LETTERS TO THE EDITOR

HOW TECHNOLOGISTS CAN GAIN THE MOST OUT OF CONTINUING EDUCATION

To the Editor: I would like to respond to a recent letter to the editor, written by Mary E. Klug regarding the growing shortage of nuclear medicine technologists.

Nuclear medicine has become a firmly established discipline. Yet there is already increasing pressure for further specialization as the volume and complexity of tasks performed by nuclear medicine technologists increase. Today nuclear medicine is in a state of flux. Tremendous changes are occurring, particularly in radiopharmacy, instrumentation, and dynamic imaging. In some instances, there may be a dozen acceptable ways to perform a procedure.

Continuing education should be an important and vital function for all nuclear medicine technologists. As professionals, we should recognize the complexity and fulfillment of our role in the health care delivery system. Some have found that continuing education is becoming important in their employment status, either in the hiring or promotional aspect. As consumer groups grow, there is even more importance put on continuing education relative to the technologists' duties.

The question most often asked is, "Where do I go for continuing education?" But perhaps we should first ask ourselves, "What do we want out of continuing education?"

There are many avenues open for continuing education, some of which can be pursued in your own department. Some of these you might wish to consider are:

1. **Formal Education.** Going back to college is perhaps the easiest way to get credit for your efforts. An "in vivo" technologist may know little about the "in vitro" procedures. By going back to school or enrolling in classes at a nearby teaching hopital, a technologist can then pursue a new specialty.
2. **Seminars.** Attending local seminars given by professional associations can be a good source for updating technical education. One drawback to seminars and workshops is rising costs. Some hospitals may have limited funds available to technologists wishing to attend such courses.
3. **Journal Clubs.** Even if you can afford to go back to school, nothing is more important to your education than reading professional journals. In some departments, journal clubs meet at least once a month to review new developments.
4. **Writing.** There may have been many times you have had to write papers, and by the time you have completed the research, you have learned more about the subject than you knew before you started. Many hospitals have in-house newsletters that are published to help others learn about your specialty. This can be a useful tool in sharpening communication skills.
5. **Research.** Setting up new procedures, revising old ones, or getting rid of outdated ones requires a certain amount of research. Letting your supervisor know of your research may result in an excellent tool for growth in your department.
6. **Audiovisual Aids.** Programmed learning aids are now accessible to many departments through professional societies. The expense of these self-instruction aids can be kept to a minimum by renting. Some aids are available free of charge from many suppliers. If you are really energetic, you can even make your own tapes and slides.
7. **Hospital Events.** Many hospitals hold "in-house" seminars that can be of great benefit in developing your clinical education.
8. **Communication.** Don't be afraid to ask questions. When you have a specific problem, don't hesitate to call or write another institution to get advice about a particular new procedure that they may be performing.

Continuing education, as a source of developing skills, has many paths that can be explored. These are just a few options that might be open to you. If you define your needs and goals, you can discover alternative paths better suited for your needs.

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STEREOISOMERS OF HMPAO VERSUS PRIMARY AND SECONDARY FORMS OF TECHNETIUM-99m-HMPAO

To the Editor: We read with great interest the timely commentary by Karesh on the preparation of technetium-99m- (^{99m}Tc) exametazime (*1*). However, we can only assume that this commentary was read by very few chemical scientists, as it appears to contain scientific errors. In particular, the author displays a lack of appreciation of the stereochemistry of the radiopharmaceutical exametazime (more commonly referred to as hexamethyl propyleneamine oxime or HMPAO) about which he is writing. It seems that confusion exists in the author's mind as to the distinction between the *meso* and *d,l* stereoisomers of the parent chelate and the primary and secondary forms of the ^{99m}Tc complex of HMPAO. Karesh does not actually refer to the *d,l* and *meso* isomers, instead he appears to confuse the primary and secondary technetium complexes with stereoisomers.

In a study of the structure of the ^{99m}Tc-HMPAO complexes which used x-ray crystallography, NMR spectroscopy, IR spectroscopy, and UV-visible spectroscopy, Jurisson et al. (*2*) did not mention any stereoisomers of ^{99m}Tc (*d,l*) HMPAO. They do, however, clearly differentiate

between the ^{99m}Tc complexes of *d,l*-HMPAO and *meso*-HMPAO. The ^{99m}Tc (*d,l*) HMPAO complex has no asymmetric centers other than the two giving rise to the stereochemistry of the parent chelate. Thus, any stereoisomerism relates to the parent chelate and is not a factor of the complexation with technetium. The *d,l* and *meso* isomers are separated prior to the kit production and subsequent labeling with ^{99m}Tc does not result in the formation of other stereoisomers. Concerns with respect to the stereoisomers are relevant to the preparation of the radiopharmaceutical kit, however, once separated the *d,l* isomer is not subject to significant conversion to the *meso* form. Interconversion of stereoisomers of this type involves the breaking of a covalent bond for which there is a very high barrier: 50 kcal/mole or more. Interconversion is difficult, and, unless one deliberately provides conditions to bring it about, it is negligibly slow (*3*).

As a result, the contamination of the *d,l* isomer with the less desirable *meso* form is the responsibility of the kit manufacturer. It is also important to recognize that this aspect of quality control cannot be evaluated by techniques available in most nuclear medicine laboratories. Specifically ^{99m}Tc (*meso*) HMPAO cannot be separated from the ^{99m}Tc (*d,l*) HMPAO by the three-chromatogram method recommended by the manufacturer and referred to by Karesh. This method is intended to separate the primary and secondary forms of Tc-HMPAO formed during labeling. Furthermore, on the HPLC system used to separate the primary and secondary complexes of ^{99m}Tc (*d,l*) HMPAO (*4*), the ^{99m}Tc (*meso*) HMPAO complex exhibits a similar pattern with both primary and secondary complexes, i.e., the majority of the complex is recovered with a long retention time (lipophilic), while a very small portion has an intermediate retention time (more hydrophilic). The most common method of evaluating the relative proportions of *d,l* and *meso* is NMR spectroscopy on the purified parent chelate.

On the other hand, the terms 'primary' and 'secondary' (*4*) refer to different forms of the ^{99m}Tc complex with the HMPAO chelate. Sometimes the primary is referred to as the lipophilic complex and the secondary as the hydrophilic complex. Since these complexes are formed during the ^{99m}Tc labeling process and/or after the labeling process, they are the responsibility of the nuclear medicine laboratory and must be detected during the quality control process. The primary (lipophilic) complex is the desired product. The structure and identity of this complex is known (*3*), while that of the secondary complex is not yet well understood. However, the secondary (hydrophilic) complex has been identified chromatographically, both by thin-layer/paper techniques and by HPLC (*4*).

The secondary complex is significantly less lipophilic than the primary complex, and it is consequently not capable of crossing the blood-brain barrier. This is in contrast to the distinction between the *d,l* and *meso* stereoisomers, which are both known to cross the blood-brain barrier (*5*). The *d,l* form has better imaging properties because it is retained within the brain cells while the *meso* form is washed out quickly. The exact identity of this secondary complex has yet to be determined, nor is it clearly evident as to its origin. It could be that it is produced during the labeling procedure by a process such as the chelation of the parent chelate with a different oxidation state of technetium to that which forms the primary complex, or it could be a degradation product formed from the primary complex and then subsequently decomposes itself to give free pertechnetate.

As previously indicated, it is the purpose of the hospital's quality control procedure to evaluate the level of radioactive impurities formed as a result of the labeling process. In the case of ^{99m}Tc (*d,l*) HMPAO, these are the secondary (hydrophilic) compound, the free pertechnetate, and the reduced hydrolyzed technetium. As indicated by Karesh (*1*), the procedure recommended by the manufacturer involves three chromatograms, silica gel with methyl ethyl ketone as solvent, silica gel with saline as solvent, and a paper chromatogram with 50% aqueous acetonitrile as solvent. This procedure enables the quantitation of all four components. The saline ITLC identifies the free pertechnetate, while the MEK ITLC enables the evaluation of the combined secondary complex and the reduced hydrolyzed technetium. The paper chromatogram in 50% acetonitrile distinguishes between the secondary complex and the reduced hydrolyzed technetium.

The introduction of this radiopharmaceutical represents the beginning of an era of new and more complex radiopharmaceuticals in nuclear medicine. The language as well as the chemistry will be new and confusing to many whose primary training is not in the area of organic chemistry, and many older practioners will have to reach far back into their memories to fully understand the technical terms used. In order to avoid confusion, great care will have to be exercised to ensure that the correct terms are used consistently. It is unfortunate that Karesh's important and useful commentary should have been so marred by such confusion of terms.

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