PVP—A PRACTICAL STABILIZER FOR ^{99m}Tc-SULFUR COLLOID

It would appear that with the steadily increasing population of patients undergoing technetium-sulfur colloid liver and spleen scans, the occurrence of reactions—albeit few—and the universal awareness of the possibility of such undesirable side effects have drawn attention to the stabilizing component of the colloid as the agent potentially responsible, thus raising the question of the necessity of using a stabilizer while simultaneously stimulating the search for a more suitable reagent by a number of investigators. In a recent communication to the *British Journal of Radiology* in response to a letter by Rosemary French (*1*) we expressed views similar to those held by Larson and Bennett (*2*) although our approach to the problem of preparing a satisfactory technetium-sulfur colloid has differed in the constituent we have selected as a stabilizer.

Of 1,343 patients undergoing liver and/or spleen scans during the period in which dextran-stabilized technetium-sulfur colloid was in clinical use in our institution, reactions occurred in 11 patients, resulting in an overall incidence of side effects of less than 1%. Although the rare fatal reaction to dextran encountered in the literature has usually been associated with large doses, the use of even small amounts of such an agent is disquieting.

Having convinced ourselves of the necessity of using a stabilizer in the preparation of a satisfactory colloid, we then gave consideration to other large-molecular-weight sugars such as mannitol and sorbitol for this purpose. However, for technical reasons requiring the additional step of passing the eluate through an ion-exchange column to remove small traces of alumina which adversely affect the final product, we abandoned this procedure. With certain misgivings we undertook the use of gelatin as a stabilizer. The shortcomings of gelatin have already been cited by many; its pharmacological uses are currently limited to oral preparations. Commercially available gelatin can be pyrogenic, and since it constitutes an excellent culture medium, fresh solutions must be prepared, sterilized and submitted to pyrogen testing frequently. Instances of patient reactions to this product have been recorded as well.

We have therefore explored the suitability as a stabilizer of the time-tested polymer polyvinylpyrrolidone (PVP) which has the distinct advantage over gelatin of availability in a sterile, nonpyrogenic, pharmaceutical-grade intravenous solution.

Garzon and colleagues (*3*) in 1965 prepared a technetium colloid by reacting colloidal antimony sulfide with pertechnetate. This method offered the advantage of providing a preformed colloid that could be labeled with technetium before injection. In their antimony sulfide they incorporated PVP as a stabilizer and claimed that this preformed colloid was stable for 3 months. Degrossi and colleagues (*4*) used the product in patients and expressed great satisfaction with the scans they obtained. Yet since 1965 little reference has been made to the method, and reasons for its relative obscurity are open to speculation. It is conceivable, however, that the preliminary preparation of antimony sulfide colloid based upon Harper's method (*5*) may have proved cumbersome with the advent of more streamlined radiopharmaceutical procedures. Thus with the method relegated to the rank of those of historic interest, the potential usefulness of an individual constituent may have been overlooked.

Our product incorporates PVP into the method of Larson and Nelp (*6*), which uses the reaction of thiosulphate and pertechnetate.

PREPARATION OF TECHNETIUM-SULFUR COLLOID STABILIZED WITH PVP

To sterile vial containing 3.5 cc $Na_2S_2O_3$ solution
↓ (12 mg)
add
6 cc $^{99m}TcO_4^-$ plus 1 cc 1 *N* HCl.
↓
Place vial in boiling water bath for 3 min.
↓
Remove vial and add 4-cc buffer containing
$Na_2HPO_4 \cdot 7H_2O$ 372 mg.
$NaH_2PO_4 \cdot H_2O$ 21.6 mg.
Finally add 0.5 cc PVP solution—3.5%.
↓
Shake vial and cool under tap water. Assay for total activity.
Final volume 15 cc.
Final PVP concentration 1.17 mg/cc.

As indicated in the procedure above, the preparation of PVP-stabilized technetium-sulfur colloid requires the addition of PVP as the final constituent; if added with thiosulphate *in lieu* of dextran or gelatin, very poor binding results. Experimental work comparing PVP- and gelatin-stabilized technetium sulfur colloids has shown similar binding on chromatography and comparable specificity of both products for the reticuloendothelial elements of the liver and spleen. The colloid has remained stable for the duration of the working day, and initial trials in patients have yielded excellent scans.

PVP forms a stable colloid in aqueous solution and can be sterilized by autoclaving. Large-scale clinical applications which span three decades reveal no evidence of toxicity or incidence of antigenicity. In the radioiodinated form, PVP has been available as an investigative tool for a number of years.

For the small nuclear medicine department which provides organ-scanning facilities without the benefit of a trained radiopharmacist, the use of PVP as a stabilizer would entail far fewer manipulative procedures than that of gelatin, which, as previously indicated, involves frequent preparation, sterilization and pyrogen testing or makes autoclaving of the final product mandatory before patient use.

PVP may also prove a better substitute for human serum albumin which can be affected adversely by the temperature of the solution to which it is being added, is more expensive and finally should be kept available for therapeutic purposes.

This macromolecule has proved so satisfactory a constituent of technetium-sulfur colloid that we are exploring its potential use in the preparation of indium products. While the current availability of whole blood and human serum albumin has removed PVP from high on the list of priority therapeutic items, its stable physical properties and availability in sterile nonpyrogenic solution ready for intravenous use may render it a versatile, useful reagent on the radiopharmacist's shelf.

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SPECIAL METHODS FOR THE DETERMINATION OF THYROID UPTAKE OF IODINE

Two papers have appeared in the *Journal of Nuclear Medicine* dealing with two presumably high quality, research-type methods for the measurement of thyroidal uptake of iodine (*1,2*). The former method uses two sodium iodide crystals in a 90-deg arrangement, applied to the skin of the patient's neck; the latter uses a lithium-drifted germanium detector that looks at the thyroid isthmus from directly in front (distance not specified). For convenience let us refer to these as the "two-crystal method" and the "germanium method." I have misgivings about both. They are related because thyroid uptakes measured with the two-crystal system are cited as confirming those made with the germanium detector.

The germanium paper discusses several sources of error but fails to mention the problem of the patient's extrathyroidal body background. The detector is described as "uncollimated," and the neck count is taken with the patient straddling the Dewar flask that supports the germanium detector. The Plexiglas phantom in which the dose standard is counted contributes, of course, no extrathyroidal background, and it is not made clear why we should assume that the patient's neck and adjacent areas similarly do not. A 30-hr uptake is reported as 2.0%, implying that it is known to be neither 1.9 nor 2.1%. Thus we are asked to believe, without benefit of evidence, that the extrathyroidal tissues contributed no more than a negligible counting rate in comparison with 2% of the dose. Isn't a reader entitled to just one scrap of experimental evidence to justify this assumption?

A figure of 1.7%, obtained by the two-crystal