# THE CLEARANCE OF INTRA-ARTICULARLY ADMINISTERED RADIOCOLLOIDS FROM THE KNEE JOINT

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The utilization of intra-articularly administered colloidal particles as drug delivery systems for the treatment of rheumatoid arthritis requires detailed analysis of the various sytems in joint cavities. Studies with radiocolloids have suggested that particle size is probably a major factor in influencing clearance and lymphatic localization from joints (Strand and Persson 1979).

In an attempt to elucidate the pharmacokinetics of particles administered to the kneejoint, the clearance of various particles of different sizes was measured using gamma scintigraphy. Five types of colloidal particles were examined namely polystyrene latex, sulphur colloid, antimony sulphide colloid, soy bean oil emulsion and egg lecithin liposomes. The latex particles were labelled by irradiating a small volume of latex and $^{131}I$ with a $^{60}Co$ source (3-3.5 M Rads). Free $^{131}I$ was removed by centrifugation and continuous dialysis and the suspension made up to volume with pH 7.4 phosphate buffer saline. The Tc-99m sulphur colloid was prepared by adding sodium pertechnetate and 0.2% sodium thiosulphate solution to a sealed vial boiled and buffered. The Tc-99m antimony sulphide colloid was prepared by adding antimony potassium tartrate to saturated $H_2S$ containing 3.5% PVP. Tc-99m sodium pertechnetate was added to antimony sulphide colloid, and the product boiled and buffered. $^{131}I$ liposomes were prepared according to the method of Hardy et al (1980).

The $^{123}I$-soy bean oil emulsion was prepared by dissolving 2 ml soy bean oil in 6 ml ether and mixing with an equal volume of $^{123}I$, iodide-thio sulphate. The resultant lower layer was removed (7 ml) and mixed with 3 ml of 8% w/v Tween 80, and ultrasonicated for 2 min and filtered. Particle size was determined using electron microscopy and Coulter Nanosizer analysis. 0.1 ml of each labelled preparation was injected into the right knees of New Zealand White rabbits (3 per group) and each rabbit placed in a Perspex restraining box prior to scanning. Scintigraphic examination of each rabbit was carried out at intervals over a 5 day period following intra-articular administration.

A plot of half life ($t_{\frac{1}{2}}$) for the clearance of latex particles from the knee joint versus particle size exhibited a minimum of (0.4μm), with longer $t_{\frac{1}{2}}$ (>100h) compared with free Na-$^{131}I$ solution ($t_{\frac{1}{2}}$<0.2h). Studies with the other colloids showed more rapid clearance than the latex, with $t_{\frac{1}{2}}$ of 10.5h for the sulphur colloid, 8.8h for antimony colloid and 15.5h for soy bean oil emulsion. For liposomes, a more rapid clearance of small (0.1μm) vesicles ($t_{\frac{1}{2}}$=18h) occurred compared with the large multilamellar (1.5μm) liposomes ($t_{\frac{1}{2}}$=33h). This size effect is different from the clearance kinetics previously observed for i.v. administered liposomes (Juliano and Stamp 1975).

Histological investigation indicated that latex and liposomes had no demonstrable inflammatory effect on the synovium. Antimony sulphide produced marked local inflammation and the sulphur colloid caused only limited localized reactions. Thus present findings indicate separate particle size dependency on the clearance from the knee joint of the inert polystyrene latex and the degradable colloidal particles.

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