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Review

The role of macrophages in osteolysis of total joint replacement

Eileen Ingham[a,*], John Fisher[b]

[a] School of Biochemistry and Molecular Biology, Institute of Medical and Biological Engineering, Division of Microbiology, University of Leeds, Leeds LS2 9JT, UK

[b] School of Mechanical Engineering, Institute of Medical and Biological Engineering, University of Leeds, Leeds, UK

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Abstract

The osteolysis associated with conventional polyethylene on metal total joint replacements is associated with the formation of an inflamed periprosthetic membrane rich in macrophages, cytokines and implant-derived wear particles. There is a wealth of evidence to indicate that the presence and activation of macrophages in the periprosthetic tissues around joint replacements is stimulated by UHMWPE particles. Particles within the size range 0.1–1.0 μm have been shown to be the most reactive. Animal studies have provided increasing evidence that, of the milieu of cytokines produced by particle-stimulated macrophages, TNF-α is a key cytokine involved in osteolysis. Recent advances in the understanding of the mechanisms of osteoclastogenesis and osteoclast activation at the cellular and molecular level have indicated that bone marrow-derived macrophages may play a dual role in osteolysis associated with total joint replacement. Firstly, as the major cell in host defence responding to UHMWPE particles via the production of cytokines and secondly as precursors for the osteoclasts responsible for the ensuing bone resorption.

Keywords: Macrophage; UHMWPE; Osteolysis; Osteoclast; Cytokines; Hip replacement

Contents

*Corresponding author. Tel.: +113-343-5691; fax: +113-343-5638.
E-mail address: e.ingham@leeds.ac.uk (E. Ingham).

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1. Introduction

There are approximately 1 million total joint replacements carried out world-wide each year. The vast majority of total joints replaced are hip joints (circa 800,000 [1]). There is no doubt that hip joint replacement was the most successful surgical procedure developed during the 20th century [2]. The vast majority of hip replacements still follow Charnley's low frictional torque principle [3] comprising an ultra-high molecular weight polyethylene (UHMWPE) acetabular cup articulating against a hard femoral head made of either metal or ceramic with or without polymethylmethacrylate (PMMA) cement fixation. In knee prostheses, the materials of choice are a UHMWPE tibial tray articulating against a highly polished metal femoral component.

Improvements in the prevention of infection, material properties of the components and methods of fixation have meant that total joint replacement is the most cost-effective means of restoring function and mobility to millions of patients with osteo- and rheumatoid arthritis. Given good surgical technique over 75% of hip prostheses may succeed beyond 25 years in elderly recipients [4]. However, the success of this procedure has meant that increasing numbers of prostheses are being implanted into younger and more active patients who place added demands on the implants [2]. The survivorship of total hip replacements in young, active patients is reduced [2,4–6]. The need to understand the mechanisms of failure and develop prostheses with increased longevity is paramount within the orthopaedic community.

Understanding of failure modes of total joint replacements has come through studies of total hip replacements since this procedure has been carried out successfully for 40 years. The expectation is that modern knee replacements will follow similar patterns of failure. In order of occurrence following implantation, the major factors that currently limit the function and longevity of the total hip replacement are the surgical technique, fixation of the implant to the bone, osteolysis and long-term bone remodelling [2]. The most frequent mode of failure is aseptic loosening due to osteolysis in the medium term [7]. Following a degree of wear, the fixation of the joint into the bone fails and the joint becomes loose. This leads to pain and instability necessitating the need for revision surgery. While this review will concentrate on osteolysis and the role of macrophages in that process, the influence of surgical technique and failure of fixation leading to mechanical loosening in the short term should not be underestimated. Poor alignment, poor fixation leading to micromotion [8,9] and the lack of initial stability of the implant [10] have been identified as important predictors of later symptomatic loosening.

Osteolysis of the bone surrounding total joint replacements is diagnosed radiographically and is characterised by areas of radiolucencies in the bone adjacent to the implant/cement mantle. Clinically, periprosthetic osteolysis can lead to aseptic loosening of one or both of the components and massive bone loss that may in extreme cases lead to fracture of the bone. There is extremely strong evidence that the biological response to particulate UHMWPE wear debris generated primarily at the articulating interface is the key factor in the development of osteolysis. The UHMWPE wear particles enter the periprosthetic tissue where they are phagocytosed by macrophages. The macrophages then release an array of cytokines and other mediators of inflammation that lead to the development of an inflamed granulomatous tissue adjacent to the bone. Eventually, osteoclasts are recruited and/or activated to resorb the bone leading to osteolysis and eventually loosening of the prosthesis.

2. Relationship between wear particles, macrophages and osteolysis

2.1. Evidence for the role of UHMWPE wear particles in osteolysis

Particulate debris can be generated following total joint replacement as a result of either wear or corrosion. Wear of the polyethylene acetabular cup articulating against the hard metal or ceramic femoral head leads to the generation of UHMWPE particles. Wear of the non-bearing surfaces rubbing together such as back-side wear of an acetabular liner, fretting of the morse taper in modular stems, stem/cement or stem/bone fretting wear in cemented and non-cemented hip prostheses, respectively, may lead to the generation of metal and PMMA wear particles. Wear particles produced by this type of wear can lead to an inflammatory reaction and osteolysis [11,12]; however, this type of wear is not intentional whereas the wear of UHMWPE is an inevitable consequence of the normal function of the prosthesis.

While several modes of wear may occur simultaneously in vivo, wear of the UHMWPE component accounts for the majority of the wear particles generated in initially well fixed and functioning prostheses [7]. This is the major factor that limits the longevity of the current total hip replacements. There is extremely strong evidence from in vivo and in vitro studies that osteolysis is mainly a UHMWPE particle-related phenomenon.

Several authors have reported on the relationship between wear of the UHMWPE acetabular cup and osteolysis [13–16]. The penetration rate of the head into the polyethlyene acetabular cup has been shown to be linear over time with an average penetration of