PITFALLS IN RADIOMETRIC STERILITY ASSAY

The article by Chen, et al (*1*) presents unwarranted conclusions as to the use of a radiometric assay for rapid sterility testing. These erroneous conclusions may arise from consideration of only a small sample size and/or incomplete consideration of the instrumentation or analytical methods used.

During the past 3 years, The University of Michigan Nuclear Pharmacy has utilized the radiometric assay system and the United States Pharmacopeia method for routine sterility testing of over 4,000 radiopharmaceuticals, pharmaceutical injections, and biologicals. Recognizing that gamma radiation contributed significantly to background radiation of the ionization chamber readings, we instituted two remedial actions.

1. Lead shielding was installed around the incubation vial to reduce gamma exposures.
2. A background measurement was performed with the sample vial in the "test" position but not attached to the air-sampling needles.

These two simple procedures have eliminated the problems with the technique as used by Chen, et al.

The data presented in Fig. 1 (*1*) are perplexing, as by the authors' criterion the ^{99m}Tc-RBC samples tested represent a positive sterility test (5 nCi). The authors should note that viable red blood cells in culture will metabolize ^{14}C-labeled substrates (i.e., ^{14}C-glucose) and evolve measurable amounts of $^{14}CO_2$. Therefore, radiometric sterility testing of RBC cultures must include a "background" correction for the production of $^{14}CO_2$ based upon nanocuries of ^{14}C evolved per number of red blood cells per cubic millimeter.

The use of radiometric methods to test the sterility of radiopharmaceuticals labeled with potentially volatile radionuclides (i.e., radioiodine and radiomercury) does significantly limit the radiometric sterility assay. Volatile radionuclides give rise to false-positive determinations, however, not false-negatives, as the authors conclude. The United States Pharmacopeia sterility test procedure is the method of choice in assessing aseptic product preparation for volatile radionuclides.

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THE AUTHORS' REPLY

Although Hetzel and Ice have reservations concerning our conclusions, the point with which we all appear to agree is that radiometric sterility testing of radiopharmaceuticals is a highly useful and important technique, and that its effective use requires attention to the problems of sample size, volatile radionuclides, variable background due to uncontrolled external radiation sources, and high background due to metabolism of samples such as ^{99m}Tc-labeled red blood cells.

In order to increase the usefulness of this technique, reports of extensive studies such as those carried out at the University of Michigan Medical Center should be published. Of particular value would be a comparison of this method with the United States Pharmacopeia method for detecting the wide range of organisms inhabiting a hospital or a radiopharmaceutical manufacturing environment. When data such as these are published, we expect that this method will become more widely used. Preliminary studies in our own laboratory show that several common organisms are not detected by the United States Pharmacopeia method but are detected by the radiometric method (*2*). For example, in an initial series of 58 anaerobic cultures positive by the radiometric method, only six were detected by conventional methods. Included were organisms such as bacteroides oralis, anaerobic diphtheroids, and streptococcus fecalis. We are hopeful, therefore, that other investigators will report the results of their studies, particularly carefully controlled comparative studies.

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REFERENCES

1. CHEN M, RHODES BA, LARSON SM, et al: Sterility testing of radiopharmaceuticals. *J Nucl Med* 15: 1142–1144, 1974

2. DEBLANC HJ, WAGNER HN: Automatic detection of bacterial growth. In *Pediatric Nuclear Medicine*, James AE, Wagner HN, Cooke RE, eds, Philadelphia, WB Saunders, 1974, p 455