

TABLE I

Age, sex and laboratory results in four patients with RA and concomitant HCV infection

Patient	Age	Sex	IgM RF	HCV RNA	
				Serum	Synovial fluid
1	65	M	+	negative	negative
2	67	M	+	positive	negative
3	57	F	-	negative	negative
4	33	F	-	negative	positive (?)

Emeryville, CA, USA). Informed consent was obtained from all patients.

In three patients, HCV infection was community acquired and in the fourth it occurred after blood transfusions. Two patients had consistently negative results both on serum and SF. One patient had consistently positive results in the serum on four occasions ( $26.09$  to  $61.35 \times 10^5$  copies), whereas all three SF specimens were negative. In the fourth patient, HCV RNA was not detected in three different tests in the serum, but was present at the low concentration of  $5.92 \times 10^5$  copies in 1/3 SF specimens. HCV RNA was searched for in an arthroscopic biopsy of the SM by PCR with a negative result. Her disease was classified as Still's disease, although the criteria for RA were also fulfilled. The patient had complained of arthritis since age 4 after smallpox vaccination. She had a remission at age 12, but later arthritis recurred with high spiking fever, severe anaemia, leucocytosis, pericarditis, and hepato- and splenomegaly. IgM rheumatoid factor (RF), ANA, anti-DNA and anti-ENA antibodies were negative. Interestingly, arthritis recurred a few years after the blood transfusions that most probably caused HCV infection.

In our experience, HCV did not show a tropism for the SM, despite the inflammation-related increase in permeability and vascularization, since even the patient with consistently positive tests in the serum had no detectable amounts of HCV RNA in the simultaneously aspirated SF samples. Moreover, the only positive test in the SF was not confirmed when the SM was evaluated. The diagnosis of HCV infection was made on the basis of positive ELISA and Western blot tests, and should not have been influenced by the possible interference of IgM RF [6] or by high concentrations of IgG [7]. Our data indicate the need for further studies on the role of the SM as a site for HCV persistence, and on SF analysis for viral RNA as a tool for differentiating RA and concomitant HCV infection from HCV-associated arthritis.

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### Does Application of Radiographic Contrast Medium in Radiation Synovectomy Influence the Stability of Yttrium-90 Colloid?

SIR—Radiation synovectomy is a well-established method of non-surgical synovectomy for chronic inflammatory arthritis [1-5]. It is carried out by an intra-articular (i.a.) injection of a radiopharmaceutical. It is necessary to ensure that the needle is positioned correctly in the joint space before injecting the radiopharmaceutical. This is to prevent the spread of radioactive material in the adjacent joint structures. Radiographic contrast medium can help to confirm the correct position of the needle in the joint, and can provide information about the spread of the radionuclide in the joint space and adjacent bursae. For that aim, 1 ml of radiographic contrast is sufficient. Radiographic contrast medium is especially used when there is only a small amount of effusion, as we often saw in pigmented villonodular synovitis [2] and in haemophilic haemarthrosis [6].

Some radiographic contrast media contain chelating compounds e.g. ethylenediaminetetra-acetate (EDTA). In the information sheet of the European Association of Nuclear Medicine (EANM), entitled 'Radionuclide therapy: from palliation to cure', it is reported that yttrium-90 (Y-90) colloid has an affinity to some chelates (e.g. EDTA, which is used in iodine contrast medium). This may lead to a separation of the radionuclide from the colloid and hence, because of altered biodistribution after intracavitary administration, add to the bone marrow radiation dose [7].

So, the Y-90-EDTA complex can migrate into the blood circulation and be cleared by the kidneys. It may give undesirable radiation exposure of the whole body and possibly a decreased therapeutic effect in the inflamed joint. We have not found studies in the literature on this phenomenon.

We have therefore examined the influence of radiographic contrast medium on the biodistribution of Y-90 colloid injected in the knee joint. A controlled comparative trial was carried out comparing Y-90 colloid and radiographic contrast medium Omnipaque (containing EDTA), Y-90 colloid and radiographic contrast medium Urografine (without EDTA), and



Y-90 colloid with saline. The injections in the knee joint were followed by collection of the urine for 48 h and the radioactivity in the urine was measured.

Fifteen patients with an active chronic synovitis of the knee joint, which persisted after adequate treatment with anti-inflammatory drugs and i.a. corticosteroid injections, were included in this study. Patients who were treated with Y-90 colloid i.a. in both knees simultaneously were excluded for this study. All patients had given informed consent. The design of the work conforms to standards currently applied in the Netherlands. The patients were randomly divided into three groups of five patients: one group of five patients received an i.a. injection of 1 ml Omnipaque (Nycomed) containing 0.1 mg EDTA, a second group of five patients received i.a. 1 ml Urografine 60% (Scheding) without EDTA and a control group of five patients received i.a. 1 ml saline. Thereafter, each patient received an i.a. injection of 185 MBq (5 mCi) Y-90 citrate colloid (CIS bio international).

Preceding the Y-90 colloid treatment, the following inflammatory activity variables of the knee joint were scored: tenderness, swelling, effusion and warmth on a four-point scale (0 = absent, 1 = slight, 2 = moderate, 3 = severe). Furthermore, the ESR, the CRP, serum creatinine and an X-ray of the knee joint were performed. The X-rays were scored according to Larsen *et al.* [8]. The method for radiation synovectomy has been described before [2, 3]. Briefly, 185 MBq Y-90 colloid were diluted in the vial up to 3 ml with saline and transferred into a 5 ml syringe. With the patient in a supine position and using an aseptic technique, the injection site was cleaned. With a standard medial or lateral approach, a needle was inserted into the synovial cavity and the knee was drained as completely as possible. Using a three-way tap, 1 ml of one of the contrast media or 1 ml of saline was injected and followed by 185 MBq Y-90 colloid, then the needle was flushed with 1 ml of saline. Next, the needle was withdrawn, pressure applied to the injection site and the knee flexed twice before being immobilized in full extension with a bandage and/or a splint. The patient was then confined to bed for 3 days.

The urine of each patient was collected for 48 h. The total volume of each urine sample was determined and 4 ml of each urine sample were used for counting the radioactivity. Five microlitres of the solution of the injected doses were used as a standard and mixed with 4 ml of blank urine. Also 4 ml of blank urine were counted. To each urine sample of 4 ml, 16 ml of scintillation solvent were added (Hionic Fluor Packard). The  $\beta$ -radiation of the Y-90 was counted in a liquid scintillation counter for 10 min. Calculation of the percentage Y-90 in the urine was performed as follows: % of the dose in the urine =  $[(A/4) \times (C - B)] / [(3000/5) \times (S - B)] \times 100$ , where  $A$  is the volume of a urine sample,  $C$  is the count of the urine sample in c.p.m.,  $B$  is the count of the blank urine sample in c.p.m. and  $S$  is the count of the standard in c.p.m.

TABLE I

Nature and dose of radiographic contrast medium and urine radioactivity after Y-90 colloid measured as a percentage of the dose administered in the knee joint

No. of patients	Radiographic contrast medium	Radioactivity in urine (mean $\pm$ S.D.)
5	Omnipaque 1 ml	3.0 $\pm$ 1.8
5	Urografine 1 ml	3.0 $\pm$ 3.7
5	Saline 1 ml	3.1 $\pm$ 3.6

Quality control of three batches of Y-90 citrate colloid was performed by paper chromatography (Whatman 3 in acetone).

About 3% of the radioactivity administered into the joint was found in the 48 h urine sample (Table I). No differences in radioactivity counts were found between the three patient groups. There was no correlation between the radioactivity in the urine and the inflammatory activity variables of the knee joints, such as tenderness, swelling, effusion, warmth, ESR and CRP. Serum creatinine was normal. No relationship was found between the radiological score [8] and the amount of radioactivity in the urine. Our radiochemical quality control showed a purity of Y-90 colloid of >99%.

In this study, no significant differences in radioactivity excreted in the urine were found between three groups of patients treated with radiosynovectomy for a knee joint synovitis, whether or not a contrast medium, with or without EDTA, was added. Although on theoretical grounds one could expect some differences between these patient groups, no such differences could be determined. There was also no relationship between the inflammatory activity parameters or the radiological score [8] of the treated knee joint and the radioactivity excreted in the urine. In this small group of patients, we cannot confirm the suggestion in the EANM information sheet that for radiation synovectomy simultaneous administration of Y-90 colloid i.a. and iodine contrast media containing EDTA should be avoided.

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#### Re: Rheumatology in Israel

SIR—We have read with interest the International Letter 'Rheumatology in Israel' by Ehrenfeld *et al.* (*British Journal of Rheumatology* 1996;35:778-80).

Your readers may be interested to learn of the important part played by British rheumatology in the development of rheumatology in Israel. The Rheumatology Department of the Rambam Medical Centre in Haifa, which opened its doors in 1974, was firmly established in the best traditions of Taplow, Guy's and the Kennedy where Professors Yehuda Scharf and Menahem Nahir (neither mentioned in the Ehrenfeld article) received their specialist training in the 1970s. The Rambam unit remains, to this day, the only designated university rheumatology in-patient unit in Israel, having 12 beds (not 18 as reported in the article) dedicated for the treatment of rheumatic diseases.

It was from there that the first president of the fledgling Israel Society of Rheumatology was elected in 1984, that the successful struggle leading to the heavily resisted recognition of the speciality was waged, that the curriculum of the Specialty Board in Rheumatology was developed and where, until 1994, all qualifying examinations for the boards were held. Over the years, an impressive, modern and popular service has been built up spanning rheumatology in the widest sense, and matched by a commensurate programme of wide-ranging clinical and laboratory research (of which, contrary to what is stated in the report, AIDS research plays no part).

Of particular importance to patient care in this unit has been, firstly, the introduction of the rheumatology nurse practitioner (based on the Leeds model) and, secondly, a uniquely close collaboration with their two British-trained rheumatological surgical colleagues, Professors Daniel Reis and Michael Besser. The most recent British influence came when Ms Helen

Whitelock, from the RNHRD in Bath, acted as external adviser on a scheme to develop a much-needed hydrotherapy pool, which opened last year.

The Rambam Rheumatology Unit has a distinguished international reputation. The list of rheumatological world leaders who have contributed to its academic programme reads like an international 'Who's Who'!

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#### Erythrocyte Sedimentation Rate (ESR) at Presentation is a Prognostic Indicator for Duration of Treatment in Polymyalgia Rheumatica (PMR)

SIR—Dolan *et al.* [1] have compared ESRs in PMR patients still on prednisolone after 24 months with ESRs in those off prednisolone at 24 months. They describe a higher pre-treatment ESR and higher ESRs at 12 and 24 months in the group who were still on prednisolone after 24 months. However, they state that the prednisolone dose was reduced 'according to disease activity and ESR'. This would create a 'self-fulfilling prophecy' whereby patients with higher ESRs on treatment would be continued on higher doses of prednisolone for longer. This, in turn, raises the possibility that the apparent association of pre-treatment ESR and duration of prednisolone treatment is due not to true prediction of disease activity, but purely to prediction of later ESR levels regardless of clinical disease activity. In other words, are individuals who tend to run higher ESRs in health likely to have the higher ESRs at presentation of inflammatory disease such as PMR?

We are in the unusual position of having a cohort of PMR patients recruited without the requirement for raised ESR at presentation, and in whom relapse was diagnosed clinically without reference to ESR. This cohort is, therefore, a valid group in which to examine the usefulness of ESR at presentation as a prognostic indicator for the duration of treatment in PMR. This cohort has been described previously [2], and of those 44 patients 40 have now been followed either until successfully off prednisolone for 6 months or still requiring prednisolone at 48 months. Of the 40 patients, 29 were female and the median age was 71.5 (range 51-87) yr; 25 had pure PMR, six pure giant cell arteritis (GCA) and nine had both. Six had biopsy-proven GCA. Median ESR at presentation was 46 (range 7-112). Twenty-six patients suffered at least one clinical relapse and the median duration of treatment was 34.5 months (range 12 to >48 months). Both ESR at first relapse and ESR during disease suppressed on treatment did show weak correlations with ESR before treatment ( $r_s = 0.229$  and  $0.297$ , respectively), but this did not reach statistical significance ( $P = 0.261$  and  $0.149$ ) in this group of 26. This does not convincingly rule out a spurious association of pre-treatment ESR and duration of