Comparison of ⁹⁰Y ferric hydroxide colloid with the citrate and resin colloids

A preliminary animal study

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This was a preliminary evaluation of ⁹⁰Y ferric hydroxide colloid for the Radiochemical Centre before using it in patients. Autoradiographs of rabbit knees, both inflamed and non-inflamed, showed that the material was evenly distributed in the synovium, and that there was no evidence of aggregation *in vivo*. Table I shows the retention of ferric hydroxide colloid in the knees of nine rabbits killed at different intervals, compared to a standard aliquot dispensed at the same time. Three separate batches of ferric hydroxide colloid were used. After the animals had been killed, the knees, liver, and popliteal and inguinal lymph nodes were removed and the radioactivity counted. One batch of resin colloid and one batch of citrate colloid were similarly studied. We were surprised to find as much liver uptake with resin colloid, which Gumpel, Williams, and Glass (1973) had noted only once in humans, but this may be a reflection of the difficulty of scanning techniques in man. The popliteal node figures are similar in time distribution to those we found in a comparison of citrate and resin (Gumpel, Farran, and Williams, 1974). No uptake was found in inguinal nodes.

There is an interesting difference in the retention of isotope in inflamed and non-inflamed knees Table II. Each rabbit had been sensitized and one knee injected with gamma globulin to produce a Dumonde-Glynn type of arthritis, while the other knee was not inflamed. The ferric hydroxide was retained equally well in inflamed and non-inflamed knees, while the citrate and resin were appreciably less well retained in the inflamed knees. There was no overlap in the figures for inflamed and non-inflamed knees.

Table I Comparison of ⁹⁰Y colloids in rabbits

Retention in the knee and extra-articular spread

⁹⁰ Y colloid	Mean retention in the knee (hrs)			Uptake in	
	24	48	168	Liver	Popliteal lymph node
Ferric hydroxide (Amersham)	93 (6)	95 (6)	65 (6)	0.3 (8)	0 (9)
Resin (Amersham)	66 (2)	67 (2)	41 (2)	4.5 (3)	0 (3)
Citrate (Saclay)	85 (2)	69 (2)	51 (2)	0.4 (3)	0.6 24 hrs 0.1 48 hrs 0.0 168 hrs

Percentage of injected dose, corrected for decay.
() No. of organs counted for each mean.

Table II Retention of radiocolloids in inflamed and non-inflamed knees

Radiocolloid	Mean retention in the knee		
	Inflamed	Non-inflamed	No. of knees
Ferric hydroxide	82	76	6
Resin	47	76	3
Citrate	49	95	3

This differential retention is most interesting, and points to the need for further work on the factors influencing retention of radiocolloids.

Discussion (of papers 3 and 4)

DR. GUMPEL I should like to ask one question of both Dr. Peake and Prof. Ingrand. Although Prof. Ingrand showed particle sizes for the citrate, *in vivo* the citrate has been shown to dissociate quite considerably (Bontoux, Marignan, and Bali, 1968). Do these particle sizes stand *in vivo* or would you say that it is no longer associated with its carrier? Dr. Peake: when you have injected your new ferric hydroxide do you think it parts from its carrier or remains with its carrier?

PROF. INGRAND I have no answer to your question.

DR. PEAKE We have no evidence to answer this question with any certainty, but the evidence that we have in saline and related media suggests that the ⁹⁰Y does stick to the ferric hydroxide very strongly indeed. In fact, in no experiments, apart from those in which we have reduced the pH down to about pH 3, have we found the ⁹⁰Y to part from the ferric hydroxide at all.

DR. WEBB Did you have a chance to look at the histology of the lymph nodes draining the knees in these rabbits?

DR. GUMPEL Yes, we have looked at them in a preliminary way. We have not seen any autoradiographic appearance of isotope coming into the lymph nodes, and we have not seen any major histological changes.

DR. DOLPHIN I should like to comment on Dr. Peake's answer. He said that the yttrium stuck with the ferric hydroxide if you changed the pH, but *in vivo* I think there must be some competition between the proteins and the other molecules in the knee joint for the yttrium which is originally bound to the ferric hydroxide.

DR. PEAKE I think your comment is probably justified. The only evidence that I have to go on is *in vitro* experiments which do suggest that the ^{90}Y sticks to the ferric hydroxide colloid over a range of chemical conditions.

DR. BOYD It is known, surely, that iron tends to aggregate in the synovial fluid and in the inflamed synovium of rheumatoid arthritis. Is it not possible that, quite apart from the advantages of iron as a vehicle here, it may be encouraging the retention of ^{90}Y within the joint for this very reason.

DR. PEAKE The levels of iron that we see in the hydroxide colloid are very tiny indeed, less than $1\text{ }\mu\text{g./ml.}$ I do not know whether this is an answer to your question.