2. **The electrolytic cell.** A 15-ml zirconium crucible (Wa Chang Corp., Albany, Ore.) can serve conveniently as the anode. A micro platinum electrode with mercury for electrical contact (Sargent S-30420) attached to a synchronous rotator (Sargent S-76486) can be the cathode. With proper care the same electrodes may be used over and over again (*4*).

3. **Chemicals.** Chemicals used are 1 *N* hydrochloric acid, 25% human serum albumin, ^{99m}Tc-sodium pertechnetate in normal saline, and saturated sodium bicarbonate solution for final pH adjustments.

If various ingredients in the electrolytic solution are in the proportion 5 ml $NaTcO_4$ (saline), 0.5 ml 1 *N* HCl, and 0.05 ml 25% human serum albumin, the charge required for 90–100% labeling will be 4.2–4.3 coulombs. The estimated quantity of zirconium in the total volume of this preparation is approximately 1 mg, and the specific activity is usually in the range 2–10 mCi/ml depending upon the technetium generator. There is no toxicity at this level for several zirconium compounds administered to higher animals through different routes (*5–11*). The technetium activity remains bound to the protein for a wide range of pH (pH 1–8) and temperatures (0–100°C) so that micro- and macroaggregation can be effected by suitable pH adjustment and heat treatment.

Traces of oxidizing agents such as O_2^{2-}, ClO_4^-, MnO_4^-, ClO^-, etc. will inhibit this reaction. The presence of ReO_4^- seems to have no effect on the labeling efficiency.

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FISSURE SIGN IN LUNG PERFUSION SCINTIGRAMS*

Visualization of the region of interlobar fissures in perfusion pneumoscintigrams may indeed be a sign of pulmonary microembolization, as described by Eaton et al (*J Nucl Med* 10: 571–574, 1969), but their paper presents *no* factual data substantiating this conclusion. Since patients are referred for lung scintigraphy usually because of a clinical probability of embolization, it is obvious that any scan finding in this population will demonstrate the association described. This is not proof of a causal relationship. The statement regarding their two patients studied at autopsy is at best ambiguous. Apparently no microembolization was documented pathologically, and if larger emboli were found "in the region of perfusion defects," the fissure sign was diagnostically noncontributory and may have been due to other causes. Of the 200 scintigrams reviewed to April 1968, the number in which the authors en-

* Letter dated Sept. 26, 1969.

countered this sign is not disclosed, nor do they offer a statistical analysis of the frequency of the fissure sign with various other abnormalities which might account for the defects noted.

We originally noted the fissure sign in May 1966, and during the next several months we documented its quite regular association with pleural fluid by physical examination, x-rays, and in several cases by thoracentesis or at autopsy within hours or days of scan. Occasionally the fissure sign was seen in the absence of demonstrable fluid. In two of those latter cases autopsied within 12 hr and 3 days of scan, neither pleural fluid nor emboli were found; sections from lobar edges above and below the fissure showed no microemboli. This information was presented in January 1968 at a "Lung Scan Workshop" held at Mount Auburn Hospital under the sponsorship of the New England Chapter of the Society of Nuclear Medicine. At that time I commented that anything impairing pulmonary arterial blood flow uniformly to the periphery of lung tissue may result in the fissure sign being seen by scan; in addition, decreased lobe size might not be appreciated at the periphery of the lung but would manifest itself as a gap when two lobes are adjacent.

We subsequently extended our observations and have developed specific information from scintigrams to establish with great confidence the diagnosis of pleural fluid. A report detailing these findings has been submitted for publication. The importance of this information is not primarily to make the diagnosis of pleural fluid since x-rays are satisfactory for this purpose, but to avoid misinterpreting perfusion pneumoscintigrams as showing embolization when effusion or some other process is present.

We have performed lung scans on 1,480 patients, 98% of which have been done in at least posterior and left and right lateral views while about 50% also include an anterior view. Of these 1,480 scans, 106 are indexed as demonstrating unilateral or bilateral fissure sign. Since all positives were probably not so indexed, I estimate that we have seen the fissure sign once for each 12–15 cases in the group referred to us for scanning; 55% showed fluid by x-ray on the same side as the fissure sign appeared by scan. Since many of these patients had only recumbent A-P x-ray chest radiographs on the day of scan, and conventional upright P-A x-ray films showed fluid one or several days before or after the pneumoscintigrams, this 55% figure is undoubtedly too low. We have seen the fissure sign, without pleural fluid, associated at autopsy with one or several of the following: pulmonary edema (most commonly), bronchopneumonia, emphysema, metastatic carcinomatosis of the lung, and pulmonary embolization. The data above from our larger series suggest that Eaton et al should have found the fissure sign in at least 14 of the 200 scintigrams they reviewed and that pleural fluid should have been found in more than half of the group. Their only positive statement in this regard is that "the scintigrams *chosen for illustration* (italics mine) are of patients whose concurrent roentgenograms were . . . without . . . pleural effusion. . . ." The excellent illustrations accompanying their paper show only six individual lungs with the fissure sign from an undefined number of patients. Unfortunately, the authors provide no data clarifying the relationship between fluid or other demonstrable pathology in the unillustrated patients with fissure sign.

At the present state of our knowledge, we can only speculate about the pathogenesis of fissure sign in that less than 45% of scans are not associated with fluid in our series. This percent may include peripheral pulmonary arterial blood flow impairment due to functional or mechanical blockage, disturbances in peripheral lymphatic flow, generalized peripheral mal-ventilation, and acute or chronic generalized or fissure-localized inflammatory pleural disease. We are engaged in a continuing investigation in this area. Until more precise pathologic correlations in this group are made, we believe the fissure sign is not evidence of pulmonary embolization in most cases and should not be interpreted as such.

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