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REPLY: I am delighted that the authors read my editorial "Something Borrowed, Something Blue" (*1*) and felt sufficiently moved to correspond to correct a literal misperception. I agree completely with the somewhat more detailed description of the physical phenomena "randoms" and "scatter" as described by Drs. Ostertag and Belleman, but I think that my allusion to these phenomena was correct.

The phenomenon of "randoms" is *limited* to distintegrations characterized by coincident events, whereas "scatter" involves the interaction of gamma photons and matter quite *independent* of count rate regardless of whether they are single or coincident photons. Hence, I characterized "scatter" as a "more generic and fundamental phenomenon" in the *literal* rather than the *physical* sense; that is in terms of the *frequency* with which it is encountered. In this regard, "frequency" is also used in the literal sense.

This correspondence confirms that *degradation* is inherent in the transfer of information as well as energy. This phenomenon needs to be understood by nuclear physicians, scientists and editors.

Stanley J. Goldsmith, Editor-in-Chief,
The Journal of Nuclear Medicine

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Adverse Allergic Reaction to Technetium-99m-Mebrofenin

TO THE EDITOR: Adverse reactions to radiopharmaceuticals are rare, with an estimated annual incidence in the United States of one to six reactions per hundred thousand (*1*). A much higher incidence, between 1/1,000 and 1/10,000 has been reported in the United Kingdom in a 7-yr period between 1977 and 1983 (*2*). In the United States, only two allergic reactions to ^{99m}Tc-DISIDA were described between 1976 and 1981 (*1*). True incidence of adverse reactions to radiopharmaceuticals is speculative since it is difficult to document cause and effect. Intradermal skin testing, however, may correlate well with systemic reactivity and predict and/or confirm allergic response (*3*). The following case strongly suggests an adverse reaction to ^{99m}Tc-mebrofenin.

A 53-yr-old, cholecystectomized, female volunteer underwent a hepatobiliary scintigraphy with ^{99m}Tc-mebrofenin (Cis Biointernational) as part of a clinical trial. Hepatobiliary scintigraphy was to be performed twice in a 1-wk interval. The routine biochemical tests and physical examination of this subject were normal. She was taking no medications but had a history of allergic reactions to penicillin.

Hepatobiliary scintigraphy was performed with 7 mCi of ^{99m}Tc-mebrofenin. Ninety minutes after injection, the subject was asymptomatic. After 1 wk, at the time of the second scheduled imaging session, she was complaining of fatigue, nausea, dizziness, headache, pruritis, flushing and a rash on her face and extremities. These symptoms and signs began 8–12 hr after radiopharmaceutical injection and gradually decreased during the following week. Upon physical examination, a maculo-papuler rash was seen on her face and extremities. An allergic reaction to ^{99m}Tc-mebrofenin was suspected prior to the second hepatobiliary scintigraphy session. An intradermal skin test was performed by injecting 0.02 ml of ^{99m}Tc-mebrofenin intradermal with a tuberculin syringe. Skin testing was read at 15 min; an 8 × 10-mm erythematous induration was observed at the injection site. This was accepted as a positive skin test and the second scintigraphy session was cancelled. The subject again complained of fatigue and dizziness after the radiopharmaceutical test dose. The patient's biochemical tests, blood counts were normal except for eosinophilia (8.8%).

Various allergic responses to radiopharmaceuticals have been reported. These allergic responses may occur as simple symptoms such as fatigue, nausea, dizziness, rushing and pruritis or as severe a systemic reaction as anaphylaxis (*3–6*). Intradermal skin testing may correlate well with systemic reactivity and predict an allergic response to bone imaging agents (*3*). In this case, the patient's symptoms secondary to an allergic reaction to ^{99m}Tc-mebrofenin is based on the positive skin test and the lack of another explanation.

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Out of Sight, Out of Mind!

TO THE EDITOR: Recently, ^{99m}Tc-teboroxime (CardioTec™), a new myocardial perfusion agent (*1,2*), was recalled temporarily from the world market. Regrettably, this has implications in the clinic and for the industry. The chromatography procedure suggested in the manufacturer's product monograph indicated greater than 90% binding throughout the first 6 hr after reconstitution. The solution was clear immediately after preparation, but within

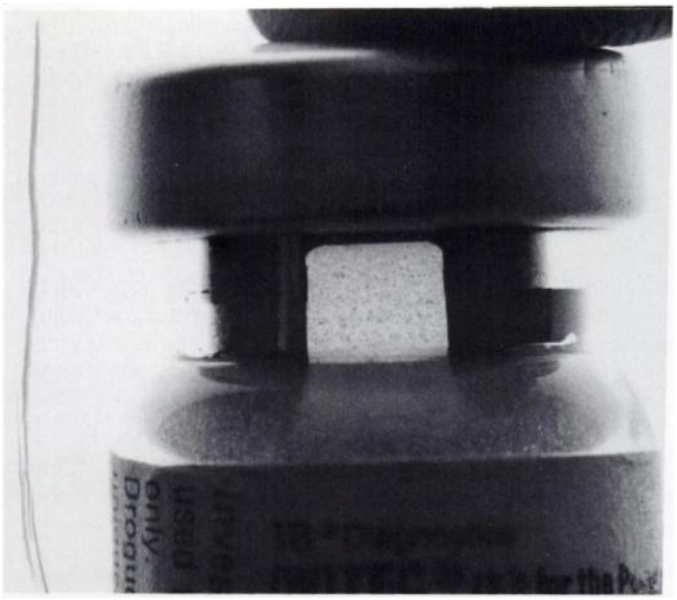

FIGURE 1. Flocculation of reconstituted ^{99m}Tc-teboroxime.

30–60 min of reconstitution severe flocculation (Fig. 1) occurred in the vial, regardless of the heating procedure or whether air was present in the vial. This has been carefully documented in our department over the last 6 mo (and corroborated at Princess Margaret Hospital in Toronto).

The reason for writing this letter, however, is to draw attention to an important yet frequently overlooked issue vital to in-house quality control of radiopharmaceuticals. Once kits have been reconstituted (which often includes a heating step employing a water-bath, microwave oven or heating block), we perform chromatography on the product, check the clarity of the vials and promptly hide them in lead vial containers. Seldom, if ever, do nuclear medicine staff look at the integrity of the product during the rest of its shelf-life. This is not necessarily an oversight, but the result of confidence instilled by claims on the package insert that the drug is stable for 6–8 hr postreconstitution. However, this is not the case with the teboroxime product, and an important lesson should be learned from this experience. It also emphasizes the irony of our anxiety to comply with radiation protection standards (i.e., the vial in the lead pot), thereby running the risk of neglecting pharmaceutical quality.

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