

THE AUTHORS' REPLY

This second letter to the editor concerning radio-nuclide venography (RNV) is further evidence of the widespread interest in the diagnosis and eventual treatment of deep venous thrombosis (DVT).

We have no experience with thermography. However, any test that adds additional information for the diagnosis of DVT in patients is welcomed.

As one moves further away from directly imaging the venous system itself, the diagnostic accuracy diminishes. Our experience with Doppler ultrasonography documents this.

We would raise the question as to whether arterial disease, decreasing perfusion to one of the lower extremities, would make the other appear falsely "hot." This theoretical consideration should be pursued.

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LUNG RETENTION OF ^{99m}Tc-SULFUR COLLOID

The discussion in the *Journal* (1,2) about the retention of ^{99m}Tc-sulfur colloid in the lungs and about gel chromatography as an analytical tool for ^{99m}Tc radiopharmaceuticals (3) has prompted us to add a few observations made during a comparative study of most of the commercially available ^{99m}Tc-liver colloid preparation kits (4).

We used the technique of Persson and Strand (5). A Sephadex G-25 column was scanned using a chromatogram scanner after developing a 30-cm column with 15 ml of 0.9% NaCl solution. We noticed a great difference in the behavior of different ^{99m}Tc-sulfur colloid products as can be seen from Table 1. Mean values and standard deviations of four determinations are given. Each product was tested with two different ^{99m}Tc generators. Pertechnetate will appear at 5-10 cm and only small amounts were registered with preparation C.

Stannous chloride-reduced-technetium is bound at the top of the column and can, as the technetium bound at 0 cm from the sulfur colloid, only be removed after treatment with hydrogen peroxide and ammonia.

All preparations studied were based on the thiosulfate/hydrochloric acid systems. Preparations A,

B, and C contained gelatin as a stabilizer. Preparation D contained Haemacell®, preparation C contained perrhenate, and preparation A contained EDTA.

Table 1 also gives the results of filtration through micropore filters. Filtration through Nuclepore® filters (1 micron) and Millipore® filters (8 microns) showed that Millipore filters also have the ability to bind ^{99m}Tc from ^{99m}Tc-sulfur colloids. There is close correlation between the percentage bound to Sephadex columns and to Millipore filters. Nuclepore filters (8 microns) were not available to us but 5-micron filters gave results as expected from 1-micron filters and microscopy of the colloids.

From these experiments we draw the conclusion that ^{99m}Tc is bound with different strength in the different types of preparations and that this might well be of importance when discussing lung uptake of ^{99m}Tc from ^{99m}Tc-sulfur colloids. We find that our experiments might support the idea that under some in vivo conditions, ^{99m}Tc might be transferred from colloids to particles that subsequently are taken up in the lungs or otherwise bound to lung tissue.

Our experiments have shown that different types of ^{99m}Tc-sulfur colloids do have different physico-chemical properties although they are based on the

TABLE 1. DISTRIBUTION OF ^{99m}Tc-SULFUR COLLOIDS ON SEPHADEX COLUMNS AND ON MICROPORE FILTERS

^{99m} Tc-sulfur colloid preparation	Distribution on Sephadex G-25 column				Percent remaining on filter			
	0 cm	Percent	30 cm	Percent	Nuclepore (1 micron)	Percent	Millipore (8 microns)	Percent
Manufacturer								
A	93 ± 5		3.5 ± 2		1.1 ± 0.2		54 ± 7	
B	34 ± 12		58 ± 12		22 ± 6		26 ± 4	
C	64 ± 6		30 ± 13		27 ± 13		48 ± 10	
D	6 ± 6		83 ± 12		0.5 ± 0.1		15 ± 0.5	

same components. They might therefore also have different biologic properties. It has become the practice of journals to refer to the radiopharmaceutical used just as ^{99m}Tc -sulfur colloid. In order to be able to correlate preparation data with clinical results, we should like to urge authors to give preparation details as long as it is not possible to describe com-

pletely the composition and structure of a ^{99m}Tc -sulfur colloid.

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We share the concern of Kristensen and Pedersen over the need for a clear statement of the method of preparing the radiopharmaceutical in any reports of unusual observations obtained when using that particular radiopharmaceutical. A review of the preparation procedures for various ^{99m}Tc -labeled radiopharmaceuticals published in the *Journal* in the last few years reveals that there are a number of different preparative procedures for most commonly used ^{99m}Tc radiopharmaceuticals. In order to establish the significance of any particular result, it is helpful to know what preparation technique was used and what quality control, if any, was carried out. In this way it is possible to predict the likely byproducts of the preparation technique and whether or not the quality control would have detected those byproducts. However, in this respect the discussion on lung retention (1-9) of ^{99m}Tc -sulfur colloid cannot be faulted, since each author in his original article either gives a reference for his preparation procedure or details it in the article. It is interesting to note in this respect that each investigator(s) reporting lung retention of ^{99m}Tc -sulfur colloid in the *Journal* has used a different procedure for preparing the labeled colloid. In addition, we have also seen rare cases of lung retention of ^{99m}Tc -sulfur colloid associated with severe liver disease. We use a preparative procedure based on that of Webber, et al (10) which is again different from these other reports. The quality control on our sulfur colloid involves thin-layer chromatography on silica gel with an 85% methanol solvent, the required purity being greater than 95%, and an

inspection of a sample of the preparation on a hemacytometer slide to insure that no particles are larger than 2 microns in size. In order to compare our preparation with those described by Kristensen and Pedersen, we carried out a gel filtration separation using Sephadex G-25 and found that $90 \pm 10\%$ (this being the mean value and standard deviation of three determinations) migrated as colloid with the remainder being bound to the top of the column. Thin-layer chromatography indicated a 97% incorporation of the ^{99m}Tc into the sulfur colloid. This would suggest that our preparative procedure results in a ^{99m}Tc -sulfur colloid in which the ^{99m}Tc is firmly bound to the colloid.

Because of the wide variation of preparations used in these studies, and the demonstrated relatively firm binding of the ^{99m}Tc to the colloid in our preparation, we believe that the reason for the lung uptake is not of a chemical nature, but rather of a physiologic one which manifests itself in a small fraction of patients with severe liver disease.

It is also interesting to note that last year three cases were reported in the *Journal* (11,12) in which renal uptake of sulfur colloid was observed. All three patients were suffering from congestive heart failure. It would therefore seem that uptake of ^{99m}Tc -sulfur colloid by an unusual organ may be a disease-related phenomenon.

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Relative to the comments of Kristensen and Pedersen about the quality of ^{99m}Tc -sulfur colloid, we investigated the ^{99m}Tc -antimony sulfide colloid (1,13) by the technique of Persson and Strand (5) and by filtration through Millipore filters (0.45 micron). After developing a 30-cm Sephadex G-25 column with 0.9% NaCl solution, we obtained the results shown in Table 1. The gel filtration showed a good yield of the ^{99m}Tc -antimony sulfide.

Filtration of the colloid solution three times

through a Millipore filter (0.45 micron), using a new filter each time, gave the results shown in Table

TABLE 1. GEL CHROMATOGRAPHY COLUMN SCANNING OF ^{99m}Tc -ANTIMONY SULFIDE

Column (cm)	Percent of total activity
0-6	5.0
6-10 ($^{99m}\text{TcO}_4^-$)	5.5
25-30 ($^{99m}\text{Tc-Sb}_2\text{S}_3$)	82.0