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INFLUENCE OF WEAR DEBRIS ON BEHAVIOUR AND BIOMECHANICAL PROPERTIES OF BONE–IMPLANT INTERFACE

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Abstracts. The aim of this paper is to describe the effects of wear particles, generated during articulation of the bearing surfaces of the total joint prosthesis on bone-implant interface. Submicron particles migrate into effective joint space and stimulate cells present in the fibrous tissue to release molecular signal. Cytokines activate the osteoclasts and in consequence bone loss may result. It weakens the bone-implant fixation and may cause aseptic loosening of the prosthesis.

Key words: wear debris, bone–implant interface, total joint replacemtnt.

1. Introduction

Millions of total joint arthroplasty surgeries are performed annually to improve quality of life of the patients by relieving pain and offering increased mobility by restoration of joint functions. However, often the total joint arthroplasty fails after few years, causing pain and reducing the joint range of movement. Finally a revision surgery is needed. The most common reason for such a surgery is loosening of the prosthetic components (cause of 66 % of hip revisions, 20 % of knee revisions and 40 % of shoulder revisions). The loosening is primarily due to formation of fibrous tissue layer around the implant, caused by mechanical and biological factors. Mechanical factors include implant micro-motion and the excess fluid pressure and velocity [47]. Bone osteolysis caused by wear particles is known as a biological factor contributing to the implant loosening [43]. Since causes about 74 per cent of all hip revisions are strongly related to wear debris – induced osteolysis [5], there is a strong need for studying the wear in total joint revision.

Wear particles are produced when the implant material is removed from the articular surface. It is a mechanical process; the stresses associated with surface damage exceed the strength of the material and particles are liberated. Generally, wear is proportional to load and sliding distance, and inversely proportional to molecular weight of polyethylene (PE). However, the wear process of an implant is complex and depends on numerous factors. The main ones are design factors including the geometry of prosthesis, loading, motion and lubrication conditions. Other factors affecting wear are related to the material (its properties, manufacturing process, sterilization method and atmospheric exposure that can lead to oxidative degradation), to the patient (weight, activity and bone properties) and are of surgical nature (positioning and fixation method).

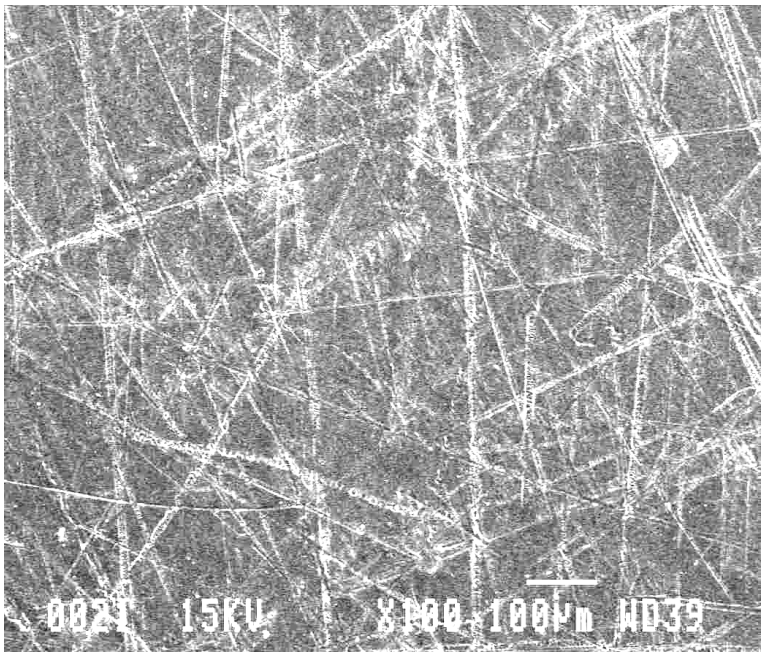

Fig. 1. Scratches of polyethylene surface of glenoid component.

This comprehensive paper focuses on the influence of wear debris on biomechanical properties of bone-implant interface. This is believed to be important for the late aseptic loosening.

2. Generation and migration of wear particles

In artificial joints, relative movements of bearing surfaces under high and cyclic joint loads results in generation of wear particles due to abrasive, adhesive and fatigue wear mechanisms [48].

Adhesive wear occurs when small portions of the polyethylene surface adhere to the opposing metal bearing surface and relative motion breaks the bond junctions and wear particles are generated. This generates small particles, usually of the weaker material, in the range from 0.1 to 10 ?m in diameter as well as thin sheets up to about 10 ?m in width. As a result of polyethylene removal, pits and voids appear on the articulating surface of the weaker component.

Abrasive wear occurs when the plastic surface is cut by hard asperities of the metal surface or by third body particles (i.e. metal, acrylic cement, or bone). The harder surface scratches (Fig. 1) the softer material, releasing particles [35]. Wear particles have a micro-chip shape and are smaller than 1 ?m.

Finally, fatigue delamination wear is caused by fatigue phenomenon. High subsurface stress leads to initiation of multiple cracks oriented horizontally, which propagate upward towards the surface, causing the loss of weaker material to a depth of a few millimetres. The evidence of fatigue wear includes large (>10 ?m) flake-like wear particles, cracks and delamination on the articulating surface.

Adhesive and abrasive wear mechanisms are typical for conforming joints such as the hip, while delamination dominates in less conforming joints, like the knee. In the case of the shoulder replacement, the components are conforming as well as nonconforming so the adhesive, abrasive as well as fatigue wear is expected.

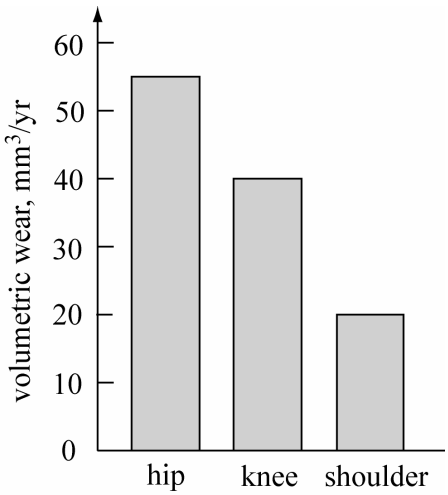

Fig. 2. Comparison of volumetric wear rates in total joint replacements.

The generation of small wear particles in the case of adhesive and abrasive wear can be associated with cyclic high contact stresses acting at the polyethylene surface under multiaxial loading. The subsurface cracks and delamination in fatigue type of wear can be related to the maximum shear stresses. For the polyethylene components, the contact stresses can easily exceed the yield point of the polyethylene, resulting in the failure of the material.

For instance, the wear factor for the UHMWPE acetabular cup increases rapidly as the stress levels increased from about 12 to 15 MPa. In the knee, an early structural failure of UHMWPE tibial component can occur due to excessively high contact stresses (up to 30 MPa) resulting from the incongruent joint geometry. The analysis shows that the peak stress generated in glenoid components under normal conditions can be as high as 25 MPa. All these contact stress values exceed the yield strength of PE (about 10 MPa). Since the hip cup has the biggest contact area, the volumetric wear for total hip joint is also the biggest (Fig. 2).

Ultrahigh-molecular-weight polyethylene acetabular cups, articulating against smooth femoral heads, have been shown to wear at a rate of approximately 40 mm^3/year. This corresponds to up to 1000 ? 10^9 particles per year, with the majority of particles of submicron size. For comparison, metal-on-metal prostheses have been clinically shown to have wear rates of approximately 1 mm^3 /year, with very small wear particles (from 20 to 50 nm in diameter). Alumina/alumina hip prostheses have also been shown to generate very low wear rates (1 mm^3/year) [26], with the particle size being of the order of 0.1 to 1 μm.

The particulate debris (PE, metal, ceramic or cement) is able to penetrate via the periprosthetic interface and migrate so effectively, that they can be found at the tip of femoral stem or at the dome of the acetabulum. This penetration is possible due to the effective joint space at the interface between bone and implant, which is accessible to joint fluid and thus accessible to particulate debris. The fibrous tissue surrounding implant exudes fluid under compressive loads, and this might provide mechanism for transporting particulate debris from the joint cavity. The debris migrates at the implant-cement or implant-bone interface, because this interface does not constitute a closed space. Massin et al. [21] however, showed that particles are also able to migrate through cancellous bone due to three-dimensional microarchitecture of trabecular bone.

3. Biological response to the wear particles from implant materials in arthroplasty

The problem of biological response to wear debris is a complex phenomenon, first studied by John Charnley in 1960s. He suspected that teflon wear particles would cause

inflammatory reaction, so he decided to implant them into his own, healthy thigh. After few weeks he obtained painful confirmation of this theory [45].

In 1987, Jones and Hungerford introduced the term “cement disease” to describe osteolysis connected with aseptic loosening around cemented total joint replacement [13]. Nevertheless, the inflammatory tissue response and osteolysis has been seen also after cementless total joint replacements proving that particulate (debris) disease is better and more adequate term for this situation. Acute biological reaction is present in case of contact with wear particles of any material used in arthroplasty [40] and is often the reason of aseptic loosening. Aseptic loosening is the term used to describe bone loss surrounding prosthesis in the presence of a peri-prosthesis inflammatory tissue in the absence of infection.

Wear particles present around implant are in 90 % less than 1 ?m in size [18]. Particles of this size are found to be the most biologically active [10]. They stimulate the periprosthetic bone resorption and expanding of the fibrous tissue, what subsequently leads to implant loosening. The accumulation of prosthetic wear debris around the joint in quantity exceeding $1 \cdot 10^{10}$ per gram of tissue, results in induction of cascade of biological reactions [32]. Biological response to wear debris is complex and involves all cells present in periprosthetic tissue. Each milligram of polyethylene has been estimated to generate $1.3 \cdot 10^{10}$ particles [42].

3.1. Fibrous tissue. Early instability of an implant creates a potential space around the prosthesis, where connective tissue can enter. Deposition of extracellular matrix, composed of proteoglycans and collagen fibers begins filling the gap between bone and implant. In well-fixed implants osteoblasts can change this matrix, into woven bone. This weak woven bone can convert into mature bone, with stronger and thicker lamellae. In stable implants, healing tissue subsequently disappears and the implant and bone remain in direct contact.

If the implant is unstable, the healing tissue becomes fibrous. Micromovements are reported to induce differentiation of fibroblasts from reparative fibrous tissue into cartilage- or bone-forming cells [3]. The direction of differentiation depends on magnitude of micromotion. When the volume of the movements is greater than 150 ?m, the fibrocartilaginous tissue is formed around implant, if the volume is less than 20 ?m the tissue differentiates into bone [7] and the osteointegration is possible. Any implant, which is exposed to a large motion, will not become stable [2], because fibrous tissue extends very intensively and replaces healthy bone. When the region becomes fibrous, the adjacent bone section supports the load. This leads to elevated strain in this section, which in turn becomes fibrous. The fibrous tissue weakens the contact between bone and implant, what may contribute to the aseptic loosening. Fibrous tissue cannot withstand the pressure to which it is exposed [39] and no osteointegration between bone and implant take place. Additionally, wear debris induces proliferation of fibrous tissue. Aseptic loosening is attributed to a combination of mechanical and biological factors.

Histological analysis of a fibrous tissue layer showed a number of macrophages, fibroblasts and some lymphocytes (Fig. 3).

A macrophage is a type of white blood cell (the biggest: 12-20 ?m in diameter), deriving from monocytes. When monocytes enter the tissue from blood, they become macrophages and undergo several changes. They grow and increase the amount of intracellular lysosome, allowing better phagocytosis. A primary function of the macrophages is to eliminate foreign substances. They work by engulfing whatever they do not recognize as healthy tissue, including pathogens. Macrophages produce various cellular mediators and proteinases during inflammation.

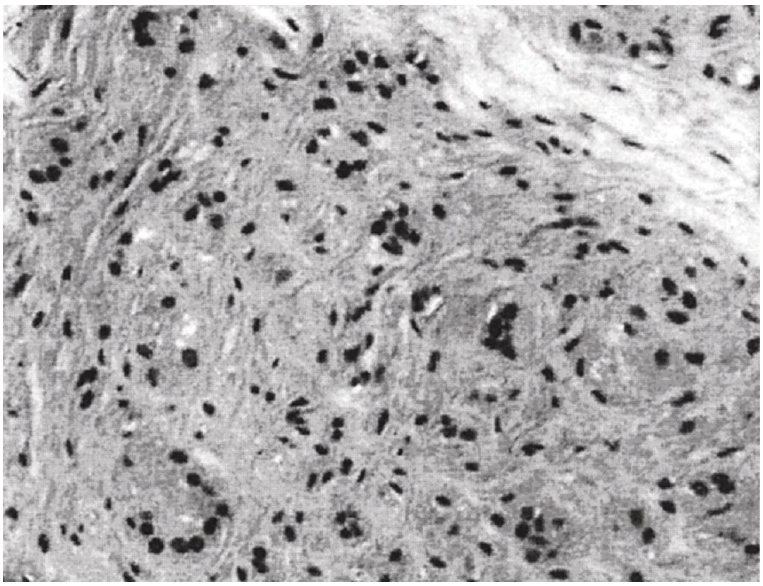

Fig. 3. Microscopic examination of hematoxylin and eosin staining of tissue from a failed total hip replacement shows macrophages containing polyethylene wear particles that are seen as white fibers and flakes under polarized light, after Wright, T.M. and Goodman S.B. [49].

A fibroblast is ubiquitous cell in connective tissue, mesodermally derived. Fibroblast secretes fibrillar procollagen, fibronectin, glycosaminoglycans, reticular and elastic fibers and glycoproteins found in the extracellular matrix. Active fibroblasts can be recognized by their abundant rough endoplasmic reticulum. Inactive fibroblasts, which are also called fibrocytes, are smaller and spindle shaped. They have a reduced rough endoplasmic reticulum. Tissue damage stimulates fibrocytes and induces the mitosis of fibroblasts. In case of the aseptic loosening of implant, the growth of fibroblasts has been reported [40]. Fibroblasts can give rise to other cell types.

A lymphocyte (6-8 ?m in diameter) is a type of white blood cell involved in the human body immune system. There are two broad categories of lymphocytes, namely T cells and B cells. Lymphocytes play an important role of the body defences. In the presence of an antigen, B-cells become much more metabolically active and transform into plasma cells. Plasma cells are large lymphocytes with large nuclei. They produce antibodies. Lymphocytes are agranulocytic leukocytes that normally make up a quarter of the white blood cell number, but their volume increases in the presence of inflammation.

3.2. Tissue reaction to wear debris. When wear debris appears in the fibrous tissue, the immune system recognises it as an antigen (any substance that stimulates the production of antibodies and elicits an immune response by the organism). That causes chronic inflammatory foreign body reaction. The immune system is designed to destroy biological antigens, not indigestible chemical components like polyethylene, but it can use only this kind of weapon.

The cells activated by the presence of antigens, release histamine. It is a multifunctional chemical compound, which induces spreading blood vessels, it also causes vasodilatation. Histamine attaches to receptors on nearby blood vessels. Increased blood flow, blood circulation and activated endothelium cells from vessels (increased permeability of blood vessel walls) contribute to intensive migration of monocytes from blood to the jeopardised tissue. Monocytes accumulate in the inflammatory region. Monocytes circulate in the peripheral blood prior to migration to the target tissue. They are able to effect phagocytosis. In the target tissue they differentiate into adult form – macrophages and become resident in connective tissue.

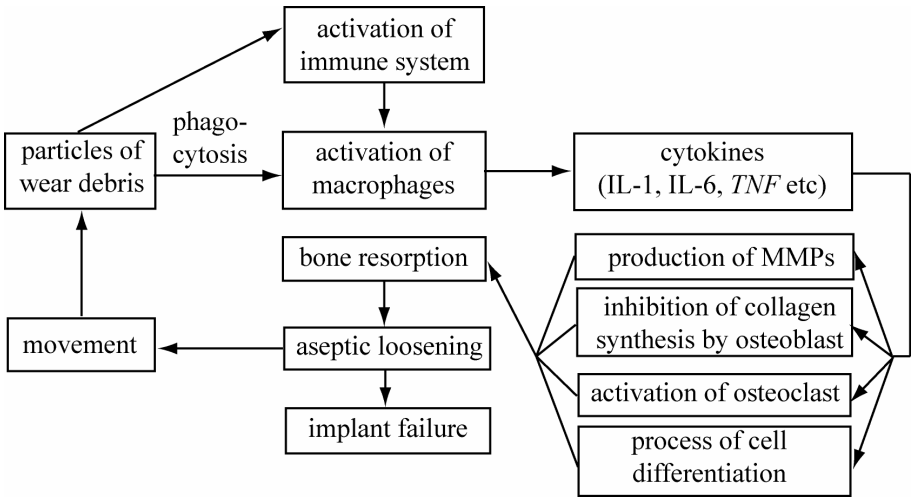

Fig. 4. Biological response to the wear particles from implant materials in arthroplasty.

Macrophages are the key cells in biological response to wear debris (Fig. 4). They phagocytize wear debris. That starts the cascade of inflammatory reactions. There are about 25-times more macrophages around loose implant compared to bone surrounding well-fixed implants [14], because continuos wear requires a constant supply of phagocytes. In this tissue there can be more than 4000 cells per mm^2 of tissue [4].

3.3. Phagocytosis. Phagocythosis is a process of engulfing and ingesting of foreign particles by the white blood cells (phago – "eating", cytos – "cell"). Phagocytosis begins by nonspecific binding of particulate wear debris to the cell surface. The macrophage cell surface invaginates, forming a pocket from the cellular membrane and composing phagosome. Phagosome fuses with lysosome, forming phagolysosome. Lysosome contains big amount of different degradative enzymes – acid hydrolases. Lysosomal enzymes work effectively in acidic pH values, at pH about 4.8, where many proteins denature and are easier to degrade. Lysosomal enzymes include Dnase (deoxyribonuclease), RNase (ribonuclease), proteases, phosphatases and lipases – enzymes that break large molecules down to their respective subunits. When a phagolysosome forms, oxygen burst is observed. Stored sugar is used to produce NADPH (nicotinamide adenine dinucleotide phosphate), which is an electron donor for oxygen. In reaction of the NADPH oxidase, toxic and reactive oxygen species (ROS) such as peroxide (H_2O_2) and superoxide (O_2^-) are formed. All of these molecules are highly reactive and cause extensive chemical damage to contents of the phagolysosomes. Lysosomal enzymes and ROS promote digestion of organic antigens, but particles of wear debris cannot be digested. After macrophage activation, wear particles are removed from the cell without any changes and they can be phagocytized by other macrophages. The presence of nondegradable particles results in a constant state of activation of all cell types present in fibrous tissue.

3.4. Cytokines. Phagocytosis of wear debris by macrophages activates intracellular signalling pathways, regulates gene expression and subsequently releases many chemical substances with inflammatory and degradative action, in particular the cytokines. Cytokines (cytos – cell, kinesia – movement) are small (in the range of 5-20 kDa), soluble glycoproteins (complex proteins, which contain molecules of carbohydrates), which move in extracellular space. They often operate locally and in very low concentration (of 10^{-12} M). The main function of these molecules is communication among immune system cells, and between immune system cells and cells belonging to other tissue types. They can (like hormones in the endocrine system), produce local effect on other cells.

Cytokines act as inflammatory mediators and modulate the functional activities of cells and tissues. Cytokines work by binding to their cell-specific cytokine receptor. This

receptor is located in the cell membrane and triggers a starting signal cascade, which regulates gene transcription. Cytokines influence growth, proliferation and activation cells, which participate in the inflammatory reaction. Cytokines operate as a network [16] in which every component controls and regulates each other. Functioning network of the cytokines depends on many elements: of quantity of cytokines, receptors and kind of cells present. The net effect of cytokines is based on interaction between them. The most important attributes of interaction are: redundancy, pleiotropy, synergism and antagonism. Redundancy is ability of different cytokines to induce the same response from the target cell. Pleiotropy is multiple biological actions. The same cytokine may cause different effects in different circumstances [27]. Synergism is an intensified effect of two cytokines, which is greater than the sum of their individual effects. Antagonism is the ability of certain cytokines to cancel the effect of other cytokines

The big group of cytokines can be divided into 5 subgroups: interleukins, chemokines, family of TNF (tumor necrosis factor), interferons and hematopoietic cytokines.

Interleukins is a collective term for a group of structurally and functionally distinct soluble proteins. They are involved in processes of cell activation, cell differentiation, proliferation, and cell-to-cell interactions.

The family of tumor necrosis factors limits tumor development and is very important during inflammation.

Chemokines define cytokine subgroup with a distinctive role on chemotaxis and inflammation. Chemokines are specifically trophic molecules, which signal different cells to move in a specific direction. The cells direct their movements according to the gradient of chemokine concentration.

Interferons are proteins, which show a virus-unspecific antiviral activity. This unspecific immune response process is mediated predominantly by monocytes/macrophages. Interferons are synthesized by virus-infected cells and protect other non-infected but virus-sensitive cells against infection for some time. The antiviral activity requires new synthesis of RNA (ribonucleic acid) and proteins and is not observed in the presence of suitable RNA and protein synthesis inhibitors. Apart from their antiviral activities, interferons also engage in antiproliferative and immunomodulating activities and influence the metabolism, growth and differentiation of cells in many different ways.

Hematopoietic cytokines act on cells of the hematopoietic system (hematopoiesis is used to describe blood formation).

Macrophages and other cells present in the fibrous tissue produce a lot of cytokines, which are the most important mediators produced by the synovial-like membrane. Cytokines can be separated into proinflammatory (cause bone resorption) and antiinflammatory (contribute to bone formation). The production of proinflammatory cytokines is more intensive around failed implant. The expression of antiinflammatory cytokines is not sufficient to counteract the imbalance. The equilibrium in bone remodeling is upset and the chronic inflammatory process can be observed. The most important proinflammatory cytokines in implant failure are IL-1, IL-6 and TNF [29]. These cytokines have been shown to be strongly involved in bone resorption. They cause directly bone resorption and indirectly induce synthesis of other cytokines, which contribute to bone resorption.

3.5. Cytokines most important in biological response to wear debris

Interlenkin-1 (IL-1). Interleukin-1 has many functions; it affects many different cells. IL-1 is secreted by a number of cells including macrophages, monocytes and dendritic cells. There are two known species: IL-1 alpha and IL-1 beta. IL-1α is associated with the cell membrane and acts via cellular contact. IL-1β is the prototypical proinflammatory cytokine [30].

The synthesis of IL-1 can be induced by other cytokines including TNF-alpha, IFN and also by bacterial endotoxins, viruses and other antigens.

IL-1 affects nearly every cell type in the organism, has a wide range of biological and physiological effects, including fever, prostaglandin synthesis (e.g., fibroblasts, muscle and endothelial cells), T-lymphocyte activation, and interleukin-2 and other cytokine production. It also favours maturation and clonal expansion of B cells. IL-1 is one of the most important mediator of inflammatory reactions [8]. Many researchers associate IL-1 with bone remodelling. IL-1 stimulates osteoclastic bone resorption by enhancing osteoclast operation [9]. It increases osteoclast survival by blocking apoptosis [12]. IL-1 can also stimulate mature osteoclasts indirectly, through other cells [16]. The production of Il-1α in the periprosthetic tissue of loose implants is positively related to osteolysis around them [37]. IL-1 also promotes wound healing. This activity is thought to involve effects on angiogenesis, and the promotion of fibroblast proliferation. IL-1 may as well induce the expression of matrix metaloproteinases [15], what can cause extracellular matrix degradation and facilitate monocytes migration. IL-1 stimulates both collagenase and gelatinase activities [17]. IL-1 also has an inhibitory effect on osteoblast function. The circulation half-time of IL-1 is 6 minutes.

Interlenkin-6 (IL-6). Many different cell types produce interleukin-6. The main sources of IL-6 are stimulated by monocytes, fibroblasts, osteoclasts and endothelial cells. Macrophages, lymphocytes (T and B), granulocytes, smooth muscle cells, eosinophils, chondrocytes and osteoblasts also produce IL-6 after stimulation. Interleukin-6 may be considered as the prototypic pleiotrophic cytokine [6]. IL-6 has overlapping activities with Il-1 and TNF.

In fibroblasts, the synthesis of IL-6 is excited by IFN-beta, TNF-alpha and viral infections. IL-1 influences osteoblasts to produce IL-6. It, in turn, in high concentration, activates mature osteoblasts, in small concentration induces osteoclast formation [41]. IL-6 acts on lymphocytes B promoting their differentiation into plasma cells and antibody secretion. This cytokine is always found in increased concentration in sites of inflammation and is likely to be very important in inflammatory regulation. It suppresses tumor necrosis factor (TNF) production. IL-6 contributes to extensive MMPs production [17]. It has been described as both proinflammatory and antiinflammatory molecule [6]. The IL-6 gene is directly regulated by sex steroid (estrogen and androgen protect skeleton, because they inhibit IL-6 production and bone degradation this way) [20].

Tumor necrosis factor (TNF). Tumor necrosis factor (TNF) is produced by many normal (macrophages, monocytes, neutrophils, T-cells) and tumor cells in response to a wide variety of stimuli, including viruses, bacteria, parasites, cytokines and foreign antigens. Production of TNF is stimulated by IL-1. TNF has influence on growth, differentiation and many functions of healthy and tumor cells.

TNF-alpha is a growth factor for normal human diploid fibroblasts and has necrotizing effect on tumor cell lines. TNF is an extremely pleiotrophic cytokine due to the ubiquity of its receptors and thanks to its ability to activate multiple signal transduction pathways and its ability to induce or suppress the expression of a wide number of genes. TNF is a proinflammatory cytokine that provides a rapid form of host defence against infection but is fatal in excess quantity. TNF induces the synthesis of IL-1 and prostaglandin E2. It also stimulates phagocytosis and the synthesis of superoxide dismutase in macrophages. TNF stimulates differentiation of osteoclasts, but not their activation [44]. It was shown that addition of anti-TNF antibody was able to inhibit bone resorption by supernatants from particle-stimulated macrophages [1]. TNF controls bone remodeling. It is produced by osteoblasts under the influence of Il-1. TNF is one of the most important cytokines involved in wear particles induced osteolysis [11].

The half-time of TNF is less than 20 minutes [30]. This time is sufficient to evoke marked metabolic changes and activate mediator distally in the cytokine cascade.

Each cytokine must not be considered in isolation, but should be considered as a part of a big good working network of interacting mediators.

3.6. The role of cytokines in bone resorption. Cytokines released primary by the macrophages and other cells present in the fibrous tissue after contact with debris particles may stimulate bone resorption (dissolution of the mineral phase and matrix degradation) by many modes, in direct or indirect way. The most important are: induction of matrix metaloproteinase synthesis, inhibition of new bone formation, osteoclast activation and osteoclast differentiation.

3.6.1. Matrix Metaloproteinases. Matrix metaloproteinases (MMPs) are family of zinc and calcium dependent endopeptidases. They are involved in physiological and pathological connective tissue remodeling, wound healing, inflammation, etc. MMPs are able of breaking down any extracellular matrix component [40]. There are 23 known human members in this family [24]. Matrix metaloproteinases can be divided into 4 subgroups: collagenases (MMP-1, MMP-8, MMP-13 and MMP-18), gelatinases (MMP-2 and MMP-9), stromelysins (MMP-3 and MMP-10) and membrane-type metaloproteinases (MMPs-14-17) [22].

MMPs are secreted as zymogens (proMMPs), which are activated by a variety of proteinases. Their activities are regulated at multiple levels, such as the activation of proenzymes and the inhibition of active enzymes by TIMPs (tissue inhibitor of metaloproteinases; TIMP-1, -2, -3, and -4).

Many inflammatory cytokines cause intensification of MMPs production. It was shown that wear particles of orthopaedic biomaterials induce the release of matrix metaloproteinases by activated macrophages [24]. MMPs show the first signs of inflammatory response to wear debris [38]. These enzymes are involved in bone resorption. Osteoblasts and osteoclasts also produce MMP-13 (collagenase 3), MMP-2 and MMP-9 (gelatinases A and B) [18, 31]. These enzymes (especially collagenases) are responsible for degrading the connective tissue and the nonmineralized osteoid layer covering bone surface. That process exposes mineralized bone to osteoclasts. The imbalance between the level of MMPs (overproduction in response to inflammatory cytokine) and their inhibitors is one of the most important causes of total joint failure. The degradation of bone matrix without a compensatory increase in bone matrix synthesis results in net bone loss.

3.6.2. Inhibition of new bone formation. Proinflammatory cytokine can also inhibit new bone formation through influence on osteoblasts. The most important function of osteoblasts is the synthesis and secretion of the organic matrix of bone, including type I collagen (a protein that constitutes 90 % of the bone matrix). Exposure of osteoblast to TNFα and Il-1β and other cytokines results in suppressed proliferation of osteoblasts [46], suppressed procollagen mRNA expression and subsequently can lead to reduction of type I collagen synthesis [22], which is crucial for formation of osteoid. Also wear debris directly can influence osteoblasts. Osteoblast surface interacts with wear particles, what also leads to limited synthesis of procollagen [33]. Equilibrium between new bone formation and bone destruction is unsteady. Then the process of bone resorption is more intensive what results in Ca^{+2} ion release from bone and the bone mass decreases. Osteoblasts can not compensate the bone loss.

3.6.3. Direct influence on osteoclasts. Osteoclast is highly specialized, multinucleated (3 – 20 nuclei), large in size (20 – 100 ?m in diameter) cell, which is responsible for bone resorption. Osteoclasts are formed by fusion of bone marrow-derived mononuclear phagocyte precursors.

Many cytokines released in response to wear debris stimulate the survival of osteoclasts, prevent osteoclast apoptosis [12] and also contribute to their activation. IL-1 acts on osteoclast directly through their IL-1 receptors and regulates their function without other stromal cells [12]. Cytokines can also activate osteoblasts to stimulate osteoclasts.

Osteoclasts have also been shown to be able to engulf particles, which results in their activation [48]. They are able to produce an acid subosteoclastic space. At the low pH values bone hydroxyapatite $Ca_{10}(PO_4)_6(OH)_2$ is dissolved and the bone loss occurs.

3.6.4. Differentiation of osteoclasts. Activated macrophages release cytokines, which are responsible for the recruitment of osteoclast precursors and their subsequent differentiation into mature osteoclasts capable of bone resorption. Macrophages associated with wear particles are also capable of differentiation into multinucleated cells, into osteoclast-like cells, that have capacity to carry out extensive bone resorption [28, 34, 35]. In vivo studies have shown that the number of osteoclasts is increased (20 times and more) in tissue around loose implant when compared with bone surface in well-fixed implant [14].

4. Discussion

Surface interaction of wear debris, direct phagocytosis of them and indirect induction of cytokines affect bone turnover negatively. Osteolysis is a consequence of cellular response to wear debris. Osteolysis on the bone - implant interface causes loss of the implant support, and with cyclical loading, leads to aseptic loosening. The patient requires surgical treatment, a revision arthroplasty with removal of the loose prosthesis and re-implantation of a new prosthesis. The results of revision arthroplasty can never be as good as the primary arthroplasty. The bone, into which consecutive implant is inserted, is not well vascularized, has a lot of fibrous scar tissue and also may contain residual foreign material (wear debris particles), so it is substantially weakened. Therefore it is very important to limit the possibility of primary implant loosening.

Polyethylene wear and its result, osteolysis, still remains a serious problem for all patients who have had a total joint arthroplasty When osteolysis occurs, it seems that a surgeon has finally no other choice than revision arthroplasty.

To prevent the generation of polyethylene particles a lot of work has been done and still needs to be done. Efforts are made to reduce the effects of the wear process by changing the geometry of the implants (i.e. using a small femoral head, adequate polyethylene thickness). The new methods for cross-linking and sterilization are elaborated to improved polyethylene wear resistance. Moreover, decreasing PE oxidation by an annealing treatment and antioxidant (i.e. Vitamin E) is used. Finally, to reduce wear a non-polyethylene articulation (i.e. metal-metal or ceramic-ceramic) has been tried and shows a big potential. Despite technological efforts, wear debris could not be completely eliminated. An accurate understanding of cytokine cascade, which plays an important role in aseptic loosening in response to wear debris may deliver information on how can we modulate this process, using pharmacological methods. However, the pre-clinical testing of any new material for joint replacement must also include the analysis of the wear particle characteristics and their biological reactivity.

Acknowledgements

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ВЛИЯНИЕ ЧАСТИЦ ИЗНОСА НА ПОВЕДЕНИЕ И БИОМЕХАНИЧЕСКИЕ СВОЙСТВА ПОВЕРХНОСТИ КОСТЬ–ИМПЛАНТАТ

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Цель данной статьи – описать влияние частиц износа, образующихся при сочленении несущих поверхностей тотального протеза сустава, на поверхность кость–имплантат. Субмикронные частицы мигрируют в эффективное пространство сустава и стимулируют клетки, находящиеся в фиброзной ткани, испустить молекулярный сигнал. Цитокины активируют остеобласты и вследствие этого может наступить потеря костной ткани. Это ослабляет фиксацию кость–имплантат и может вызвать асептическое расшатывание протеза.

Ключевые слова: частицы износа, поверхность кость–имплантат, тотальная замена сустава.

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