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Radionuclide Imaging in Pulmonary Edema

TO THE EDITOR: The studies in dogs by Slutsky and Higgins (*1*) with oleic acid injury to the lungs was an outstanding investigative work on acute respiratory distress syndrome (ARDS). It is now clear that increased thallium-201 (Tl-201) lung uptake may be seen in patients with ARDS and in patients with LV failure (*2,3*). While the animal study was well conducted and the data obtained were valuable, we feel the authors may have overextended the possible clinical applications of these findings. A cautionary note is warranted before an expensive test is utilized and judgments are made without further experimental evidence to substantiate the validity of this test in this specific clinical setting.

The authors suggested that serial pulmonary imaging may provide useful noninvasive monitoring of therapeutic results in patients with ARDS. Presumably this would be an indirect way of measuring decreases in extravascular lung water (EVLW) as the ARDS resolves due to proper therapeutic intervention. The problem we have with this suggestion is that while EVLW is increased in ARDS, disturbances in gas exchange are not characterized by similar changes in EVLW content. In fact, animal studies in sheep with endotoxin-induced ARDS showed that the EVLW bore no relationship to the measurement of gas exchange expressed as the alveolar-arterial (A-a) oxygen gradient (*4*).

The primary danger to the patient with ARDS is organ damage due to severe hypoxemia from the large R-L shunting caused by blood perfusing poorly ventilated or unventilated, liquid-filled lung units. Hence, the first step in managing the patient with ARDS is to improve gas exchange, usually by ventilatory support, oxygen, and PEEP. This treatment modality is known to improve gas exchange and promote survival, but not directly by decreasing EVLW, as has been well documented experimentally (*5*). In fact, PEEP may actually promote an increase in the EVLW even though gas exchange is improved (*6*). Other effects of PEEP, such as a decrease in the cardiac output, require that careful hemodynamic monitoring be utilized while high levels of PEEP are employed. To promote the use of lung Tl-201 measurements of EVLW in such a setting could lead to erroneous or confusing data regarding the clinical response to treatment.

A similar cautionary note is warranted for the suggestion by the authors that a dual-radionuclide study might be used to examine noninvasively the pulmonary fluid shifts in cardiogenic pulmonary edema. The use of such a technique for clinical research is acceptable, but the use of radionuclide pulmonary imaging as a clinical tool to characterize the flux of lung fluids in cardiogenic pulmonary edema seems unnecessary. Accurate hemodynamic monitoring is essential and limited information is available noninvasively with the use of radionuclide cardiac angiography or nuclear probe. On the other hand, since these fluid shifts often lag behind the hemodynamic changes, pulmonary radionuclide imaging would be an expensive means for yielding the same information that the stethoscope and chest radiography have provided for years.

We would like to stress that the study by Slutsky and Higgins was confined to dogs and should not be extrapolated to humans without first confirming that pulmonary Tl-201 imaging in cardiogenic and noncardiogenic pulmonary edema gives clinically useful and reliable information that is not otherwise easily available.

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REPLY: While the initial comments by Drs. Movahed and Wait were gratifying, the majority of their comments made me feel a bit like the innocent man asked to state when he'd stopped beating his wife. In fact, I feel somewhat like a "straw man" for expensive medical technology, who neither volunteered for the job nor asked to stand in the "cornfield." I reread the article in question and believe that Drs. Movahed and Wait have made their assertions based on comments in the article on the potential clinical uses (all of which would need any variety of clinical studies involving many possible questions).

It should be pointed out that Dr. Higgins and I are quite familiar with the effects of PEEP (*1*), therapy (*2*), and phase lag (*3-5*) on pulmonary congestion and gas exchange. Furthermore, we are also familiar with the potential problems with scintigraphy in hydrostatic pulmonary edema (*6*). We alluded to these concepts, pitfalls, and potentials in the discussion of our article.

Drs. Movahed and Wait are kind enough to review the standard clinical approaches to medical management of ARDS and cardiogenic edema. While undoubtedly familiar to most

clinicians, a brief review is certainly of interest to those not likely to be familiar with them. Drs. Wait and Movahed should remember that mixed forms of edema may occur (*7*), confounding some of the clinical information.

Regardless, Drs. Wait and Movahed are correct in stating that pulmonary scintigraphy in pulmonary edema should not be applied and billed to patients without further investigation about its utility. In the article under discussion, I suggested with Dr. Higgins some interesting clinical avenues of research, I am quite content to stand on that little isolated portion of the aforementioned "cornfield."

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Brain Tumor Imaging Using C-11-Labeled L-Methionine and D-Methionine

TO THE EDITOR: Positron emission tomography (PET) allows the characterization of local brain function in normal and pathological states (*1-4*). Carbon-11-labeled amino acids, DL-valine, DL-tryptophan, and aminocyclopentane carboxylic acid have been used to image brain tumors (*5,6*). In a case report, Bergström et al. (*6*) demonstrated differences in the imaged size of a brain tumor by CT and PET, using Ga-68 EDTA, C-11-glucose, and C-11 L-methionine. From in vitro studies with an amino acid analyzer (*7*) and from nutritional support studies (*8*), it is known that methionine provides especially high tumor-to-nontumor ratios in gliomas and metastatic brain tumors.

In preliminary in vivo studies of brain tumors with C-11-labeled L- and D-methionine, we have also found significant uptake ratios with both isomeric forms. Production of C-11-labeled D- and L-methionine is described elsewhere (9). The D and L forms were analyzed for optical purity. Seven patients with brain tumors and without previous treatment were studied, each of them providing informed consent to the protocol. PET scans were performed with a positron camera 20 min after i.v. injection of 30 mCi of tracer, when the blood level is sufficiently low (*5*). Up to nine slices of 1.6-cm thickness were reconstructed. The diagnosis was ascertained clinically and by angiography, CT, and NMR, and histologically in six of the seven patients. Relevant details and PET findings are given in Table 1.

In two patients with disruption of the blood-brain barrier (BBB) according to scintigraphic findings with Tc-99m DTPA, no significant methionine uptake could be found. In one patient with a grade 1 astrocytoma I, an uptake of C-11 L-methionine occurred, but no BBB breakdown could be verified. The regional uptake ratio of tumor-to-contralateral tissue increased with tumor grade and was highest in a grade 4 astrocytoma. The accumulation of the L form is slightly higher than that of the D form in most cases. A sample PET image is shown in Fig. 1.

Generally the uptake of C-11-labeled methionine may be due to BBB breakdown and/or incorporation into the protein fraction of tumor tissue. Our preliminary findings suggest that the accumulation is not governed by BBB breakdown but that at least a considerable fraction of the accumulation is due to an active metabolic process. The high uptake of D form methionine, which hitherto had not been observed, seems to indicate that the metabolic process is quite unselective and that it may provide a measure for the degree of malignancy of the tumor. If this holds true, quantification of this phenomenon could be helpful in the grading of brain tumors.

Quantification models for in vivo amino acid metabolism in the brain have been developed by Phelps et al. and Bustany

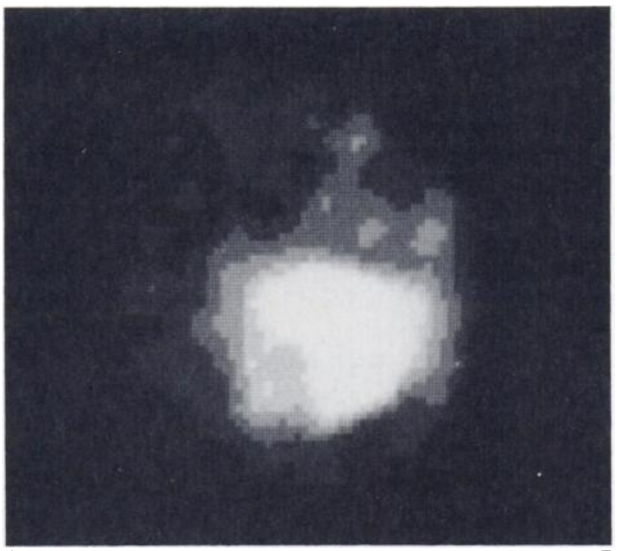

FIGURE 1
PE tomogram of C-11 L-methionine uptake in astrocytoma IV (4 × 5 cm) in right occipital lobe close to midline.