Effect of premedication with intra-articular hydrocortisone on the retention of ¹⁹⁸Au in the knee joint in rheumatoid arthritis

Use of ^{99m}Tc in assessment

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Intra-articular radioactive colloids are most often used to treat rheumatoid arthritis of the knee when joint effusion persists in one or both joints after general measures and simple local measures have failed. Almost certainly an intra-articular steroid will have been tried. Even when long-term help is not obtained by intra-articular steroids, there is usually temporary subjective benefit and often objective evidence of reduced activity.

When I first premedicated knee joints with hydrocortisone 4 years ago I considered two possible advantages from even such transient benefit. One was that it might eliminate any reactive inflammation to colloidal radioactive gold. I believe Delbarre, Cayla, Aignan, Roucayrol, Menkes, and Ingrand (1968) used intra-articular steroids at the same time as colloidal radiogold for this purpose, and also for clearing the needle of radioactive material. The other possible advantage was that, by reducing the effusion and perhaps the thickness of the synovium, the short range β -emission of the colloidal gold would be more effective.

Subjective improvement from intra-articular steroids may take up to 2 days or more to reach its maximum. If joints are aspirated at intervals after injection with intra-articular steroids, change in the joint fluid occurs over 2 or 3 days, with the fluid gradually becoming clearer and more viscid. From these clinical observations, an interval of 2 or 3 days seemed desirable between the premedication with intra-articular hydrocortisone and the administration of the radioactive colloid. Long after the synovial fluid has reverted to its previous cloudy watery state, subjective benefit may continue, so that objective criteria are needed to judge the optimal interval.

The first four patients treated in this way had bilateral knee effusions. 50 mg. (25 mg. in one case) hydrocortisone for intra-articular use was injected into one knee of each patient, and 2 days later 10 mCi. colloidal radioactive gold (particle size 20–30 m μ) was given by intra-articular injection to *both* knees. Scans of the groins and abdomen 3 to 8 days

later showed no leakage to the inguinal, para-iliac, or para-aortic glands on the sides which had received premedication, but three out of the four sides not premedicated showed leakage to the glands.

It was purely serendipity which revealed that premedication with hydrocortisone reduced the leakage of colloidal radioactive gold. Subsequently we looked into this question alone and tried to find the optimum interval between premedication and therapeutic injection by varying the interval. Standard premedication was used with 50 mg. hydrocortisone. Some knees were not premedicated. In this paper, 'leakage' means *any* loss of radioactivity to inguinal, pelvic, or intra-abdominal glands as shown on scans mainly done between 1 hour and 2 days after the radioactive gold was injected. No attempt was made to assess grades of leakage. 52 knees (28 patients) gave the results shown in Table I. All the patients had rheumatoid arthritis and most were seropositive. There were ten men and eighteen women. All but one were over 50 years of age, most of them being over 60. One woman had both knees treated in 1969 and again in 1972.

Table I Leakage from the knee joint with and without premedication

Premedication	Interval before radioactive gold injection (days)	No. of knees	Percentage showing leakage
None	—	23	78
50 mg. hydrocortisone	1	11	55
	2	12	25
	7	6	33

Comparing the premedicated group with the unpremedicated the difference is significant at the 1 per cent. level. The results suggest that an interval of at least 2 days is desirable but this does not stop leakage in all patients. A longer interval or a larger

dose of hydrocortisone or both may give better results. So far exploration of these possibilities has been limited to 100 mg. intra-articular hydrocortisone to five knees in four patients. Three of these knees showed a leakage of colloidal radioactive gold given 1 day later.

Arthrograms in rheumatoid arthritis sometimes show filling of lymphatic vessels by contrast medium. Marked lymphatic filling occurs only in joints with the most active inflammation; it does not occur in less active joints.

Radioactive colloidal particles are much larger than the molecules of water-soluble contrast media, but if the increased inflammatory activity of a joint encourages a loss of contrast media *via* the lymphatics, it might influence loss of colloidal particles too.

The inflammatory activity of knee joints has been assessed using a clinical thermal index and also a technetium index. The clinical index is based on the warmth of the anterior aspect of the knee as felt by the palm in relationship to the anterior thigh and to the calf when both lower limbs are completely exposed. The technetium index is a knee/calf ratio of uptakes at 1, 2, 5, 10, and 15 minutes after the intravenous injection of pertechnetate. There is a close statistically significant relationship between these two indices, which show good reproducibility.

In most of the patients treated these indices were measured before treatment with colloidal radioactive gold. In premedicated joints these same assessments done before premedication and immediately before the therapeutic injection indicated that in joints showing leakage the disease activity was less well suppressed on the whole than in those showing no leakage, but the difference was not great.

In the presence of an effusion, Dixon and Grant (1964) have shown that use of the knee joint produces high intra-articular pressures. These high pressures may also encourage the leakage of joint fluid *via* the lymphatic vessels. If this is so one would expect less leakage from inpatients (especially those resting in bed) than from outpatients. Our figures confirm this and show that premedication benefits both outpatients and inpatients (Table II).

Table II *Results of premedication in inpatients and outpatients*

Patients	Inpatients		Outpatients	
	Leaking	Not leaking	Leaking	Not leaking
Knees				
Premedicated	2	6	9	10
Not premedicated	7	3	10	1
Totals	9	9	19	11

In a trial carried out 3 weeks ago we tried splinting alone for 1 day before and 2 days after the therapeutic injection in four knees of three patients, but leakage

occurred from all four knees. This experience showed me that, even with splinted knees, the amount the knee was rested depended also upon other factors, such as the availability of porters, manoeuvrability of patients, and the shape of leg for splinting.

Technically, premedication with hydrocortisone may make the subsequent injection of colloid harder, as the smaller amount of viscid joint fluid may be more difficult to aspirate. When I have been unable to aspirate joint fluid I have injected 10 to 20 ml. normal saline to satisfy myself of free flow and to produce an observable effusion to ensure that the needle is free in the synovial cavity.

Treatment with intra-articular radioactive colloids is a very simple matter for the patient. Unlike surgery this procedure can be given without fear of extra strain on other joints. Loss of flexion is not to be expected as a result of treatment.

Intra-articular radioactive colloids are almost wholly used in older patients and often in the elderly with a short life expectancy. It would be a pity if theoretical hazards reduced the use of this treatment in such patients or if sophisticated methods using more time, bed space, and money meant that fewer patients could be treated.

Summary

Intra-articular hydrocortisone premedication of the knee joints in rheumatoid arthritis 2 days before the use of intra-articular colloidal radioactive gold stops leakage to the lymph nodes in a useful proportion of patients.

We should like to acknowledge the help when this work began of Dr. Adel Fam, who is now in Toronto.

Discussion

PROF. INGRAND Dr. Goode has pointed out the importance of the synovium in the phenomenon of leakage. I should like to show some slides which emphasize this. Figs 1 and 2 show data concerning ^{186}Re and $^{99\text{m}}\text{Tc}$ distribution in the same joint.

(1) 24 hrs after the injection of a tracer dose of colloidal ^{186}Re , external counting gives 58,036 counts per minute in the knee and 11,223 counts per minute in the groin. The distribution of radioactivity is shown in Fig. 1.

(2) 12 days later colloidal $^{99\text{m}}\text{Tc}$ was injected into the same knee and the scan shown in Fig. 2 was obtained.

The pattern of distribution is obviously rather similar and we were tempted to conclude that the state of the knee joint is more important than the colloidal characteristics. But another observation led us to reconsider this conclusion (Fig. 3). In another patient external counting after an injection of ^{90}Y into the knee indicated 9,100 counts per

FIG. 1 Scintigrams of groin after injection of a tracer dose of ^{186}Re into the knee. At this time the count rate over the knee was 58,036 c.p.m. and over the groin 11,223 c.p.m.

FIG. 2 Scintigram in same patient as in Fig. 1 after injection of $^{99\text{m}}\text{Tc}$ into the knee (see text).

minute at the point of injection and 1,700 counts per minute in the groin. 4 days later a $^{99\text{m}}\text{Tc}$ injection into the same knee disappeared entirely from the joint and was found in the inguinal and pelvic lymph nodes. In that case the properties of the colloids played an important part.

FIG. 3 Scintigram of lower abdomen of a patient 4 days after injection of a tracer dose of ^{90}Y citrate and 4 hours after injection of $^{99\text{m}}\text{Tc}$, both into the knee. While the count rates for ^{90}Y were 9,100 c.p.m. in the knee and 1,700 c.p.m. in the groin, all the activity for the $^{99\text{m}}\text{Tc}$ was found in the groin and none in the knee (see text)