers of total hip replacements at risk of becoming loose, research to improve the biocompatibility, tribology, and durability of total hip replacements seems worthwhile (Santavirta 1998). The hypothesis is that if amorphous diamond in particulate form, considering what is already known about biological THR loosening, appears to be inert and likely to cause only a low-grade host-response reaction, such material should be tribologically tested for THR coatings. Further, tribological studies should clarify the potential of such amorphous diamond coating for THR bearings.

2 Purpose of the study

This study program focused on the following topics with the aim to find relevant answers to each of the next questions:

- What is the biologic response to particulate wear debris from THR?
- What is the role of biocompatibility of conventional THR materials and their wear debris in implant loosening?
- Which materials can be safely used in THR prostheses?
- Can wear characteristics of THR bearings be improved?
- Is amorphous diamond biocompatible as THR material?
- Are the wear properties of the THR coated with amorphous diamond suitable for clinically applicable THR?

3 Materials and methods

Modern biological methods were used to study local host response to THR implants. Tribological tests, including simulator studies, were performed to analyze the preclinical performance of THR bearings. Materials and methods are summarized in Table I, with methodological details in the original publications included in this thesis.

Table I Materials and methods used in separate studies I to X.

Original publication	Materials	Methods
I	Interface tissue samples obtained from revised THRs	Immunohistochemistry for inflammatory cells
II	Interface tissue samples obtained from revised THRs	Immunohistochemistry for inflammatory cells, Ki-67 staining
III	Fine pulverized methylmethacrylate	Human lymphocyte cultures, 3H-thymidine incorporation, immunocytochemistry
IV	Our previous studies and pertinent literature regarding THR materials	Analysis and review
V	Our previous studies and pertinent literature regarding host response to THR materials	Analysis and review
VI	THR bearings	Tribological techniques
VII	Particulate hydroxyapatite, silicon carbide and amorphous diamond	Human monocyte cultures, immunocytochemistry
VIII	Particulate diamond	Bone-harvesting chamber studies in rabbits
IX	Diamond-coated versus conventional THR bearings	Tribological techniques
X	Diamond-on-diamond THR bearings	Hip-simulator tests

4 Results

The general results are summarized in Table II. Detailed results appear in the publications included in this thesis.

Table II Main conclusions of studies I to X THR materials

Original publication	Main results
I	Aggressive periprosthetic granulomatosis is a mainly monocyte-macrophage-dominated adverse foreign-body-type tissue reaction with fibroblastic reactive zones.
II	Around loose THRs, more cell-rich areas and a higher number of activated cells were detectable than around well fixed implants.
III	Methylmethacrylate is immunologically essentially inert.
IV	Cobalt-chromium alloys, methylmethacrylate and polyethylene are still the basic THR materials, showing biologically and tribologically acceptable function.
V	Theoretical and experimental testing is mandatory before introducing new implant materials in a clinical setting.
VI	Metal-on-metal, alumina-on-alumina, and highly cross-linked polyethylene bearings improve tribological properties of THRs.
VII	Diamond particles in a serum-free human monocyte culture are inert, whereas SiC has a stimulatory effect comparable to that of hydroxyapatite.
VIII	SiC and diamond particles were harmless and caused no reduction in bone formation in the bone-harvesting chamber.
IX	Diamond-coated THR bearings offered superior stability and good tribological performance in comparison to any previous THR bearings.
X	After 15,000,000 simulator cycles, diamond-on-diamond THR bearings show no delamination nor measurable wear.

5 Discussion

5.1 Background

The concept of Charnley´s original low-friction arthroplasty was based on ultrahigh molecular-weight polyethylene acetabular and metallic femoral components, which were attached to bone with the use of methylmethacrylate. From the beginning, this procedure was clearly more successful than several previous trials that failed because of poor designs and unhappy choice of materials. However, with time it became clear that even in the best series, total hip components gradually tend to become loose, and aseptic loosening still remains the single most important complication of total hip replacement (THR). Wear of articulating and nonarticulating surfaces of the prostheses and of the cements used for fixation, as well as biological and mechanical damage caused by, among other things extensive continuous cyclic loading of the implants cause loosening over a long period of time. Understanding of the biological- and material-related physical processes occurring in the totally replaced hip form the basis of attempts to improve the currently existing level of THR. The goal of this thesis was to clarify the adverse response to particulate wear debris and learn how this response might be mitigated. Further, the ultimate goal was to produce a nonwearing and highly biocompatible THR prosthesis. The present discussion briefly reviews studies I to X on which this thesis is based.

5.2 Aggressive granulomatous type of loosening

In order to better understand the process of aseptic THR loosening, we focused our interest in 1989 on the aggressive granulomatous type of loosening. At that time, aggressive granulomatosis around cemented THRs had been reported among others by Harris et al (1976), Jasty et al (1986) and Tallroth et al (1989). All these reports confirmed that in some patients aggressive granulomatous lesions may lead to rapid bone lysis around apparently stable cemented arthroplasties in the clear absence of infection and sepsis or of primary mechanical failure (Carlsson et al 1983). We found that 4.6% of our revision THR arthroplasties showed radiographic evidence of these lesions. At that time the cause of aggressive granulomatous lesions was debatable. Today, much knowledge has accumulated but the actual reason why in some THRs this process is

initiated and in others not is still to be found. Harris et al (1976) suggested that cement mantle fragmentation and failure of implant fixation should be blamed, but our results (I) contradict this. Wear of cement caused by micromotion and patient-specific hypersensitivity were at that stage considered hypothetical trigger mechanisms. Goldring et al (1983) had pointed out that the synovial-like biomembrane around the cement was active in production of bone resorption mediators such as prostaglandins and collagenases. In our series, the speed of growth of aggressive granulomas was unpredictable; some doubled in size during only a few months. Pain is the first clinical sign of aggressive granulomatosis. When pain has developed, the granola may be large, even though the prosthesis may still be well fixed. Fragmentation of the cement allows deleterious penetration of the wear particles deep into the interface tissue.

In early reports describing histology of aggressive granulomatous lesions (Bell et al 1983, Goldring et al 1983), these granulomas were reported to include histiocytes of various sizes and numerous giant cells. In order to trace the reason for aggressive granulomatosis, we performed immunopathological studies (I).

Immunohistological evaluation revealed that most cells in the aggressive granulomatous tissue were multinucleated giant cells and C3bi-receptor and nonspecific esterase-positive monocyte-macrophages. Aggressive granulomatosis leads to a relative paucity of fibroblast-type cells. This cytological finding suggests a foreign-body-type reaction compatible with the rapidly progressive lytic nature of the lesion, which was shown radiologically in Study I. It appeared evident that granulomatosis involved an uncoupling of the normal sequence of the monocyte-macrophage-mediated clearance of foreign material and tissue debris that is normally followed by fibroblast-mediated synthesis and remodeling of the extracellular matrix (Konttinen et al 1988). What might the foreign material debris be, which irritates the monocyte-macrophages? Charnley (1975, 1979) studied the tissue reaction around cemented prostheses using conventional histology methods and concluded that methylmethacrylate cement was relatively inert, causing little tissue reaction in the well-fixed THR. Among others, Jones and Hungerford (1987) suggested that aggressive aseptic loosening of THR prostheses may be caused by methylmethacrylate cement; this process was called the "cement disease".

One of the problems with aseptic loosening is that on each occasion some part of the original bone stock is destroyed. In multiple revisions, a common and feared complication is the loss of periprosthetic bone substance (Amstutz et al 1982). As we analyzed our patients´ outcome after multiple THR revisions, we found good primary results but major loss of periprosthetic bone (Wirta et al 1995). Consequently we started to revise loose THRs using cementless implants. With time, we noticed that this did not completely solve the problem. Clearly, there appears to be a need to improve THR technology to reduce wear and loosening.

5.3 THR as a pseudojoint

After surgery, the THR complex is gradually organized into a jointlike space, often referred to as a pseudojoint. Histologically, this pseudojoint shows signs of organization

into synovial-like structures with a lining cell layer of fibroblastlike and macrophagelike cells which grow directly on loose connective tissue (Santavirta et al 1991). This synovial cell layer also produces hyaluronate and releases it into pseudosynovial fluid, where it is found in concentrations far exceeding those of peripheral blood and resembling concentrations observed in synovial joints (Saari et al 1993). Local proliferation of fibroblasts and vascular endothelial cells in periprosthetic tissues may reflect healing and active tissue remodeling in the so-called pseudocapsule of the artificial joint, whereas activation of the same cells in the interface tissue between implant or implant-cement-complex and bone may reflect local connective tissue activation caused by foreign bodies or cyclic loading or both (Jiranek et al 1993, Kim et al 1993, Goodman 1994). Cytofluorographic studies have implied that cells synthesizing DNA are significantly more numerous in such tissues (Santavirta et al 1990). To assess the eventual activation and proliferation of local cells in periprosthetic tissues in loose THRs, samples of such tissue were stained with specific antibodies directed against a cell proliferation marker known as Ki-67 antigen (Brown and Gatter 1990) (II). The fibrous areas and, in particular, the cell-rich vascular areas of the interface tissue (between implant and bone) and the pseudocapsule around aseptically loosened implants contained higher numbers of proliferating cells than did the tissues around well-fixed implants. In addition, the pseudosynovial lining occasionally contained some Ki-67-positive proliferating cells. It became clear that reactive (interface tissues) and adaptive (pseudojoint capsule) tissue changes occurr in loosening THRs which result from proliferation of local fibroblastlike cells. These activated mesenchymal tissues, however, showed no malignant changes.

5.4 Cement disease?

Methylmethacrylate is one of the most common materials implanted in man. Earlier histologic studies of human retrieval samples (Charnley 1979, Linder and Hanson 1983) and of animal-experiments (Draenert 1981) have demonstrated that long-lasting close contact between cement and bone may be achieved without signs of tissue irritation. However, at that stage, research regarding immunocompatibility of methylmethacrylate cement was based on indirect evidence. We therefore analyzed whether or not finely pulverized methylmethacrylate in human peripheral blood lymphocyte cultures was immunologically inert (III). Phytohemagglutin (PHA) lectin, purified protein derivate of tuberculin (PPD) antigen, or culture medium alone served as positive and negative controls on study days 0, 1, 3 and 5. Major histocompatibility complex locus II antigen (MHC locus II antigen;Ia) and interleukin-2 receptor (IL-2R);Tac) expression were analyzed by the ABC method, and lymphocyte DNA synthesis by 3H-thymidine incorporation and beta-scintillation counting. The results suggested that although methylmethacrylate is essentially an immunogically inert implant material, it seems, however, to induce inflammatory mononuclear cell migration and adhesions, leading to a slightly nonspecific lymphocyte and macrophage reaction (Wimhurts et al 2001). The nonimmunological type of monocyte activation which we detected may also be

responsible for the cellular profile observed in periprosthetic tissue in THR loosening (Brooks et al 2000).

5.5 Cemented versus cementless hip arthroplasty

Because of increased numbers of loosened cemented arthroplasties, it became popular to perform primary and revision THR arthroplasties without the use of methymethacrylate cement (VI). Some surgeons still considered that the adverse effects of mechanical loosening to be overemphasized, and for many years it was thought that the polyethylene and methylmethacrylate wear debris was of benign nature (Wroblewski 1979, Editorial, Lancet 1990). In Finland, the cementless THR became the common clinical choice in the 1980s, and its primary clinical success was good. Because of poor design, such as threaded acetabular cups, after a few years these prostheses usually failed. The threaded cups were later replaced by press-fit components, but in some designs the locking mechanisms between metallic component and polyethylene liner were insufficient. Moreover, in small cups the thin polyethylene liner fractured easily. In cementless titanium based THRs also articulating titanium-based balls were used in the early period. This caused excess metallic and polyethylene wear, which accelerated the loosening process (Agins et al 1988). The elasticity modules of different metals and bone were also quite different, which in cementless THR, made true bonding of the whole implant surface and bone practically impossible. Today, we know that some of the cementless stems have been very successful (Lord et al 1988), but the different cementless acetabular components have usually had shorter survival times than have their cemented counterparts, a fact shown in several Scandinavian implant register studies. It also became clear that better preclinical studies were necessary before introducing any new THR designs into clinical use.

In order to improve cementless fixation, hydroxyapatite coating of the implant surface (often titanium) was considered the method to improve bonding between implant and bone. Hydroxyapatite is very biocompatible, but easily becomes delaminated from the implant and then pulverized into small-particle wear debris (Santavirta et al 1991). Experimental and developmental work has now improved the quality of hydroxyapatite coatings, and the newer hydroxyapatite-coated THRs probably produce a solid and long-lasting bonding to bone.

Lord et al (1988) and Santavirta et al (1990) reported adverse bone reactions leading to loosening in cementless THRs meaning that not only methylmethacrylate could be blamed for granulomatous lesions or common aseptic loosening. In clinical interface and pseudocapsular samples, CD11b- and CD68-positive cells dominate the cellular reaction mainly caused by polyethylene-wear debris (Santavirta et al 1993,A). In human lymphocyte cultures, polyethylene debris behaves very much as does methylmethacrylate; the material seems to be immunologically biocompatible but causes a foreign-body type reaction which may be more severe than from methylmethacrylate because the particles are frequently of submicron size and the shape may be very irregular.

5.6 Matrix metalloproteinases in THR loosening

Histological evidence exists that a monocyte/macrophage reaction against implant wear particles (methylmethacrylate, polyethylene, metallic, ceramic) may precede the instability and sometimes may be the primary cause of loosening (Willert et al 1996, Pazzaglia et al 1988, Pazzaglia 1990). Macrophages have been shown to produce interstitial collagenase identical to fibroblast collagenase (Konttinen et al 1991). This is suggestive of an attempt by the local phagocytic and secretory macrophages to respond to the stimulus initiating the adverse tissue reactions complicating both cemented and cementless THR arthroplasty (Santavirta et al 1993,B). It appeares likely that interstitial collagenase contributes to the sometimes rapid growth of reactive infiltrative tissue connected with loosening of the THR prosthesis. Blood and healthy tissues contain tissue inhibitors of matrix metalloproteinases (TIMP). The aggressive periprosthetic granuloma formation occasionally occurring is apparently the result of an imbalance between collagenase- and TIMP-production controlling mechanisms. Particle generation from wear of the prosthesis also plays a significant role as an inducer of nitric oxide synthase and cyclooxygenase 2 (Hukkanen et al 1998, Suh et al 2002).

We hypothesized that aseptic loosening of THR implants is usually a result of cyclic mechanical loading combined with biological responses in which proteolytic enzymes play an important role (Takagi 1996). Because extracellular matrix degradation in vivo occurs in the extracellular space at neutral pH, the extracellular proteinases, which are active at physiological pH, are important in the cascade of connective-tissue degradation both in normal and in pathological tissues. Type IV collagens are digested by gelatinase/type-IV collagenases (MMP-2/72kDa and MMP-9/92 kDa) as our studies showed (Takagi et al 1994). Zymographic and densitometric analyses revealed elevated production of MMP-2 and induction of MMP-9 in tissue extracts from both the interface tissues and the pseudocapsular tissues around loose THRs. The level of MMP-9 was higher in the former than in the latter. The pseudocapsular tissue reactions may contribute to prosthetic loosening via the production and release of matrix metalloproteinases into the synovial fluid. The pumping mechanism created by cyclic loading leads the fluid to the interphase space between bone and implant/cement complex, and through cracks in the cement, the fluid may penetrate even further.

During our studies, techniques for research on matrix metalloproteinase activity in the context of THR loosening developed rapidly. It became clear that an excess of matrix metalloproteinases, including MMP-1, MMP-2, MMP-9, MT-1 MMP, and possibly MMP13, plays an important role in the periprosthetic weakening, contributing to aseptic loosening and osteolysis around loose THRs (Takagi et al 1998). This understanding is essential if attempts are made biologically or chemically to reduce local periprosthetic matrix metalloproteinase activity.

5.7 Materials in total hip replacement

Total joint replacement is one of the most efficacious and cost effective procedures in surgery. However, issues concerning the optimal materials for THR have been of a major concern. Materials chosen must be biocompatible (both the material itself and any breakdown products), strong, resistant to fatigue, wear, and corrosion, easily accessible and reasonably priced (IV,V). For many years, the material chosen by John Charnley in the early 1960s (namely stainless steel, polyethylene, and methylmethacrylate) remained the "gold standard" for comparison (Charnley 1972). More recently, the trend has been toward modern joint prostheses employing one of the newer metallic alloys of cobalt-chrome or titanium. In general, these newer alloys are stronger and more corrosion- and wear-resistant than stainless steel (Wright and Goodman 1995). Such theoretical benefit, however, has to be seen in improved clinical outcome. Papers IV and V review our and other researchers´experience regarding currently used THR materials.

5.7.1 Stainless steel

Improved stainless steels are still used in current THR designs as the major load-bearing joint (Cook 1995). These steel materials are iron-based alloys containing appreciable amounts of chromium, nickel, and molybdenum. Stainless steel is usually annealed, cold-worked, or cold-forged to improve alloy strength. A potential problem is the relatively high modulus of elasticity of stainless steel, which is about 200 GPa. This value is about 10 times the figure for bone. Methylmethacrylate mitigates the stress-shielding effects of stainless steel, which is still quite a suitable THR material in cemented prostheses and paired with cobalt-chromium or ceramic head. In the body, stainless steel like all metallic THR materials, is subject to different types of corrosion. For example, taper fretting and corrosion are as a rule found in revised modular hip prostheses (Goldberg et al 2002).

5.7.2 Cobalt-chromium alloys

Cobalt-chromium alloys. stronger and more corrosion-resistant than stainless steel, are usually composed of 30 to 60% cobalt, 20 to 30% chromium, and 7to 10% molybdenum, and various amounts of nickel (Gibbon 1982, Cook 1995). Heat and pressure improve the strength of these alloys. Their modulus of elasticity is slightly higher than that for stainless steel (250GPa), and with cobalt-chromium alloy based THR implants, cement fixation modulates the different elasticity modules of bone and implant. Prosthetic fractures are rare. Stress shielding of the periprosthetic bone is also a potential problem, especially when the material is used for a cementless femoral component. Currently

cobalt-chromium alloy-based metal-on-metal total hip prostheses have again become popular (Rieker and Köttig 2002). Although cobalt-chromium alloys are hard and tough, there is constant metal release from prosthetic articulations based on these metals (Saikko et al 1998). In fact.dissemination of such metal particles to the liver and spleen has been reported even in the case of well-functioning prostheses (Urban et al 200). Recent research shows that cobalt ions influence the proliferation and function of human osteoblast-like cells (Goodman et al 1995, Anissian et al 2002). Cobalt-chromium alloy-based metal-on-metal THR designs were popular in the early phase of modern THR surgery. In the 1990s such designs have been improved, and clinical experience is generally good (VI).

5.7.3 Titanium alloys

Titanium alloys have become popular in THR components designed for cementless fixation. Ti- 6Al- 4V is a common alloy composed of approximately 90% titanium and almost equal parts of aluminum and vanadium. Titanium alloy is strong and corrosion-resistant, and has a modulus of elasticity (110 GPa) about half of that of stainless steel and cobalt-chromium. Theoretically, stress shielding should be less with a material having an elasticity modulus closer to that of the bone. The wear characteristics of titanium can be improved by surface treatment processes such as ion implantation, but such a surface tends to wear out very soon, and it has become clear that titanium is not suitable as an articulating component. The titanium femoral stem should be paired with head of cobalt-chromium or ceramic. Some newer titanium alloys such as Ti-13Zr-13Nb are even stronger than conventional titanium alloys and have a lower modulus of elasticity. Evidence exists that titanium may be less suitable for cemented fixation. For such use, it should probably be at least highly polished and preferably coated with a ceramic surface. There is some evidence that commercially pure titanium and titanium-based alloys may favor bone apposition and ingrowth to a greater degree, than cobalt-chromium alloys (Johansson 1991). On the other hand, titanium particles have a stimulatory effect on resident macrophages (Soloviev et al 2002). The future of THR technology is to a great extent dependent on correct choice of metallic materials (Wright and Goodman 1995).

5.7.4 Polyethylene

The THR debate in the 1990s has been focused on polyethylene wear, because increasing numbers of otherwise successful total joints have failed. The material of choice is ultra-high molecular-weight polyethylene (UHMWPE) (Santavirta et al 1993,A). The industrial production of basic UHMWPE powder involves very few manufacturers. The molding processes and recently the use of irradiation to produce more crosslinked UHMWPE surfaces both vary. In the molding process, UHMWPE powder is

heated above its melting point. Any time UHMWPE reaches an elevated temperature, the potential arises of alteration in its physical properties.

Oxidation of the polyethylene has been reported in retrieved implants as well as in new components after gamma sterilization (Li and Burstein 1994). The shelf-life of UHMWPE acetabular components has an important effect on their later wear properties (Gomez-Barrena et al 1996). Average wear in the cup is still between 0.1 and 0.2 mm/year. At least the early wear of the new highly crosslinked UHMWPE components seems clearly less (VI). The wear of polyethylene has been linked with the biological and clinical THR loosening processes (III, V). The presence of particulate polyethylene is known to be sufficient to cause an aggressive periprosthetic tissue response and in the case of an unstable interface prevents the formation of new bone (Bechtold et al 2002). Any means of reducing or totally avoiding wear for polyethylene is very important. This can be achieved by developing better polyethylenes, by tribologically better femoral heads or better prostheses, for example of metal-on-metal and alumina-on-alumina types. Each design has its advantages but also drawbacks. A prosthetic system showing little wear easily becomes too rigid or shows inferior shock-absorbing properties.

5.7.5 Ceramics

Ceramics in THR are classified into materials that are bioinert (alumina and zirconia) or bioactive (hydroxyapatite and glass ceramics). The bioinert ceramics are suitable as femoral head material and hydroxyapatite as a coating material in cementless prostheses. The wear products are abrasive and easily destroy the bearing surfaces, resulting in excessive wear. Recent work has shown that alumina-on-alumina bearings are a good alternative, and also improve the tribological properties of the THR (VI). Ceramic coating of the bearing surfaces is possible (such as with amorphous diamond). In the case of delamination of such surfaces, the particles created may, however, irritate the periprosthetic tissues.

5.7.6 Diamond

In human monocyte-culture studies, diamond particles appear quite inert (VII). In order to further study the biocompatibility of diamond in bone, we applied the bone-harvest chamber method in rabbits as introduced by Albrektsson et al (1984) and previously used for a similar purpose among others by Goodman (1994) (VIII). Our results, compared to relevant previous results indicated that methylmethacrylate, polyethylene and cobalt-chromium caused a clear reduction of bone formation, whereas, neither diamond nor SiC particles caused any such reduction in bone formation. It appeared that particles of diamond and of SiC were comparably harmless when inserted into bone. SiC whiskers can be used to improve adhesion between coating and substrate and guarantee extreme adhesion even in the case of the high internal stresses

characteristic for amorphous diamond coatings with a high sp^3 fraction of diamond bonding (Anttila et al 1995).

5.8 Registers

Methylmethacrylate (III) is still the basis of fixation in most THRs (Santavirta et al 1992). With improved cementing techniques, the 10-year survival results of the best cemented THR prostheses in the Scandinavian THR registers are better than 90%. With the help of such registers it has become easier to follow the survival trends of different THR designs and materials. Such registers do not, however, replace prospectively planned clinical studies.

5.9 Testing of materials

Studies of the host response to orthopedic implants and biomaterials have become very important in preventing clinical failures (V). To date, many different materials have been tried in attempts to reduce wear and generation of macrophage-irritating submicron-size particles or to provide more biocompatible materials. However, trials to improve the methylmethacrylate cement or to invent better polyethylene have often failed. Diamond coating of the metallic components seems promising: less wear occurs and diamond is very compatible both in bulk and in small particulate form. Extensive biological and mechanical testing is, however, necessary each time new materials and designs are planned (Goodman et al 1998).

Regarding in vitro tribological studies of total hip bearings, a variety factors influence the action of wear mechanisms (Wimmer et al 2001). For example, the effects of lubricants on the friction of total hip prostheses is very important, and nonbiological lubricants should not be relied upon in tests of new designs of total hip prosthesis bearing surfaces (Scholes et al 2000). Diluted bovine serum is currently universally accepted as the test lubricant.

Since wear debris probably causes many of the harmful processes involved in prosthesis loosening, there appears to be a definite need for a prosthetic material that has more optimal wear characteristics than the traditional materials. Currently we are working on the development of a THR prosthesis with amorphous diamond coating deposited using a novel pulsed plasma acceleration method (Anttila et al 1997).

5.10 Biocompatibility of diamond

In the case that diamond would be applied as a THR coating material, it had to be tested for biocompatibility issues. Huiskes (1993) and Harris (1994) have warned for failed innovations and have pointed out the need for profound laboratory testing of new materials. Hydroxyapatite (HA), an established THR coating material, is generally accepted as very biocompatible (Goodman 1993). Material scientists have discussed the need to strengthen the diamond coating with SiC whiskers to improve adhesion. To this end, we decided to test the biocompatiblity of these materials in small-particle form in human monocyte cultures (VII). In macrophage-particle interaction, the size, composition, and surface area are of importance (Shanbhag et al 1995). Mainly, particle sizes were for each material from 2 to 5 microns. All particles were phagocytozed, and monocyte morphology changed, except after the ingestion of diamond. Interleukin-1beta production was on average 30-fold and 38-fold in cultures exposed to HA or SiC, respectively, the production in control and diamond cultures. In some cultures, methylmethacrylate was also included, and its stimulatory effect on interleukin-1beta production was in the same range as with HA or SiC. These results clearly showed that diamond particles in a serum-free monocyte culture were inert, whereas HA and SiC had a stimulatory effect comparable to that of methylmethacrylate. Because of its excellent tribological and biocompatible properties, further studies of diamond coatings are warranted.

The bone-harvest chamber in rabbits as described by Albrektsson et al (1984) has proven to be a suitable method for testing the biocompatibility of orthopedic implant materials. Studies on cobalt-chromium alloys, polyethylene, hydroxyapatite, and methylmethacrylate have appeared, and their results serve as controls for future tests (Goodman 1994, Goodman et al 1995). We dispersed particles of diamond and SiC in hyaluron and introduced this to a canal traversing the implant (VIII). Tissue that entered this canal during the following 3 weeks was then harvested. In previous studies, each of these THR materials induced an inflammatory reaction and reduced new bone formation. In the present study, neither diamond nor SiC had any adverse effect on bone formation. It appears that particles of diamond and SiC are comparatively harmless in bone.

5.11 Tribological considerations

Proper counterface material combinations, surface finish, and tolerances of contact surfaces are important issues in minimizing friction, wear, and corrosion of THR prostheses (Saikko et al 1993). The new highly crosslinked polyethylenes, alumina-on-alumina and metal-on-metal bearings are well-functioning solutions available to improve tribological properties (VI). We studied the potential of novel amorphous diamond coatings (Anttila et al 1997, Lappalainen et al 1998), to solve some current problems in THR prostheses by using tribological tests with a hip-joint simulator and pin-on-disk testers (McKellop 1998). According to our hypothesis, a diamond coating can be used on any metallic THR material, such as stainless steel, in the bearings. A diamond-coated

femoral head can be paired with a polyethylene acetabular cup or a metallic cup, preferably also coated with a diamond layer.

In this study, "amorphous diamond coating" refers to a hydrogen-free tetrahedral amorphous carbon film prepared with physical vapor deposition methods (Anttila et al 2001). Such films are extremely hard, show a low coefficient of friction and have no open corrosion paths to the substrate. Moreover, since the deposition temperature is relatively low, these coatings do not suffer from thermally induced stress. Based on our tests, the wear of amorphous diamond was negligible compared with the wear of conventional hip joint materials and was 10,000 to 1,000,000 times as low (IX, X). The coefficient of friction of the diamond-coated artificial hip joint was 0.03 to 0.06 when tested in a saline solution with loads from 200 to 1000 kg for as many as 2 million cycles; friction remained stable throughout the tests. Methylmethacrylate (bone cement) is a typical source of third-body wear particles in cemented THRs. The wear tests showed that bone cement, containing hard ceramic particles of hydroxyapatite or zirconia, severely scratched cobalt-chromium alloy samples. These scratches accelerated the wear of softer counterpart materials, such as polyethylene, whereas diamond-coated samples remained unchanged. High quality amorphous diamond coatings offer superior stability (minimal wear-debris release in surrounding tissues) and good biomechanical performances, leading to longevity of the THR.

In order to plan a THR implant with theoretically minimal wear, we decided to test 28-mm and 35-mm femoral heads made of stainless steel (AISI3 16L) paired with a comparable acetabular cup and polished mechanically to give a typical surface roughness of 5 to 10 nm. An amorphous diamond coating was deposited on the bearing surfaces by the technique described by Anttila et al (1997). After deposition, clearance between ball and cup was about 100 microns. The wear-rate measured in a commercial 6-channel hip-simulator for 15 million walking cycles (comparable to 15 clinical THR years; Schmalzried et al 1998) with serum lubrication was negligible, i.e. 1,000,000-fold lower than in conventional metal-on-polyethylene or metal-on-metal THR pairs (McKellop 1998). The coatings remained smooth during the test and did not delaminate. It can thus be concluded that high-quality amorphous diamond coatings lead to markedly reduced wear in hip simulators.

6 Conclusions

The present studies and the cumulative work of other researchers indicate that the main total hip replacement systems are usually well accepted by the host and function well over a long period of time. Clearly, even in the best situation, the total hip implant complex represents a foreign body, and the bearings and other implant surfaces are all subject to wear. Thus, the following conclusions seem justified:

- THR loosening is a result of adverse biological reactions mainly initiated by implant wear products, in combination with mechanical cyclic loading (I,II)

- Conventional THR materials are usually very biocompatible in bulk form but their small particulate wear products cause foreign-body type cellular reactions (III,IV)

- In the THR, these wear-products irritate resident macrophages both in the interface and in pseudocapsular tissues, leading to excess production of several matrix metalloproteins, which are some of the important enzymes weakening the THR anchorage tissues (V)

- THR materials should show good biocompatibility characteristics both in bulk and in small particulate form, should be resistant to wear and corrosion, and should have reasonable elastical properties (to avoid stress-shielding) (V,VI)

- Amorphous diamond coating seems to be very biocompatible, and practically nonwearing, and provide the basis for increased longevity of the THR (VII,VIII,IX,X))

No single solution of a totally biocompatible, nonwearing, and durable total hip replacement yet exists but even small improvements in wear properties will, one hopes, result in reduced numbers for revision statistics. Amorphous diamond coating and the highly cross-linked new polyethylenes are currently the most promising innovations to improve the tribological properties of the totally replaced hip.

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