POOR LABELING OF TECHNETIUM-99m RBCS IN VIVO ASSOCIATED WITH SOURCE OF NORMAL SALINE USED FOR Sn-PYP RECONSTITUTION

To the Editor: During a three-week period in September 1989, we observed abnormal biodistribution in about half of our patients studied with technetium-99m-(^{99m}Tc) red blood cells (RBC) labeled in vivo. These patient studies typically demonstrated cardiac blood-pool-to-soft-tissue ratios that were lower than expected, frequently exhibited stomach and thyroid localization, and occasionally showed liver uptake (see Fig. 1)

Our procedure for labeling RBCs in vivo is based on the technique by Hamilton and Alderson (*1*). Briefly, a vial of stannous pyrophosphate* (Sn-PYP) is reconstituted with 6 ml 0.9% sodium chloride injection. Two milliliters of the Sn-PYP ($\sim$ 10μg Sn^{+2} per kg) is injected intravenously and is followed in $\sim$ 20 min with an intravenous injection of sodium pertechnetate. Excess Sn-PYP solution remaining in the vial is stored at 2°-8°C. for use later the same day (*2*). We have successfully used this procedure for over a decade with only rare, patient-specific problems.

Causes for poor RBC labeling with ^{99m}Tc can be broadly grouped into two categories: patient-related and product-related. Patient-related problems usually occur as single, isolated cases. Reported patient-related problems involved in ^{99m}Tc-RBC labeling include the following:

1. Infiltration of the Sn-PYP injection.
2. Injection through heparinized catheters (*3*).
3. Patient history of lupus or recent blood transfusions (*4*).
4. Patient drug therapy with drugs such as heparin, methyldopa, hydralazine, quinidine, digoxin, prazosin, propranolol, doxorubicin, and iodinated contrast media (*5*).

Product-related problems, on the other hand, are usually observed as multiple cases grouped in clusters or in a substantial fraction of patients within a given time period. Reported product-related problems involved with Sn-PYP include:

1. Variations in stannous ion content between kits (*6,7*).
2. Deterioration or oxidation of stannous ion during storage of the kits (*8*).
3. Oxidation of stannous ion over time following reconstitution (*2*).
4. Oxidation of stannous ion by room air introduced into the vial (*2,7*).

Since the problem that we observed was undoubtedly product-related, we requested repeat quality control testing by the manufacturer. The report from Mallinckrodt (Harashe LT, *personal communication*, 1989) stated the following:

> *"Our laboratories examined the returned TechneScan PYP with both the saline you returned and our saline and obtained the following results. Testing performed with the returned material and returned saline resulted in less than 60% uptake in the blood pool, yet testing performed with the returned material and our saline resulted in greater than 90%."*

The interpretation of this report is that the poor RBC labeling was associated with the normal saline used for reconstitution of the Sn-PYP.

Over the last decade we have routinely used normal saline manufactured by three companies[†‡§]. During the problem period, however, we were temporarily using normal saline manufactured by another source [¶]. Upon reinstatement of a previously used brand normal saline, the problem disappeared. Hence, we theorize that the normal saline supplied by the other source was responsible for the poor RBC labeling observed during the

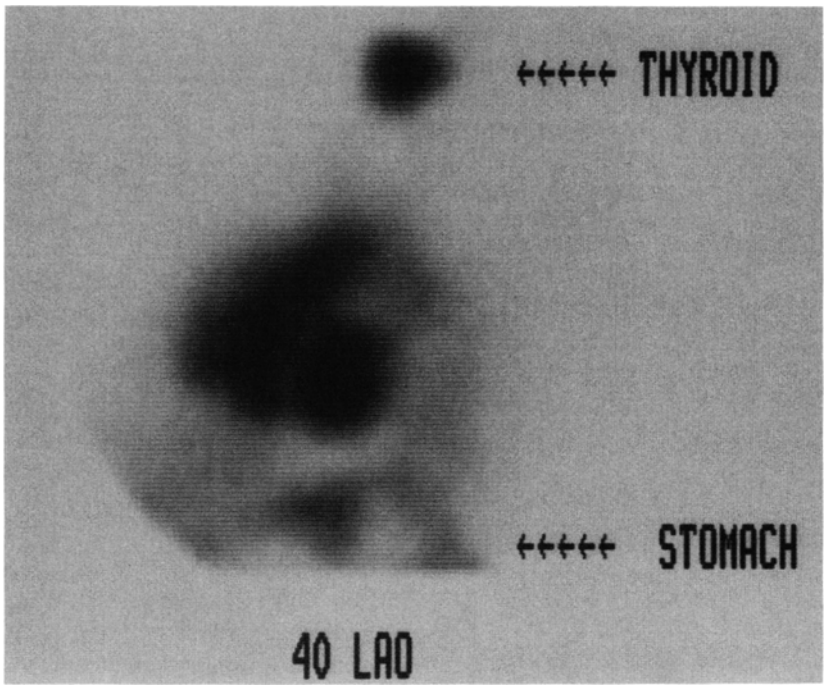

FIG. 1. Cardiac blood-pool study in a pediatric patient using ^{99m}Tc-RBCs labeled in vivo shows greater than expected soft-tissue background and marked localization in thyroid and stomach.

time of its use.

Although we have no analytic data on the content of the problematic normal saline, we believe that it may have contained excessive quantities of oxidizing agents. The presence of bacteriostatic compounds can interfere with ^{99m}Tc labeling of many radiopharmaceuticals, presumably by an oxidative mechanism (*9*); the normal saline used, however, did not list bacteriostatic agents in its labeling. One possible explanation may relate to the concentration of dissolved oxygen in the normal saline used for reconstitution of the Sn-PYP (*10*). Another possible explanation may relate to the selection of the elastomeric material used for the vial stopper since certain closures can affect the stability of stannous ion (*11*) and can leach potent chemicals used in its manufacture into the vial contents (*12*).

In summary, our observed cluster of poor quality ^{99m}Tc-RBC labeling procedures was apparently related to the source of normal saline used for reconstitution of the Sn-PYP. Product-specific incompatibility should be considered whenever product-related problems are not readily explained.

James A. Ponto, MS, RPh
Janice S. Preslar, CNMT
University of Iowa Hospitals and Clinics
Iowa City, Iowa

NOTES

* TechneScan PYP, Mallinckrodt, St. Louis.
† Abbott, North Chicago, IL
‡ Invenex, Orlando, FL
§ Lyphomed, Rosemont, IL
¶ American Regent Laboratories, Shirley, NY

REFERENCES

1. Hamilton RG, Alderson PO. A comparative evaluation of techniques for rapid and efficient in vivo labeling of red cells with [^{99m}Tc] pertechnetate. *J Nucl Med* 1977;18:1010–1013.

2. Majewski W, Zimmer AM, Spies SM. Stannous tin levels in commercial stannous pyrophosphate: effect of different preparation methods. *J Nucl Med Technol* 1981;9:146–149.

3. Hegge FN, Hamilton GW, Larson SM, Ritchie JL, Richards P. Cardiac chamber imaging: a comparison of red blood cells labeled with Tc-99m in vitro and in vivo. *J Nucl Med* 1978;19:129–134.

4. Leitl GP, Drew HM, Kelly ME, Alderson PO. Interference with Tc-99m labeling of red blood cells (RBCs) by RBC antibodies [Abstract]. *J Nucl Med* 1980;21:P44.

5. Hladik WB III, Ponto JA, Lentle BC, Laven DL. Iatrogenic alterations in the biodistribution of radiotracers as a result of drug therapy: reported instances. In: Hladik WB III, Saha GB, Study KT, eds. *Essentials of nuclear medicine science.* Baltimore: Williams & Wilkins; 1987:189–219.

6. Kowalsky RJ, Dalton DR. Technical problems associated with the production of technetium Tc-99m tin (II) pyrophosphate kits. *Am J Hosp Pharm* 1981;22:1722–1726.

7. Kowalsky RJ, Chilton HM. Stability of stannous ion in stannous pyrophosphate kits. [Letter] *J Nucl Med* 1983;24:1080–1081.

8. Ponto JA, Swanson DP, Freitas JE. Clinical manifestations of radiopharmaceutical formulation problems. In: Hladik WB III, Saha GB, Study KT, eds. *Essentials of nuclear medicine science.* Baltimore: Williams & Wilkins; 1987:268–289.

9. Study KT, Schultz HW, Laven DL. The effect of bacteriostatic saline on ^{99m}Tc-labeled radiopharmaceuticals [Abstract]. *J Nucl Med Technol* 1981;9:115–116.

10. Coupal JJ, Kim EE, DeLand FH. Effects of dissolved oxygen on Tc-99m methylene diphosphonate. *J Nucl Med* 1981;22:153–156.

11. Petry NA, Shaw SM, Kessler WV, Born GS, Belcastro PF. Effect of rubber closures on the stability of stannous ion in reagent kits for radiopharmaceuticals. *J Parent Drug Assoc* 1979;33:283–286.

12. Hamilton G. Contamination of contrast agent by MBT in rubber seals [Letter]. *Can Med Assoc J 1987;*136:1020–1021.

TECHS AS RESEARCHERS

To the Editor: After reading Maria Nagel's article "Research As An Integral Part of a Nuclear Medicine Technology Curriculum", September 1989, I had mixed feelings. The idea of teaching basic research skills to technologists *is* beneficial for a variety of reasons, notably it would improve the ability to read and evaluate the field's literature. This could be accomplished in several lectures.

In a four-year program (or even the "three and one" program), there would be enough elective hours available to add a two-credit hour course. But, how does one integrate an additional two-credit hour course into the two-year associate degree program? Especially a program whose curriculum is already overcrowded?

Her statement that "as part of the nuclear medicine team, the nuclear medicine technologist must be able to conduct and assist in research activities" struck a raw nerve. Based on manpower surveys published in the *Journal of Nuclear Medicine Technology* as well as other health-related publications, it is clear that there exists a critical shortage of nuclear medicine technologists. I feel that the first priority of any program should be to educate and train good clinical technologists. My experience, admittedly limited, indicates there are more technologists working in community-based hospitals and medical centers than in large research-oriented facilities.

Although research is an important venue, it should be subordinate to the training of competent clinical technologists. Moreover, it is imperative that we seek ways to fill vacant positions and maintain our current technologists in the field before total burnout occurs.

Are we trying to teach our students to become researchers rather than staff technologists?

Shirley G. Garrett, MA, CNMT
Mt. Sinai Hospital
Chicago, Illinois

Reply: I read Ms. Garrett's letter with interest. She made some points which I should like to address: I believe that her supposition that students could learn to "read and evaluate the field's literature" after a series of "several" "lectures" would instead give them only a superficial set of tools and would not imbue in them the ability to think independently.

Her point about there not being enough time for a two-hour research course in the two-year associate degree program is inappropriate. We have been teaching this course to not only two-year students in nuclear medicine technology and radiography, but also to students pursuing one-year pro-