

LETTERS TO THE EDITOR

Need for New Radiopharmaceuticals

There has recently been a striking reduction in the number of head scans performed because of the introduction of computerized tomographic (CT) transmission scanning. This has had a serious effect on nuclear medicine because head scans were the commonest procedure performed. All previous head scans were based on demonstrating defects in the blood brain barrier and, to some extent, gross changes in regional hemodynamics.

It has been demonstrated (1) that the i.v. injection of a substance that is lipid soluble enough to be completely cleared during one passage through the brain results in a scan of the head in which the regional isotope distribution is proportional to regional blood flow (2). ¹²³I-iodoantipyrine is useful to this end (2), but it is expensive and impractical for most laboratories.

I believe that a concerted effort should be made to develop a Tc-99m-labeled compound which is sufficiently lipid-soluble that it would undergo complete clearance in one pass through the brain (3). The only requirement is that it should not strongly bind to plasma protein and that it have an octanol/water partition coefficient greater than about 0.5. This would correspond to an olive oil/water partition coefficient of about 0.1.

Beginning immediately after i.v. injection of perhaps 10 millicuries, the head would be imaged for the next 1–2 min. After that time, the technetium would be redistributed and would no longer represent the regional blood flow. A late scan could well provide additional useful tissue characterization because it would then be distributed in proportion to the compound's partitioning between blood and various regions of brain, and this could reflect various tissue pathologies.

The compound need only remain stable in blood for 30–60 sec after which its distribution would have been finalized.

If such a technetium compound could be made—and it would not be easy—it would allow a new parameter of brain physiology to be displayed (regional microcirculatory perfusion) and would offer something that previous brain scanning with polar tracers and CT scanning cannot provide.

This letter is intended simply to encourage workers proficient in the chemistry of technetium to pursue this potentially valuable undertaking.

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Indications for Tl-201 Scintigraphy Revisited

The article by Turner et al. in the *Journal* (1) is an excellent contribution to the current controversy regarding the role of stress testing in coronary-artery disease (2). The study was carefully conceived and executed, and the conclusions seem valid. Data analysis was performed keeping in mind the experience of the conventional ECG stress test.

In patients with atypical chest pain (as defined by the criteria of Ross and Friesinger), in whom the prevalence of ischemic heart disease is 30–50%, Tl-201 imaging and ECG stress testing were equally insensitive. Combining both procedures improved sensitivity at the expense of a much lowered specificity.

Although the study did not address the relevancy of Tl-201 myocardial perfusion imaging in *asymptomatic* individuals suspected of having coronary-artery disease (2), we completely agree that it sets the stage for a more critical evaluation of indications of Tl-201 imaging after stress. Clearly it would appear that Tl-201 is *not* indicated after stress for diagnostic purposes in patients with typical or atypical angina pectoris, or in patients with previous myocardial infarction.

Most investigators now agree that interpretation of Tl-201 myocardial perfusion images is subject to interobserver variation. Acknowledging this problem the authors excluded patients with previous myocardial infarction in an attempt to limit bias related to possible reversible ischemia. The latter factor may further influence overall sensitivity and specificity of the technique. Although strategies such as comparison of normalized countrates, gating, and background subtraction have been advocated by others to make the interpretation of the test more objective, more research is needed in the area of myocardial perfusion imaging using gamma and positron-emitting radionuclides.

Finally, clinicians await comparisons between exercise Tl-201 imaging and multiple-gating of the cardiac blood pool during exercise. A recent study of 56 consecutive patients at the N.I.H. (3) demonstrated that multiple-gating of the cardiac blood pool during exercise is a highly sensitive method to indicate ischemic heart disease. This technique also has a high specificity and predictive accuracy.

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