Ann. rheum. Dis. (1971), **30**, 180

Radioactive yttrium in the treatment of rheumatoid knee effusions

Preliminary evaluation

J. F. BRIDGMAN, F. BRUCKNER, AND N. M. BLEEHEN

From the Departments of Rheumatology and Radiotherapy, The Middlesex Hospital, London

Irradiation of the synovium for the treatment of chronic knee effusions associated with rheumatoid arthritis and allied conditions is being increasingly used as an alternative to surgical synovectomy. Intra-articular injections of a colloidal solution of radioactive gold (^{198}Au) has been tried with some success (Ansell, Crook, Mallard, and Bywaters, 1963; Virkkunen, Krusius, and Heiskanen, 1967; Makin and Robin, 1968; Grahame, Ramsey, and Scott, 1970).

However, as ^{198}Au has a beta-particle maximum range in tissue of only 4 mm. and as the synovium in these chronic knee effusions can attain a thickness of greater than 1 cm., a complete synovial ablation is not produced. A serious disadvantage of intra-articular ^{198}Au is that there may be marked leakage from the joint to the regional lymph nodes, the liver, and spleen in as many as 36 per cent. of patients so treated (Virkkunnen and others, 1967). Moreover, radioactive gold possesses a significant gamma-ray component and this gives an unwanted whole body radiation to the patient. Because of these disadvantages it has been suggested that radioactive yttrium (^{90}Y) may be a more suitable agent (Ansell and others, 1963; Grahame and others, 1970).

^{90}Y is a pure beta-emitter with a maximum range in tissue of 10 mm. It has a higher maximum energy than gold, 2·26 MeV compared with 0·9 MeV, and it has a half-life of 2·7 days. The whole body distribution of ^{90}Y silicate and ^{90}Y resin after intra-articular injections has been compared (Prichard, Bridgman, and Bleehen, 1970). It was found that silicate preparations were associated with an appreciable leakage from the joint, but that the resin remained localized. It has also been shown that the ^{90}Y resin was taken up more or less evenly in both normal and inflamed rabbit synovia (Webb, Lowe, and Bluestone, 1969).

We have therefore undertaken a controlled double-blind trial, using intra-articular ^{90}Y resin in the treatment of chronic knee effusions. The preliminary results after assessment of all cases 6 months after the intra-articular injections are presented.

Patients and methods

Of 22 patients who consented to be included in the study, nineteen had rheumatoid arthritis, two hydroarthrosis associated with osteoarthrosis, and one psoriatric arthropathy. All the patients had knee effusions of an average duration of at least 6 years (range 2 to 18) and had been resistant to other forms of treatment, including repeated aspirations and intra-articular injections of hydrocortisone. One patient had previously received deep *x*-ray therapy to the knees and another had received intra-articular Thio-tepa.

There were twenty patients with the bilateral effusions who had injections of ^{90}Y into one knee and this was compared with a placebo injection of saline into the other knee. ^{90}Y was also given to two other patients with unilateral effusions. One of the authors assessed the knees before injection, afterwards at 1 week, 2 weeks, 4 weeks, and then monthly intervals for up to 6 months, under double-blind conditions. The assessments consisted of improvement or worsening in pain, subjective changes, changes in a fixed flexion, joint range, knee circumference, and effusion. 10 ml. synovial fluid were aspirated after each assessment for the measurement of cells, viscosity, transaminases, and acid and alkaline phosphatase levels. Nineteen patients were treated as out-patients and three as in-patients. The knee which was to receive the ^{90}Y was randomly selected and the dose given was 3 mc. The ^{90}Y resin was obtained from the Radiochemical Centre, Amersham, incorporated in colloidal particles of Zeocarb resin, stabilized with glucose and having particle size of 40 to 50 mμ.

Results

The results of assessments were graded as improvement, no change, or worsening. A change in the measurement of the knee circumference of more than half an inch, a change in the joint range of 10°, and a change in the fixed flexion of 5° was regarded as significant.

Table *Assessment at 6 months in 42 cases*

Parameter	*Treatment*	*No. of cases*	*No. improved*	*Significance of improvement***
1. Effusion	Isotope	22	15	0·01
	Control	20	7	
2. Knee circumference	Isotope	22	5	
	Control	20	3	
3. Joint range	Isotope	22	10	0·001
	Control	20	0	
4. Fixed flexion	Isotope	22	3	
	Control	20	2	
5. Subjective change	Isotope	22	10	
	Control	20	7	
6. Pain	Isotope	22	12	
	Control	20	9	

**Significance of improvement with respect to the total number of cases as determined by Fisher exact test

The results of assessment (Table) show that in the ^{90}Y group there has been persistent improvement of the joint range in ten patients and of the effusion in fifteen patients after 6 months. These results are statistically significant. In only seven patients had the effusion completely disappeared at 6 months. Seven of the patients who received the ^{90}Y developed reactions (lasting an average of 48 hours) and consisting of general malaise, flu-like symptoms, shivering, pyrexia, severe pain, and swelling of the knee. The symptoms usually resolved within 3 days and responded to simple treatment of rest in bed and salicylates.

There were no important changes in the synovial fluid cell count, viscosity, transaminases, or acid and alkaline phosphatases.

Discussion

The results are encouraging as far as the objective criteria of improvement are concerned. Although a large number of the treated knees were said to be subjectively improved, there was no real statistical difference compared with the placebo.

Delbarre, Cayla, Menkes, Aignan, Roucayrol, and Ingrand (1968) who used 6 mc. ^{90}Y, had good results in 55 per cent. of patients treated, with no short-term reactions, but their trial was not conducted under double-blind conditions and included patients treated with ^{198}Au.

In another series, in which 12 mc. radioactive gold were employed (Grahame and others, 1970), an exacerbation of pain and effusion in 20 per cent. of the patients came on within 1 week of the injection. Occasional skin burns around the injection site, presumed to be due to leakage of the isotope from the needle tract, were also reported.

The dose of 3 mc. ^{90}Y used in our series may have been too low. We have so far hesitated to use larger doses because of the risk of severe local and general reactions, and the possibility of producing radio-necrosis of the cartilage and malignant change in the synovia.

We are observing these patients on a long-term basis to measure the duration of the effect of the injection and to search for any adverse effects.

Summary

The results are presented of treating a series of 22 patients in a double-blind controlled trial using an injection of ^{90}Y or saline into 42 knee joints.

There was sustained improvement at 6 months in the objective changes of joint range in ten patients, and of effusion in fifteen patients. There were general and local reactions in seven patients.

We are extremely grateful to Dr. A. C. Boyle for his valuable advice and for allowing his patients to enter this study.

References

ANSELL, B. M., CROOK, A., MALLARD, J. R., AND BYWATERS, E. G. L. (1963) *Ann. rheum. dis.*, **22,** 435 (Evaluation of intra-articular colloidal gold ^{198}Au in the treatment of persistent knee effusions).

DELBARRE, F., CAYLA, J., MENKES, C., AIGNAN, M., ROUCAYROL, J.-C., AND INGRAND, J. (1968) *Presse méd.*, **76,** 1045 (La synoviorthèse par les radio-isotopes).

GRAHAME, R., RAMSEY, N. W., AND SCOTT, J. T. (1970) *Ann. rheum dis.*, **29,** 159 (Radioactive colloidal gold in chronic knee effusions with Baker's cyst formation).

MAKIN, M., AND ROBIN, G. (1968) *Proc. roy. Soc. Med.*, **61,** 908 (Radioactive colloidal gold in the treatment of chronic synovial effusions).

PRICHARD, H. L., BRIDGMAN, J. F., AND BLEEHEN, N. M. (1970) *Brit. J. Radiol.*, **43,** 466 (An investigation of radioactive yttrium (^{90}Y) for treatment of chronic knee effusions).

VIRKKUNEN, M., KRUSIUS, F.-E., AND HEISKANEN, T. (1967) *Acta. rheum. scand.*, **13,** 81 (Experiences of intra-articular administration of radioactive gold).

WEBB, F. W. S., LOWE, J., AND BLUESTONE, R. (1969) *Ann. rheum. dis.*, **28,** 300 (Uptake of colloidal radioactive yttrium by synovial membrane).