Overview

When natural body parts cease to function effectively because of disease, trauma, or overuse, it is often necessary to implant synthetic parts surgically to take on the function of the damaged organs, joints, or other tissues. While these implants are successful in the vast majority of cases, providing restoration of function and relief from pain, a small percentage of the devices fail or cease to function, necessitating further surgery. One of the causes or results, or both, of these failures is the release of particulate material debris from the devices as a result of wear, physical deterioration, or chemical attack by the harsh physiological environment.

This Special Technical Publication is the result of a symposium which was held 31 Oct. 1990, in San Antonio, Texas. At that symposium, 21 papers were presented on particulate debris from orthopedic implant materials, the clinical consequences of the tissue response to particles, and some methods used for modeling tissue responses in the laboratory. Manuscripts from 19 of the speakers were accepted for publication after passing the ASTM peer review process. In addition, the substance of one of the remaining talks was published in the *Journal of Bone and Joint Surgery*[1] and should be reviewed to supplement the clinical results presented here.

The analysis of failed implants and surrounding tissues has revealed that particulate debris is formed as a result of wear and other factors and that this debris may be found in bone and soft tissues in the proximity of the devices or at distant sites. Some reports suggest that particulate material may reside benignly in tissue, while others show evidence of tissue destruction and a resultant loss of function of the device. The clinical results reported in these papers represent, in many cases, failures of only a small percentage of the total number of implantations performed by a particular surgeon or for a particular device. In some cases, radiographic evidence of the lysis of bone around implants is reported but the devices are still clinically functional, at least at the current time.

The speakers and symposium participants were primarily concerned with attempting to explain the tissue response which is now being seen in response to particles of implant material in order to identify factors, such as material selection, surgical protocol, implant design, or postoperative prophylactic drug treatment, which might either limit debris generation or moderate the tissue response.

This publication is divided into two sections. The first section deals with clinical experience with the generation of material debris from implants. The second section contains manuscripts describing *in vitro* and *in vivo* models for the clinical situation and methods for the generation and characterization of wear debris particles which may be suitable for use in laboratory models.

The Clinical Problem

In the first section, the first two papers provide a review of the literature and a historical basis for the symposium and serve as a background for the other papers in this publication.

Next, Campbell et al. report on wear debris found around cemented and porous-coated hip surface replacement devices. This study showed that polyethylene debris was found with both types of devices but metallic debris was commonly seen only with the porous-coated devices. They conclude that histiocytes are the direct cause of osteolysis.

The next two papers deal with endosteal osteolysis around porous-coated hip replacements at two medical centers. The overall incidence of endosteal erosion in the two reports is similar (14

[1] Maloney, W. J., Complex, M., Rosenberg, A., and Harris, W. H., "Bone Lysis in Well-Fixed Cemented Femoral Components," *Journal of Bone and Joint Surgery*, Vol. 72B, 1990, pp. 966–970.

out of 308 in one study and 14 out of 474 in the other study). Most of the implants in both studies had not been revised and remained functional while exhibiting radiographic evidence of endosteal erosion. In those cases in which biopsies were taken, fine particulate was found within histiocytes and macrophages. Both authors concluded that the debris was involved in causing the osteolysis.

Kossovsky et al. performed an analysis of particles retrieved from revision cases and found the particles to be primarily in the nanometre size range, much smaller than can be detected by most analytical procedures being used in today's laboratories. This study focused on the particulate found within macrophages and periprosthetic tissues and utilized an extremely sensitive sizing procedure to identify the sub-micrometre-sized particulate. A difference was found in size between the particles recovered from tissues and those recovered from isolated macrophages, suggesting that the macrophages preferentially pick up smaller particles and, if the macrophages are implicated in osteolysis, the smaller particles may be very important to the process.

Stulberg and his colleagues submitted two manuscripts relating to the failure of patella resurfacing implants. The first details the results of an implant retrieval study on metal-backed patellas and the second presents a technique for assessing the congruity of the patellofemoral joint. These papers provide an illustration of some of the ways that product design can influence debris generation in a positive or negative way.

The section on clinical complications of debris concludes with a report from a group of researchers in Israel concerning clinical and animal experience with a number of different implant materials, some of which are experimental new materials.

Models and Experimental Results

In this section of the volume, the authors discuss results with laboratory and animal models related to debris generation and the biological response.

In a rabbit model, the synthesis of prostaglandin E_2 (PGE_2) can be measured in response to particulate implant materials. A number of manuscripts have been published based upon the model presented in the first paper, and the reader is encouraged to read those papers in the orthopedic and biomaterials literature for additional information. In this report, the response to polyethylene in different forms is measured. Because PGE_2 is known to have an effect on bone formation and resorption, the authors have looked at the effects of a nonsteroidal anti-inflammatory drug on the production of PGE_2 in response to particulate.

The next two papers present an animal model for the physiological reaction to particulate in synovial tissue. The method involves the creation of a subcutaneous air pouch in the rat, which becomes lined with synovial-like tissue. The material to be tested is then injected into the pouch and the response is assessed. In the first paper, the model is compared with an intramuscular implantation model for the testing of particulate. After assessing the response to polymethyl methacrylate (PMMA) particles with and without titanium particles, the authors believed the air pouch model to be more sensitive. The second paper describes the use of the air pouch model to compare PMMA with and without the addition of barium sulfate.

The next two papers describe *in vitro* test methods which use cell culture to measure the response of cells to metal and cement particles. In the first paper, monocytes, macrophages, and fibroblasts were exposed to particles of common orthopedic metals. The levels of PGE_2 produced by monocytes and macrophages were measured, as well as the tendency of fibroblasts to increase the production of collagen. The result was that PGE_2 synthesis and collagen synthesis were increased in the presence of metal particles. In the second paper, the production of PGE_2 and interleukin 1 (IL-1) by fibroblasts was measured. PGE_2 levels were elevated with both experimental and retrieved cement particulate but were higher for the experimental particles, which suggests that there is a difference in the physiological response to particles that have come

from the body, which thus seems to reduce their antigenicity. The significance of both those studies is that the cell culture results correlate with clinical experience, suggesting that this system may be an appropriate screening model for analysis of particles.

Kossovsky and his co-workers describe experiments to evaluate human plasma protein adsorption to experimentally prepared particulates from pure titanium, cobalt, and chromium. Bone cement particles were also evaluated. The plasma used consisted of samples from five patients undergoing primary arthroplasty and five undergoing revision arthroplasty. The proteins adsorbed into the particles were quantified using gel electrophoresis. The authors found differences between the eluted proteins on the cobalt and those on the chromium and titanium. Based on these data, they have begun further studies to see if there is truly a difference in the way plasma proteins interact with cobalt.

The particulate produced by fretting wear was analyzed by the authors of the next paper. Different metal/metal combinations were employed in a fretting wear test, and the resulting particulate was characterized for size and the composition identified. A principal conclusion of the paper was that weight loss measurements, metal ion concentrations in the wear medium (lactated Ringer's solution in this experiment), and the particle size and weight generated are all important in the full characterization of a wear experiment.

A group of researchers in Germany and Switzerland next present their method for the production of metal particles and a vehicle for use in experimental animal injections. Animal experiments showed commercially pure titanium to be the most biocompatible material, followed by titanium alloys, cobalt alloys, and iron alloys (steel).

The final two manuscripts deal with the testing of debris particles from ligament prostheses. The first article describes particulate distribution, migration, and tissue response after synthetic anterior cruciate ligament replacement. Several mechanisms of particle transport are proposed. The second paper presents the results of a cell culture test method in which particles from two synthetic ligament devices were found to activate collagenase productions in a culture of synovial cells. The results of both papers bear directly on a concern about the fragmentation which has been reported for all synthetic ligament devices currently being used in the United States. The cell culture method holds promise for further application in investigating other types of particles that could be released into the joint space.

Significance and Future Work

Since this symposium was held, a number of additional reports of corrosion or wear of orthopedic devices have appeared in the literature.

ASTM Committee F-4 on Medical and Surgical Materials and Devices has an active task force which is developing a series of protocols for the characterization of experimental and clinically derived particulate to allow uniform communication by researchers in this area and allow more accurate description of the problem, so that research toward solutions may begin.

Within the Orthopaedic Research Society and the Society for Biomaterials, an informal task force has been organized to develop characterized reference standard particulate from orthopedic metals, polymers, and ceramics which can be used in research.

Investigations concerning the causes of osteolysis around implants and other tissue responses to implant material particles are being actively pursued around the country. The concerns are real and the problem may potentially grow larger as we get longer-term experience with the newer device designs, many of which are more complex and have a greater number of interfaces with the potential for wear.

The reader is encouraged to participate in the activities of ASTM if he has the time and

interest. The lists of references contained at the end of each paper in this volume provide a good basis for expanding knowledge in the area.

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