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^{99M}Tc-PERTECHNETATE UPTAKE AFTER TOTAL KNEE REPLACEMENT IN RHEUMATOID ARTHRITIS

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In 6 out of 48 non-hinged knee joint replacements in 35 patients, ^{99m}Tc 04$^-$ uptake values were clearly increased compared with a control group. Measurements were performed an average of 3 years (range 9 months – 4½ years) after operation. Four of the six cases showed loosening of the prosthesis at arthrotomy and one showed an infection. Tests for hypersensitivity to the different components of the prosthesis and cement were normal. Histology and immunofluorescence of the synovial membrane obtained at arthrotomy in the four operated patients showed no recurrence of the synovitis. This study indicates that there is no recurrence or only a slight recurrence of rheumatoid synovitis after total knee joint replacement of the geometric type.

Key words: arthritis, rheumatoid; fluorescent antibody technique; joint prosthesis; knee joint; patch tests; synovial membrane; technetium/diagnostic use

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Recurrence of rheumatoid inflammation is frequently observed in rheumatoid arthritis patients treated by knee synovectomy (Arthritis Foundation Committee 1977, Arthritis and Rheumatism Council and British Orthopaedic Association 1976, Ranawat et al. 1971, Morgan et al. 1969). The rate of recurrence of the original rheumatoid inflammation in synovectomized knees increases with the length of the follow-up period (Arthritis Foundation Committee 1977).

We are aware of only one study (Bryan et al. 1973) mentioning that no inflammation or only a slight amount was found after knee joint replacement in rheumatoid patients.

The aim of the present study was to establish whether, in patients with rheumatoid arthritis treated by prosthetic knee joint replacement, recurrence of rheumatoid synovitis occurs in the treated joint a year or more after operation. In addition to clinical measurements we used the ^{99m}Tc04$^-$ uptake method as a procedure to detect joint inflammation (Dick et al. 1970, Boerbooms & Buys 1978, Patersen et al. 1977).

When the ^{99m}Tc04$^-$ uptake measurements were increased, a search was made for possible causes such as recurrence of rheumatoid inflammation, infection, loosening of the prosthesis or an allergic reaction to the various components of the prosthesis or the cement.

PATIENTS AND METHODS

Two groups of patients were studied. The first group consisted of 35 patients with classical or definite rheumatoid arthritis (Ropes et al. 1958), who underwent 48 non-hinged geometric arthroplasties; 28 were women and 17 men with a mean age of 64 (range 46–81 years). Forty-seven of these arthroplastic knee joints

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were examined 1 year or more (mean 3 years; range 1–4½ years) after receiving a geomedic-type metal-to-plastic prosthesis of the knee. One additional case presenting with pain and swelling of the knee joint was studied 9 months after knee replacement.

A control group consisted of 23 healthy non-operated volunteers, 15 females and 8 males, aged 19–54 (mean age 34).

All patients were examined with special attention to manifestations of gonarthritis such as tenderness, warmth, joint effusion, swelling, longitudinal pressure pain and pain during movement of the knee joint.

$^{99m}Tc04^-$ uptake measurements were made shortly (2¾ minutes) after intravenous injection of 200 μCi $^{99m}Tc04^-$, preceded by an hour's rest as described by Boerbooms & Buys (1978). In 6 patients without pains in the arthroplastic knee joints the contralateral knees were also investigated.

When the $^{99m}Tc04^-$ uptake in the prosthetic knee joint was increased as compared with the measurements in the knee joints of healthy persons, a radiological examination was made of the knee joint. Tests for hypersensitivity to the various components of the prosthesis and cement were performed in the 6 cases with clearly increased $^{99m}Tc04^-$ uptake values. For this purpose patients were patch-tested in the standard manner with various allergens as proposed by the International Contact Dermatitis Research Group. The allergens included the metal constituents of replacement prostheses, acrylic cement, chemical activators and inhibitors, and formaldehyde used for sterilization. The following substances were included in the tests: potassium dichromate 2 per cent, cobalt chloride 2 per cent, nickel sulphate 5 per cent, sodium molybdate 2 per cent, manganese chloride (methylmethacrylate) 1 per cent, polymer (polymethylmethacrylate) 10 per cent, hydroquinone 0.2 per cent and benzoperoxide 5 per cent. The patch tests were read after 48 and 96 hours and again after 1 week.

When hydrops was present in the prosthetic knee joint the synovial fluid was aspirated and examined for colour, clarity and white blood cell count; a differential count was made on a May-Grünwald-Giesma stain of the cytocentrifuged preparation; Gram and Ziehl Neelsen stains and cultures were also performed.

In addition, an arthrotomy was done and macroscopic aspects of the synovium were studied with special reference to hyperaemia and fibrosis.

Multiple synovial samples were taken (Cruikshank 1952), especially from the hyperaemic areas, and examined by light microscopy after fixation in 10 per cent formalin and staining with haemotoxylin and eosin. Inflammatory changes in the synovial membrane, including vascular changes such as vasodilatation and vascular proliferation, perivascular mononuclear infiltration, lymphoid follicles and proliferation of the synovial lining cells, were looked for. The same specimens were also viewed in polarized light for detection of prosthetic material. Immunofluorescence studies of the synovium were performed using antisera against: IgG, IgM, IgA, C1q, C3, C4, and fibrin. Bacteriological studies of synovial membrane specimens included Gram and Ziehl-Neelsen stains and cultures.

RESULTS

The $^{99}Tc04^-$ uptake values in the knee joints of normal persons, and in knee joints treated by arthroplasty 9 months or more previously, are shown in Figure 1. The mean and S.D. was 54.3±10.2 cpm/μCi for the normal knee joints and 63.5±11.2 cpm/μCi for the 42 prosthetic knee joints without clinical signs of inflammation. There was a significant difference between the two groups, Pw <0.001 (Pw = tail probability of Wilcoxon's two sample test). The maximum normal value is 75 cpm/μCi. No significant difference was found between the knee with joint surface replacement and the clinically non-inflamed contralateral knee joint in 6 patients (Table 1).

$^{99m}Tc04^-$ uptake values were markedly increased in 6 prosthetic knee joints, which were painful, especially when strained. These joints showed slight to moderate swelling, warmth and tenderness. Moreover, in 5 of these 6 knee joints pain was elicited by longitudinal pressure and the sixth (represented by an open square in Figure 1) was the only knee joint with moderate effusion. The synovial fluid aspirated from this joint was yellow and slightly turbid. The white cell count per cubic millimetre was 38,000, with 90 per cent polymorphonuclear cells. The culture was positive for nonspecific streptococci. The remaining 42 knee joints with prosthetic replacement showed no clinical signs of inflammation.

Epicutaneous patch tests for hypersensitivity to the various components of the prosthesis and to the cement in the 6 patients with markedly increased $^{99m}Tc04^-$ uptake were negative, and radiological signs of loosening of the prosthesis (Ducheyne et al. 1978) were inconclusive.

Arthrotomy was performed in the 4 cases represented in Figure 1 by open circles; loosening of the tibial component was found in all of these. The remaining patient, with a clearly increased $^{99m}Tc04^-$ uptake and with complaints of pain on weight-bearing, refused reoperation.

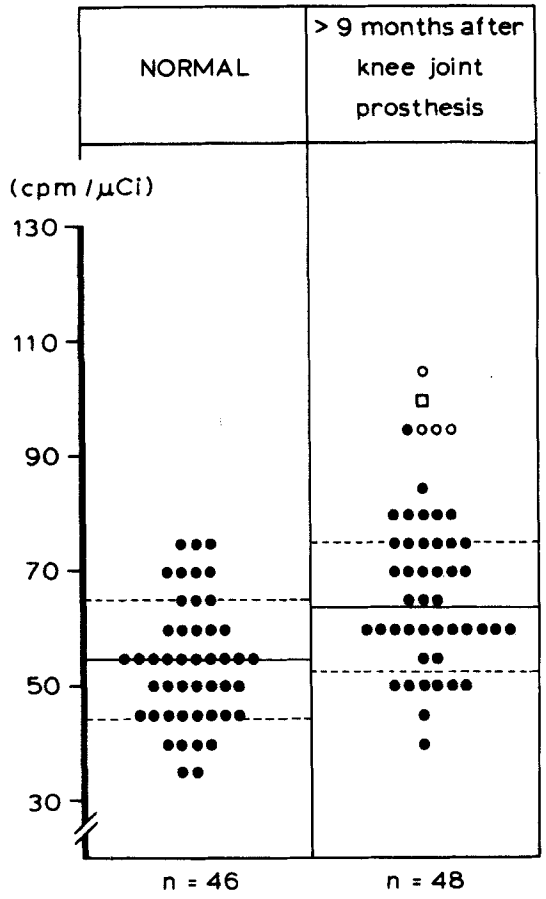

Figure 1. ^{99m}*Tc pertechnetate uptake in the knee joints,* $2^3/_4$ minutes after intravenous injection of 200 μCi, *in 23 healthy controls and 35 patients with rheumatoid arthritis who received 48 non-hinged knee joint prostheses. Open circles refer to knee joints with loosening of the prosthesis. The open square refers to the knee joint with infection.*

Histological examination of the synovial membranes generally revealed a marked degree of fibrosis, with only a few lymphocytes, plasma cells and giant cells beneath the lining cells. In the tissue around the prostheses more infiltration was seen; lymphocytes, plasma cells, and giant cells with rod-shaped bodies inside. The rod-shaped bodies showed strong positive birefringence when viewed between crossed polaroids. Immunofluorescence staining of synovial membrane for IgA, IgG, IgM, C1q, C3, C4 and fibrin only revealed the presence of fibrin on the synovial membrane surface. A few cells in the subsynovial tissue were positive for IgM and IgG. Bacteriological examination of the synovium was negative.

Table 1. ^{99m}*Tc04*$^-$ *uptake measurements in patients with rheumatoid arthritis, a non-hinged prosthesis in one knee* and no clinical signs of inflammation in the other*

Patient number	Right knee (cpm/μCi)	Left knee (cpm/μCi)
1	63*	56
2	75	68*
3	56	62*
4	73	65*
5	59	60*
6	70	60*

DISCUSSION

Rheumatoid synovitis apparently did not recur within 3 years in the prosthetic knee joints, although some of these joints showed signs of inflammation due to other causes. Only one review of 56 patients with rheumatoid arthritis followed up for more than a year after polycentric knee replacement mentions that, as a rule, no synovitis or effusion was found even in the presence of systemic activity (Bryan et al. 1973). Among 21 patients followed up for 1 year or more after synovectomy, Patzakis et al. (1973) found 14 with clinical and 18 with microscopic evidence of recurrence of the rheumatoid process in the synovium. In a previous study on synovectomized knees we found that, 1 year after synovectomy, the ^{99m}Tc04$^-$ uptake values were increased in 7 of the 8 knees (Boerbooms 1975).

Several radioisotopes, e.g. ^{99m}Tc methylene diphosphonate (Convery & Convery 1979), ^{85}Sr (Bauer et al. 1973) and ^{87}Sr (Feith et al. 1976), have been used for detection of loose or infected prostheses. In both situations increased osteoblastic activity was mentioned as the cause of the positive scintigraphy. ^{99m}Technetium diphosphonate scans were positive in 29 of the 30 joints with pain after hip joint replacement (Feith et al. 1976). Roentgenograms sometimes show a radiolucent zone around a prosthetic component, but this does not necessarily imply loosen-

ing. However, widening of the radiolucent zone on the roentgenogram, between the time immediately after arthroplasty and the time of revision, should more strongly indicate loosening of the prosthesis (Ducheyne et al. 1978). In the case of loosening of the prosthesis after total joint replacement, a high incidence of metal sensitivity was reported in patients with metal-to-metal but not in those with metal-to-plastic prostheses (Benson et al. 1975). In this study a metal-to-plastic prosthesis was used. In all cases of loosening, the polyethylene tibial component was concerned. There were no signs of hypersensitivity to the various prosthesis components as shown by epicutaneous patch tests. Phagocytosis of polyethylene in the giant cells (Revell 1979) was seen beneath the polyethylene component. So far as we know, hypersensitivity to polyethylene has not been described. The main cause of loosening of the tibial component of the prosthesis is probably mechanical (Ducheyne et al. 1978). The synovium of a knee joint with loosening of the tibial component usually showed fibrosis, but few signs of inflammation. Immediately beneath the tibial component, more signs of inflammation were found. This is probably the cause or one of the causes of the increased $^{99m}TcO4^-$ uptake.

Immunofluorescence studies of the synovial membrane obtained at arthrotomy in four cases with clearly increased $^{99m}TcO4^-$ uptake revealed only fibrin on the surface. Although fibrin masses are frequently seen in very early and active disease (Zvaifler 1973), similar findings have been reported in tissues from patients whose disease was clinically inactive when the tissues were obtained (Kaplan 1963) In patients with rheumatoid arthritis, immunofluorescence studies showed a rather wide distribution of IgG and more focally localized IgM staining. Massive distribution of both IgG and IgM has been reported in patients with rheumatoid arthritis and high rheumatoid factor levels (Kaplan 1963). Observations by Rodnan et al. (1967) indicate that the tissue distribution of C3 and C4 immunofluorescence in the synovial membrane followed the staining for IgG, suggesting the presence of immune complexes.

Why did we fail to find moderate or severe synovitis more than a year after non-hinged knee joint replacement, even when the rheumatoid arthritis was active? One difference between a synovectomized knee joint and a prosthetic knee joint is that the latter is without most of its cartilaginous structures such as menisci and articular cartilage. Recent studies have suggested that the presence of cartilage may have something to do with the chronicity of arthritic processes. Immunoglobulins and complement component have been found in hyaline articular cartilage and menisci in patients with rheumatoid arthritis (Cooke et al. 1975) and other forms of chronic arthritis (van de Putte 1978). Studies on antigen-induced arthritis in rabbits, a model for rheumatoid joint inflammation, have indicated that antigen, presumably in the form of immune complexes, persists predominantly in the vascular collagenous tissues of the joint (Hollister & Mannik 1974). Moreover, synovectomy performed in rabbits with severe antigen-induced arthritis did not protect them from recurrence of the inflammatory process (Currey et al. 1970). In this procedure the major fraction of retained antigen apparently is not removed. Extrapolating their experimental data to the human situation, Cooke et al. 1972 have suggested that retention of antigen in joint collagenous tissues such as hyaline cartilage, menisci and intra-articular ligaments, may play an important role in the perpetuation of joint inflammation. Our data on prosthetic knee joints are consistent with this hypothesis.

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