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Combined Intravenous Dipyridamole and Symptom-Related Stress Testing

TO THE EDITOR: We were very interested in the recent publication by Ignaszewski et al. concerning the use of combined intravenous dipyridamole and symptom-related stress testing with thallium imaging in patients with coronary disease (*1*).

In 1988, in our nuclear cardiology laboratory, we felt that there was a large part of the population that was not well served by the lab. Those that could stress to at least 90% of the target heart rate could get a standard Bruce protocol stress test with thallium. Those who we knew could exercise only to a very limited degree or not at all received intravenous Persantine with ^{201}Tl imaging. Unfortunately, a very large part of our patient population fits in between these two categories. They can certainly exercise to some degree but not to 90% of their target heart rate as we expected.

It was our belief at that time that combining both intravenous Persantine and whatever exercise the patient could manage would likely be better from our point of view in that we would get both a pharmacologic and physiologic stress on the patient's heart at the same time. It has been our protocol since October of 1988 to give patients a bolus of Persantine based on size, approximately a minute or two before they could not exercise further. This would be followed by a thallium injection and a further minute of exercise. While we have not done a controlled study comparing these images with patients who exercise to a submaximal rate or get Persantine alone with thallium, we feel that the images are of an excellent quality and there is certainly no problem with liver and gut uptake as is often experienced with a resting Persantine infusion.

We would like to congratulate the authors on bringing forth this information as we think that it is very important.

Our laboratory at the Credit Valley Hospital and the attached outpatient facility have now done a total of 3,595 combined intravenous dipyridamole/symptom-limited exercise stress tests with thallium imaging since October of 1988. The side effects as expected from the Persantine are minimal and our complication rate is extremely low. In fact, only two patients (0.08%) had to receive intravenous aminophylline to help reverse significant angina.

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Technetium-99m-Sestamibi Imaging in Breast Cancer: An Alternative to Thallium-201 Imaging

TO THE EDITOR: Radionuclide imaging has mainly focused on detecting distant metastases in patients with breast cancer. Bone scans now have a definite role in the follow-up of these patients. Experience in demonstrating the primary tumor with radionuclides in breast cancer is rather limited. There has been little effort to find a radionuclide allowing us to determine the nature (i.e., benign or malignant?) of the breast lesion detected by palpation and/or mammography. Lee et al. made a significant contribution to this effort with their recent study (*1*) in which they investigated the diagnostic specificity of ^{201}Tl imaging for breast cancer and its efficacy as a complement to mammography. Their results confirm the previously published reports and support a well known idea that ^{201}Tl imaging could be used in the management of breast cancer (*2,3*). They also reviewed the previous clinical trials with some other radiotracers (*1*), including ^{99m}Tc-pertechnetate, ^{67}Ga and ^{99m}Tc labeled phosphates. I would like to complete their discussion by bringing the recent efforts with ^{99m}Tc-sestamibi to your attention. Following our initial report in a limited number of patients with breast cancer in whom we compared ^{99m}Tc-sestamibi with ^{201}Tl and obtained higher detectability with the former (*4*), excellent results have been reported confirming the value of ^{99m}Tc-sestamibi imaging in the management of breast cancer (*5–10*). Considering the poor physical characteristics of ^{201}Tl (i.e., long half-life which restricts the use of larger doses for better count statistics and low photon energy which unavoidably results in some attenuation in tissues such as breast, particularly in large and dense breasts), ^{99m}Tc-sestamibi appears to be an alternative to ^{201}Tl in the imaging of breast cancer and its axillary metastasis. In addition, ^{99m}Tc-sestamibi has the practical advantages of availability in kit form, which is important in the management of breast cancer since both the surgeon and the patient are usually difficult to persuade for waiting even a few days for a noninvasive method to predict the nature of a mass in the breast before the surgeon proceeds to a biopsy. Although Lee et al. did not suggest that ^{201}Tl imaging could replace biopsy in the initial diagnosis, waiting a few days (sometimes a week to 10 days for some departments) to supply ^{201}Tl may not be tolerated by the patient even in a scenario (as suggested by Lee et al.) in which the mammogram result is abnormal yet considered indeterminate or benign and ^{201}Tl is proposed as a third alternative to short-term periodic mammography and biopsy (*1*). Technetium-99m-sestamibi imaging could replace ^{201}Tl in such a scenario in which a same-day immediate imaging could be possible only 10–15 min after the injection of this agent (*4*).

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Clinical Utility of Bone Scan Features of Pleural Effusion: Sensitivity and Specificity for Malignancy Based on Pleural Fluid Cytopathology

TO THE EDITOR: I read with interest the article by Sandler et al. in the March issue of the *Journal* (*1*). The authors report a good assessment of the sensitivity and specificity of the routine bone scan for detection of malignant pleural effusion using pleural fluid cytology as the "gold standard" (though the authors are careful to point out that pleural fluid cytology can be flawed by sampling error that would cause false-negative results). The data presented suggest that skeletal scintigraphy has a sensitivity of about 42% and a specificity of about 84% for the detection of malignant pleural effusions in patients with clinically detected pleural effusions who had cytologic examination of the fluid (perhaps creating a subpopulation from all patients with pleural effusion with a somewhat higher percentage of true positive cases of malignant etiologies).

At Brooke Army Medical Center, we performed a similar analysis utilizing a similar patient population (*2*). We found approximate sensitivity and specificity values of 51% and 44%, respectively. The sensitivity value is slightly higher than the value noted by Sandler et al. and the specificity value is considerably lower. These differences may reflect an inadequate sample of the nonmalignant pleural effusion cases (we evaluated 85 cases of which only 9 were nonmalignant) and/or a tendency toward "overcalling" the bone scan findings on our part (reading the scans "blindly," but with a heightened index of suspicion).

We applaud the work of Sandler et al. as their effort and ours provide substance to a pathologic finding seen on bone scans that has been often discussed in the nuclear medicine community, but for which the significance had not until now been carefully defined.

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REPLY: In response to the letter from Dr. Heironimus concerning our paper in the *Journal*, we offer the following response:

We appreciate Dr. Heironimus' kind words and encouragement concerning our recent paper. Because of the limited publication of his similar study as an abstract not listed in the Medline database we were not previously aware of it.

We totally agree that false-negative pleural fluid cytology tarnishes its use as a reference standard. Sampling error, degenerated cells and a significant variability in the regional skills of cytopathologists are some of the causes of this.

For that reason we choose a highly skilled cytopathologist to rereview all of our patients' cytopathology specimens as a coinvestigator. We believe that the differences between our specificity and Dr. Heironimus' 84% and 44%, respectively, very likely resulted from a higher false-negative cytopathologic outcome in his study.

Also, as we noted in our paper, we used a strict set of rules to infer the presence of pleural effusions in the bone scans. We believe that this probably decreased our false-positive rate, or at least improved interobserver agreement.

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False-Positive Radioiodine Uptake in Lung Carcinoma

TO THE EDITOR: Misaki et al. (*1*) report a case of a false-positive radioiodine uptake in a patient with squamous-cell carcinoma of the lung and state that only three cases of iodine- or technetium-concentrating lung adenocarcinoma have been reported. In 1990, we published a case of an iodine-storing primary adenocarcinoma in the right lower lobe of the lung and the simultaneous presence of a differentiated (papillary) thyroid carcinoma (*2*). Accumulation of ^{131}I was seen in both lungs and in the left femur. Histology and immunohistochemical investigation of these lesions were negative for thyroglobulin but positive for cytokeratine, confirming the diagnosis of metastastic lung adenocarcinoma. In 1993, Haubold-Reuter et al. (*3*) reported a case of ^{131}I uptake in the hilum and right lung of a patient with papillary thyroid carcinoma; histology revealed a small to medium cell undifferentiated bronchial carcinoma.

Since 1973, twelve cases of misleading radioiodine uptake have been reported in the literature (*2,3*); additionally, in 1989 about 21 cases were also mentioned by Greenler et al. (*4*).

Possible explanations for the underlying mechanism of lung neoplasms have been discussed in detail (*2,3,5*).

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