HUMAN SERUM ALBUMIN AS A STABILIZER FOR ^{99m}Tc-SULFUR SUSPENSION

Over the past few years in nuclear medicine, scanning agents have been produced that have greatly enhanced the technical quality of body organ scans. Since the introduction of ^{99m}Tc, many preparations have been made available which can easily be prepared in the isotope laboratory.

One of the more significant advances has been the use of ^{99m}Tc-sulfide colloid (*1*) for liver scanning. This greatly improves the resolution and statistics over that of the conventional ^{198}Au or ^{131}I-rose bengal scan. The desirable short half-life lets one administer larger doses with a much lower radiation dose to the patient.

For some time this clinic used the simplified preparation of Patton *et al* (*2*) with Dextran as a stabilizer rather than gelatin as suggested by Larson and Nelp (*3*). Injection of several hundred patients produced three anaphylactoid reactions which subsequently were investigated and felt to be related to the Dextran. This was later confirmed by other clinics using the same preparation (*4*). Webber *et al* (*5*) further modified the formula by eliminating the rhenium and Dextran. As is stated in their paper, this preparation produced no adverse patient reactions and was completely satisfactory for a liver scan. The absence of any stabilizer, however, proved to be a rather major disadvantage because it did not remain stable for more than an hour. This required one to make a new preparation for every patient that was scanned. In a small clinic this may not be of importance, but in a large clinic where as many as eight liver scans must be done in a day, it required excessive time in the hot lab to prepare the material. Also to be considered was the possibility that the suspension broke down not only in the vial, but in the body as well, thereby gradually decreasing the counting rate as the scan progressed. A renewed effort was made to find a reaction-free stabilizer.

A review of basic chemistry revealed that there were three significant additives to a colloid which would act as a stabilizer. These were Dextran, gelatin or other protein. From previous adverse results the Dextran and gelatin were immediately eliminated, leaving some other form of protein as the most usable substance. Perhaps the most readily available form of protein in the laboratory is human serum albumin. In minute quantities it is also the most innocuous, nontoxic, nonallergenic substance one can use. A program of using this as a stabilizer was instituted.

METHOD

Because of the effect of heat on the albumin, it was necessary to add the albumin after the original solution had been cooled for a reasonable period. Varying amounts of albumin were added and tested. The most satisfactory result was obtained with a volume of 0.1 ml of a 25% solution or equivalent to 25 mg. Any greater volume seemed to produce macroaggregates. It was unnecessary to treat the albumin in any manner. After the addition of the albumin, the solution was shaken vigorously. The phosphate buffer was added with additional shaking. One millicurie of this preparation was injected into male New Zealand rabbits at intervals of 1, 2, 3, 4, 5 and 6 hr. After each injection the rabbits were scanned on a Nuclear-Chicago Pho/Gamma camera. This procedure was repeated over a 1-week interval. Scans made at 6-hr showed excellent concentration of the material in the liver and spleen with no accumulation in the heart, lungs or bladder. Because of the short half-life, it was not possible to scan with this material at 24-hr; however, a visual observation of the solution showed that it had its original cloudy appearance, indicating no separation of reagents. The yield was checked by the Millipore method (*5*) showing an average yield of between 95 and 98%. A general observation of recent patient scans shows a higher counting rate and generally a more uniform concentration of the tracer.

All reagents are prepared with sterile pyrogen-free water and sterilized by Millipore filter.

Reagents are:

1. 1 *N* HCL.
2. Sodium thiosulfate, 10 mg/cc.
3. Phosphate buffer at pH 7.4 containing
   15.26% $Na_2HPO_4 \cdot 7\ H_2O$,
   0.92% $NaH_2PO_4 \cdot H_2O$.
4. 25% human serum albumin.

To a dry stoppered sterile vial, add 1 cc sodium thiosulfate, 1 cc 1 *N* HCL and 1–3 cc ^{99m}Tc, depending on the total activity required. Place in a

100°C water bath for 3½ min. Cool in running water for 5 min. Add 0.1 ml of albumin and shake vigorously. Add 2 cc phosphate buffer and shake again. The amount of albumin added is adequate for a final volume of 7 cc. Larger volumes of ^{99m}Tc require additional reagents in the same proportion.

It is suggested that the reagents be ordered in amounts that will be used over a 1-month period. Storage for a longer time, particularly of the buffer, increases the possibility of a chemical breakdown. There should be no interchange between old and new batches of reagents.

SUMMARY

A nontoxic stabilizer for the ^{99m}Tc-sulfur suspension has been found. Addition of human serum albumin stabilizes the suspension for 6 hr or longer. Reaction-free liver-scanning material is now available for better-quality scans. The ability to make the preparation on a one-time daily basis is a major advantage to any productive isotope clinic.

JEANNE M. LARSON
LESLIE R. BENNETT
UCLA Center for the Health Sciences
Los Angeles, California

REFERENCES

1. HARPER, P. V., LATHROP, K. A. AND RICHARDS, P.: ^{99m}Tc as radiocolloid. *J. Nucl. Med.* **5**:382, 1964.

2. PATTON, DENNIS D., GARCIA, EUGENE N. AND WEBBER, MILO M.: Simplified preparation of ^{99m}Tc sulfide colloid for liver scanning. *Am. J. Roentgenol. Radium Therapy Nucl. Med.* **97**:No. 4, 880, 1966.

3. LARSON, S. M. AND NELP, W. B.: Radiopharmacology of a simplified ^{99m}Tc colloid preparation for photoscanning. *J. Nucl. Med.* **7**:817, 1966.

4. SMITH, E. M., SMOAK, W. M. AND GILSON, A. J.: Letter to the editor. *J. Nucl. Med.* **8**:896, 1967.

5. WEBBER, MILO M., VICTERY, WINONA AND CRAGIN, MICHAEL D.: Stabilizer reaction free ^{99m}Tc sulfur suspension. *Radiology* **92**:170, 1969.

TIME FACTOR AND ITS RELATION TO ABSORBED DOSE

In a recent letter to the Journal (*J. Nucl. Med.* **9**:499, 1968) King and O'Foghludha discuss the time factor in relation to the absorbed dose in procedures in nuclear medicine. While the matter certainly deserves consideration particularly with respect to therapeutic procedures, I feel, as I think others do, that in the case of diagnostic isotope tests it is important to keep a proper perspective.

In diagnostic radiology doses of the same order as those in many isotope procedures (300 mrads) have been and are being given in times smaller by a factor of around 20,000 even in comparison with an isotope with a half-life as short as 1 hr. Moreover, in special radiological procedures 20 or more of these doses may be given in a few minutes, and in fluoroscopy up to 25 rads or more have been and are frequently given in similar periods of time.

Literally millions of these cases are available as evidence and are being added to daily by the thousands. On the other hand, the number of patients receiving isotopes, while it is growing, is still considerably less than those being examined by x-rays so that if restraint is going to be exercised on this point, surely the logical place to start is in diagnostic radiology, not only in respect to the time relationship but to the total dose administered.

While remembering that other factors such as homogeneity, distribution and type of radiation differ between diagnostic radiology and diagnostic nuclear medicine, it is perhaps time that controls and conditions imposed on the two fields should be brought somewhat closer together. Which is to move? Perhaps, hopefully, both diagnostic nuclear medicine and diagnostic radiology will move from the extreme positions of no control and somewhat repressive control that they hold at present.

K. G. LEACH
The Cardiff Royal Infirmary
Cardiff, Wales, UK

RETENTION AND STORAGE SITES OF RADIOACTIVE POLYVINYLPYRROLIDONE

The authors of the article "Retention and Storage Sites of Radioactive Polyvinylpyrrolidone" (*1*) report the results of whole-body retention, organ content and excretion measurements on mice and rats as well as of urine and fecal excretion and (in 2 cases) blood clearance in humans. They refer to Tothill's work (*2*) and disagree with his assumption that all the polymer retained in the body (50% from 24 hr onwards) was selectively stored in the liver. The authors quote a maximum of 5% of the in-