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*Case Report*

# Phagocytosis of Chromium During Patellar Osteoarthritic Remodelling Associated With a Knee Prosthesis

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**Summary.** The report is of an anatomico-pathological and electron probe microanalyzer study of a patella with osteoarthritic remodelling, that had been in contact with a cast cobalt-chromium-molybdenum prosthesis for two years and seven months.

Abrasion of the metal resulted in preferential phagocytosis of chromium, principally in the wall of an osteoarthritis cyst.

This observation indicates that a substance administered by intra-articular pathway for the treatment of osteoarthritis can become phagocytosed, and quite deeply, in the remodelled bone.

**Key words:** Osteoarthritis – Joint prosthesis – Metal phagocytosis – Chromium.

## Introduction

The present paper describes a study made by electron probe microanalyzer of the reaction of neighboring tissue to the alloy used in a knee prosthesis and gives some histopathological data concerning osteoarthritic remodelling.

## Case Presentation

*Clinical and Radiological Data.* The patient was a seventy five year old woman at the time of consultation in 1974, obese, diabetic and suffering from osteoarthritis, particularly in the knees. The left knee was affected with medial femoro-tibial and femoro-patellar osteoarthritis and total femoro-tibial prosthesis was required. The Guepar-type prosthesis implanted was made of Francobal®, a cobalt-chromium-molybdenum cast alloy of the following percentage composition: Cr = 28 – Mo = 6 – Ni ≦ 2,5 – Mn ≦ 1.00 – Si ≦ 1.00 – C = 0.25 – P ≦ 0.04 – S ≦ 0.03 – Co = about 60 (balance). Histological examination at the time of the operation revealed non-inflammatory synovial hyperpla-

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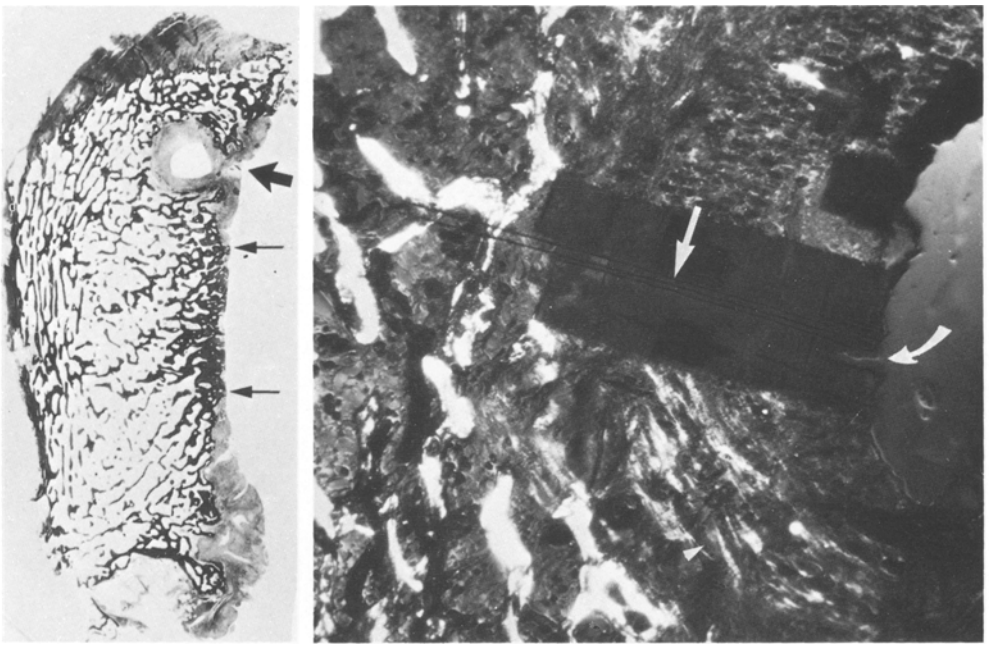

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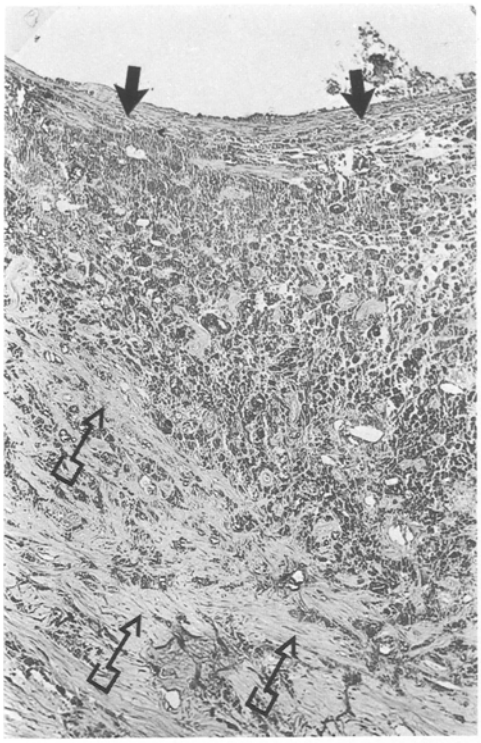
**Fig. 1. a** Sagittal section of the patella (van Gieson stain ×2).The two thin arrows define the limits of the eburnated surface. The thick arrow indicates an osteoarthritis cyst. **b** Detail of the deep part of the cystic region (unstained section ×15, studied by polarized light). Curved arrow indicates inner cyst wall facing artifactual fissure. Straight arrow is explained in Fig. 4. Collagen fibers of the wall can be seen in the right half and spongy bone trabeculae in the left half. The black rectangles indicate the surfaces burned by the electron beam scanning (X-ray images) and the black lines indicate the burned traces leading to the bone (profiles)

sia and chondrocalcinosis of the menisci. Two years and seven months after implantation of the prosthesis, the patella, which had been causing pain, was removed. It was reported (Dr P. Tschantz) that the cartilage had almost completely disappeared. There was a small amount of clear liquid in the joint space. The surface of the prosthesis appeared unchanged. No data concerning possible skin sensitivity to metals were obtained.

*Histology.* The surgical specimen (T. 15566/76) had been fixed in formalin, decalcified in formic acid (solution containing: 90 per cent formic acid: 80 $cm^3$ – 40% formalin: 50 $cm^3$ – distilled water: 870 $cm^3$) and embedded in paraffin. It revealed osteoarthritic remodelling with a distal osteophyte already detectable on the pre-operative X-ray of 1974, with marginal remnants of hyalin cartilage

**Fig. 2. a** Cyst wall containing macrophages (alcian blue stain ×65). Black arrows indicate fibrous inner wall. Pinnate arrows indicate the more fibrous area at the periphery. **b** Spongy bone adjacent to the cyst wall (alcian blue stain ×65). Short black arrows indicate macrophages in the deep part of the cyst. Long black arrow indicates a fragment of embedded articular cartilage. Pinnate arrows indicate macrophages in the bone marrow. **c** Macrophages surrounded by fibrous tissue in the cyst wall (hematoxylin-eosin ×420). **d** and **e** Unstained particles in cyst wall material after microincineration. **d** Observed by transmitted light (×530). **e** As seen on dark field (part of the region seen in **d**, with a different orientation ×420)



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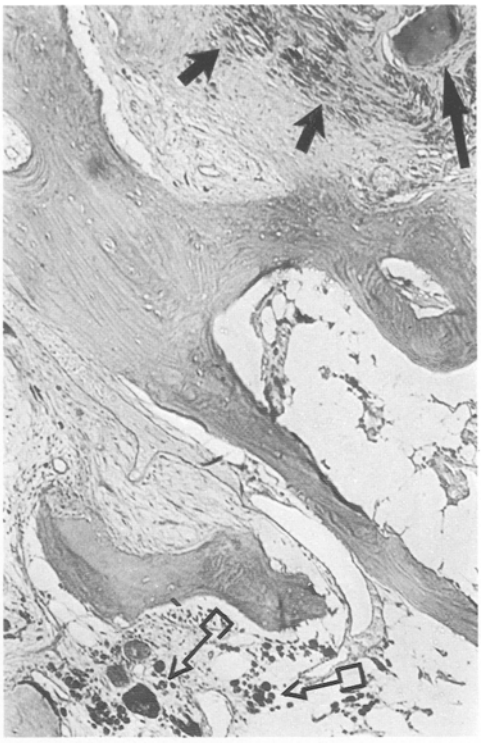

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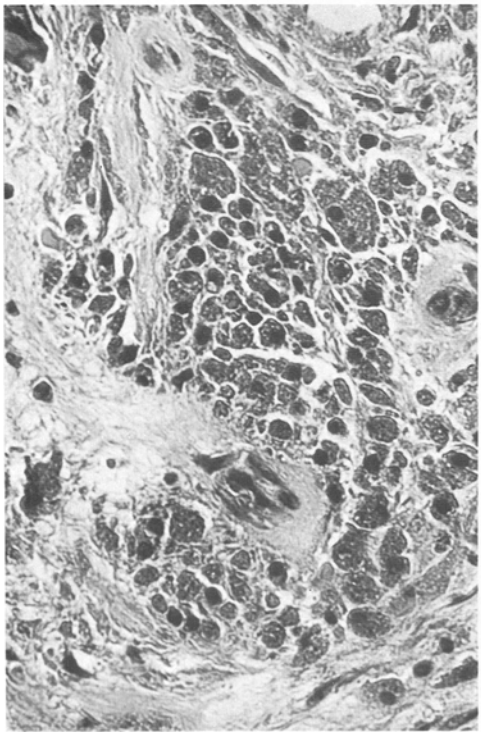

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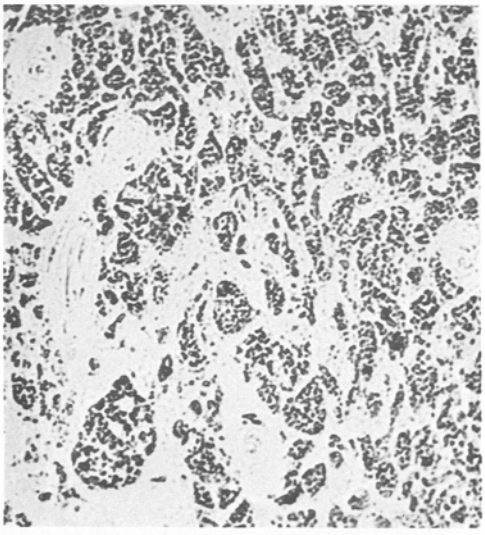

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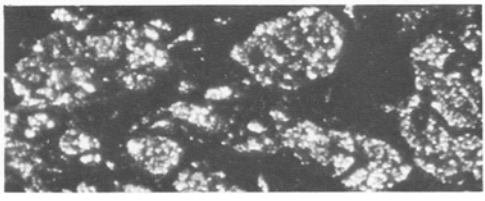

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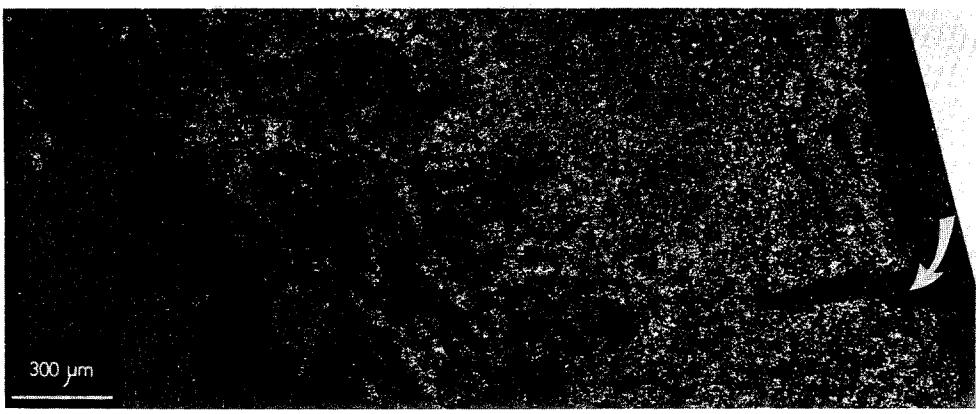


**Fig. 3.** $K\alpha_{1,2}$ X-ray image of chromium distribution on the large rectangular field shown in Fig. 1b (scanning time: 150 s). Arrow indicates the fissure shown on Fig. 1b

that showed no evidence of phagocytosis and with synovial tissue containing phagocytic macrophages. The remodelling of the naked bone resulted in a vast surface of eburnated bone with a cyst near the proximal end (Fig. 1a). The cyst wall which was slightly fibrous and showed no obvious necrosis, contained embedded debris of articular cartilage and necrotic bone (Fig. 2b). Particularly evident were the macrophages and giant cells whose protoplasm appeared brown in the sections stained with hematoxylin-eosin and turquoise blue in those stained with alcian blue (Fig. 2c). They were less dense near the periphery of the cyst (Fig. 2a). Staining with Perl's Prussian blue revealed no hemosiderin deposits. This staining of the macrophages made possible the detection of similar macrophages infiltration of the bone marrow surrounding the cyst or underlying the eburnated surface (Fig. 2b). After microincineration the cyst wall was seen to contain reflecting particles grouped in clusters and located in what could be considered cellular territories (Fig. 2d and e).

*Microanalysis.* The wall of the cyst and the neighboring bone tissue were studied by means of electron probe microanalyzer (ARL EMX-SM). Sections, 10 µm in thickness, were cut from the original block which had been, after careful removal of the paraffin, embedded in methyl methacrylate. They were then fixed with Euparal. To eliminate any possible confusion with one of the components of the prosthesis, a synthetic corundum ($Al_2O_3$) slide was used and the section was vapor-coated with aluminium.

Investigations were then made to determine the possible presence of various components of the Francobal® alloy, i.e., Co, Cr, Mo, Ni, Mn, Si (analytical conditions: 15 kV – 50 nA on benitoite, objective lens temperature −15°C) as well as of C and O (analytical conditions: 10 kV – 100 nA on benitoite, objective lens temperature −15°C). The cyst wall was radially scanned by means of 20 elemental profiles, numerous X-ray images and several point measurements (Fig. 1b).

## Results

Results showed that chromium was the only one of the chemical elements studied that was present in significant quantities. It was observed in a band between 1,200 and 1,800 µm wide which corresponds to the thickness of the cyst wall and in a few islets in the neighboring bone marrow (Fig. 3). The profiles showed an irregular distribution as indicated by the many very sharp peaks (Fig. 4). Both the profiles and the X-ray images showed that the chromium

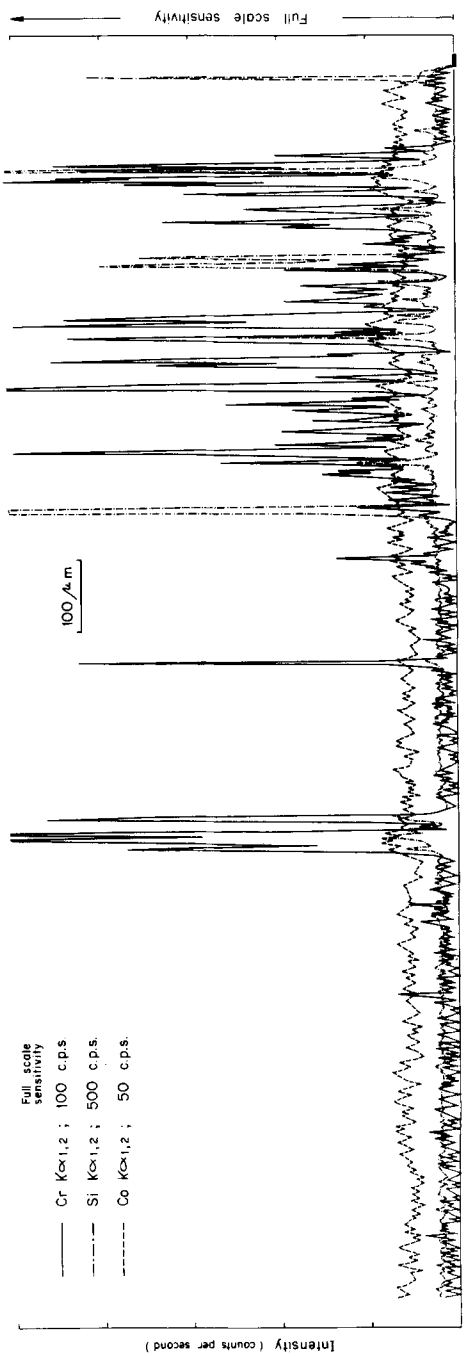


**Fig. 4.** Elemental profiles corresponding to the upper burned trace leading to the bone on Fig. 1b; from *A* (inner cyst wall) to *B* (point indicated by the straight arrow on Fig. 1b)

particles were grouped in clusters similar in size and arrangement to those of macrophages and observed in the cyst wall as well as in the neighboring marrow. This finding is compatible with histological data, particularly those obtained after microincineration (Fig. 2d and e). A chromium free band was observed at the inner border of the cyst that corresponded in size (between 40 and 160 μm) with a band of fibrosis containing no macrophages (Fig. 2a).

Results also revealed the presence of silicon, but its peaks were much less frequent than those of chromium and not congruent with them. Silicon was detected only in a narrower zone near the inner border of the cavity and some peaks corresponded with the outline of the border (Fig. 4).

Cobalt was also detected, but only in trace quantities, as indicated by very weak and rare peaks which similarly were not congruent with those of chromium (Fig. 4). No molybdenum, nickel nor manganese could be detected.

A similar electron probe microanalysis of a section after microincineration gave the same results as those obtained for the intact sections. Similar microanalyses were made of the wall of an osteoarthritis cyst from a hip without a prosthesis (T. 4118/78), of the methyl methacrylate used for embedding and of the Euparal used as fixative for the slides. The results showed no trace of the previously detected elements.

## Discussion

Although the Co–Cr–Mo cast alloy has been considered to be resistent to corrosion, there is evidence indicating that there is some release of ions into the neighboring tissue from implanted prostheses of this material (Ferguson et al., 1960). More significantly, this alloy has been found to release particles as a result of metal-metal friction (Swanson et al., 1973). Wear particles of this kind have been detected in the synovial fluid (Kitridou et al., 1969) and phagocytozed into the adjacent connective tissue (Charosky et al., 1973; Semlitsch et al., 1972; Vernon-Roberts and Freeman, 1976; Winter, 1974).

The present study not only confirmed previous observations of metal phagocytosis, but also led to interesting findings unrelated to the patient's chondrocalcinosis. It should be noted, however, that we do not consider here the following variables which are not directly related to the principal purpose of this study: the condition of the hyalin cartilage remnants (peripherally located, remodelled and with no phagocytosis) and synovial phagocytosis (a well-known phenomenon which was observed in part of the sample).

The chromium incorporated into the patella seems unlikely to be released in significant quantities by direct friction between the bone and trochlea of the prosthesis (Evans et al., 1974). It seems, rather, to be transported by intra-articular currents. In fact the erosion caused by metal-metal friction in the prosthesis occurs essentially at the femoro-tibial axis as we have observed on a used Guepar prosthesis. A similar observation has been reported concerning a Shiers knee prosthesis (Swanson et al., 1973).

The foreign material is regrouped in clusters of particles in macrophages, particularly in those present throughout the wall of an osteoarthritis cyst connected to the new articular surface. It can therefore be considered to be a label marking a histodynamic element of osteoarthritic remodelling, i.e. the migration to a certain depth of material of superficial origin. The extent of this change has been frequently underestimated, even though migration can be verified by the presence of articular debris in remodelled tissue easily detectable when the cartilage is stained black because of ochronosis (Lagier, 1973; Steiger and Lagier, 1972). This possibility should be borne in mind by the rheumatologist when giving intra-articular injections for the treatment of osteoarthritis, particularly since the release of lysosomic hydrolytic enzymes by phagocytic macrophages can by itself cause cellular or extra-cellular necrosis (Dannenberg, 1975). Osteomedullary necrosis after phagocytosis could explain the presence, in osteoarthritic remodelled tissues, of zones of aseptic necrosis which are known to become more pronounced after occasional aseptic intra-articular injections.

The metallosis of the present case appears due to a preferential phagocytosis of chromium. Although cobalt was the quantitatively predominant element of the alloy, it was only detected in trace quantities in the tissue. Silicon was also detected but in considerably smaller quantities than chromium. It is not known whether the presence of silicon in the tissue was due to some slight erosion of the silicone buffer of the Guepar prosthesis or to abrasion of alloy particles in which a small proportion of silicon might be concentrated; microprobe examination of a metal sample from another Guepar prosthesis has, in fact, indicated the presence of small concentrations of silicon.

It seems unlikely that the absence of cobalt in the tissue surrounding the prosthesis could be due to an effect of the acid used for decalcification of the bone specimen since it was a weak acid and was diluted, but this point should be clarified by further study. The preferential retention of chromium in tissue surrounding an articular prosthesis made of cast cobalt-chromium alloy has been reported in several studies in which no decalcification seems to have been performed (Coleman et al., 1973; Postel and Langlais, 1977) but was not mentioned in other studies (Winter, 1974; Evans et al., 1974). Whether the composition of the alloy used in the prosthesis was responsible for the preferential phagocytosis of chromium could not be established in the present study. Microprobe examination of the sample taken from another Guepar prosthesis and of phagocytic material from microincinerated sections did not reveal any particles of chromium carbide or chromium-molybdenum carbide, whose presence might have helped to explain the phenomenon. It is possible that biological factors, as yet undetermined, are involved.

For a better understanding of the reactions of tissue to joint prostheses, it is necessary to compare systematically the phagocytosis of the various constituents of the alloys used in the implanted prosthesis, as a function of certain biological variables and of the type of prosthesis implanted. The latter comparison would be of particular interest, since it is possible that the size of the eroded particles and consequently the area of oxidation in contact with the cells, might depend upon local mechanical conditions.

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## References

Charosky, C.B., Bullough, P.G., Wilson, P.D.: Total hip replacement failures. A histological evaluation. J. Bone Joint Surg. **55-A,** 49–58 (1973)

Coleman, R.F., Herrington, J., Scales, J.T.: Concentration of wear products in hair, blood, and urine after total hip replacement. Br. Med. J. **1,** 527–529 (1973)

Dannenberg, A.M.: Macrophages in inflammation and infection. N. Engl. J. Med. **293,** 489–493 (1975)

Evans, E.M., Freeman, M.A.R., Miller, A.J., Vernon-Roberts, B.: Metal sensitivity as a cause of bone necrosis and loosening of the prosthesis in total joint replacement. J. Bone Joint Surg. **56-B,** 626–642 (1974)

Ferguson, A.B., Laing, P.G., Hodge, E.S.: The ionization of metal implants in living tissues. J. Bone Joint Surg. **42-A,** 77–90 (1960)

Kitridou, R.C., Schumacher, H.R., Sbarbaro, J.L., Hollander, J.L.: Recurrent hemarthrosis after prosthetic knee arthroplasty: identification of metal particles in the synovial fluid. Arthritis Rheum. **12,** 520–528 (1969)

Lagier, R.: Anatomo-pathologie des arthropathies ochronotiques. In: Arthropathia ochronotica. S. Sitaj und R. Lagier. Acta Rheumatologica et Balneologica Pistiniana, N° 7. Piestany 1973

Postel, M., Langlais, F.: L'usure des prothèses totales de hanche en stellite. Mesures «in vivo» et conséquences cliniques. Rev. Chir. Orthop. **63** (suppl. II), 84–94 (1977)

Semlitsch, M., Vogel, A., Willert, H.G.: Investigation of joint endoprostheses abrasion products in the connective tissue of the joint cavity. Sulzer Techn. Rev, **2,** 136–144 (1972)

Steiger, U., Lagier, R.: Combined anatomical and radiological study of the hip joint in alcaptonuric arthropathy. Ann. Rheum. Dis. **31,** 369–373 (1972)

Swanson, S.A.V., Freeman, M.A.R., Heath, J.C.: Laboratory tests on total joint replacement prostheses. J. Bone Joint Surg. **55-B,** 759–773 (1973)

Vernon-Roberts, B., Freeman, M.A.R.: Morphological and analytical studies of the tissues adjacent to joint prostheses: investigations into the causes of loosening of prostheses. In: Advances in artificial hip and knee joint technology, M. Schaldach, D. Hohmann in collaboration with R. Thull, F. Hein (eds.), pp. 148–186. Berlin, Heidelberg, New York: Springer 1976

Winter, G.D.: Tissue reactions to metallic wear and corrosion products in human patients. J. Biomed. Mater. Res. **5,** 11–26 (1974)

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