JOURNAL OF NUCLEAR MEDICINE 7:1-22, 1966

Radioisotope Photoscanning In Pulmonary Disease[3]

James L. Quinn III, M.D.[1], Louis R. Head, M.D.[2]

Chicago, Illinois

With the development of a suitable pharmaceutical (1) and the first reports of its successful use in patients (2,3) the lung became a scannable organ. Since that time lung scintiscanning, using aggregates of iodinated human serum albumin, has been used to evaluate many pulmonary disease states with varying degrees of clinical usefulness (4). Perhaps the most important application of lung scanning using the albumin aggregate is in the evaluation of pulmonary embolism.

A newer scanning procedure for pulmonary study is in the inhalatory scan. A radionuclide is administered using a nebulizer and positive pressure (5-8). This results in a gross representation of bronchial patency.

LUNG SCANS WITH INTRAVASCULAR PARTICLES

Material: Aggregates of ^{131}I human serum albumin 10-50 μ in diameter can be produced by lowering the pH to 5.4 and heating at 80° C for 15 minutes. If high specific activity albumin is used 200-300 μC will contain approximately 0.1 mg of albumin. This material, when injected intravascularly, is held up in the first arteriolar-capillary bed it reaches. As gravity causes nonuniform blood flow even in healthy persons, so does the position of the patient at the time of aggregate injection cause nonuniform distribution. If the patient is injected in the sitting position, there will be decreased distribution in the apices. If the patient is injected lying on one side, the dependent areas will receive the greatest amount of aggregate. The aggregates are broken down into smaller particles

[1]Assistant Professor of Radiology, From the Departments of Radiology and Surgery, Northwestern University School of Medicine and the Nuclear Medicine Laboratory, Chicago Wesley Memorial Hospital

[2]Associate in Surgery

[3]This work has been supported in part by grants from U.S. Public Health Service General Research Grant No. # 1-S01-FR-05070-01 and the James Picker Foundation on recommendation of the committee on Radiology, National Academy of Science-National Research Council.

which pass through the capillary bed and are removed by the reticulo-endothelial system of the liver and spleen. It is estimated that the albumin dose safety factor of the aggregate in the normal lung is approximately 1500 (9) but may be less than 700 in acute cor pulmonale. This is, none the less, an acceptable safety range. We do not administer more than 1.0 mg of the aggregate at any one time in patients. To date we have had no untoward patient reactions attributable to the aggregate in over 500 injections, many of whom have had pulmonary hypertension and several of whom have had acute cor pulmonale.

Technique: With the patient supine, 120-180 μC of ^{131}I albumin aggregate are injected. Nuclear-Chicago three inch rectilinear scanners with 19 hole focusing collimators and photo-recording were used to obtain the scans. The lung scan is performed immediately following injection with the patient usually prone and occasionally supine. The scan is started at the inferior margin of the rib cage and proceeds upward so that accumulation of smaller particles in the liver and spleen from large aggregate breakdown do not interfere with interpretation of the lung base activity distribution. If the aggregate is of smaller particle size, it will pass through the pulmonary bed and be picked up by the liver and spleen. One of our early shipments resulted in such a scan recording. The material was injected and a posterior prone scan of the liver and spleen was recorded (Fig. 1a). The material, already at pH 5.4, was reheated at 80° C for 15 minutes and the scan was repeated the next day (Fig. 1b), at which time a normal lung scan was ob-

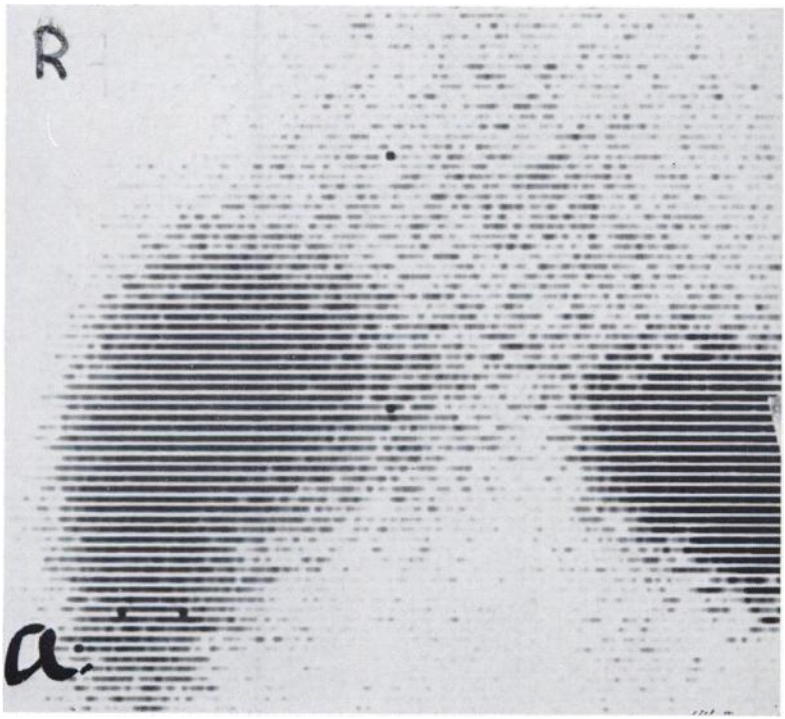

Fig. 1a. Posterior scan using aggregated ^{131}I albumin showing uptake in the liver and spleen indicating the material is of the small aggregate particle size.

tained. At a scanning speed of 90 cm/min, the posterior scan is completed within 15 minutes. One of our rectilinear scanners was modified increasing the scanning speed to 190 cm/min. Less than 10 minutes is required to perform the scan using the modified machine.

One cc of saturated KI solution is administered orally at the time of injection to reduce thyroid uptake of iodine-131.

Internal Dose Calculation: The disappearance of the ^{131}I aggregate has been reported to follow at least two half-times (10), the initial being approximately three hours and the second about 12 days. The estimated dose to the lungs from 200 μC of ^{131}I albumin aggregates is 1.2 rads.

LUNG SCANS WITH AEROSOL DEPOSITION

The pattern of deposition of positive pressure nebulized particles in the pulmonary air passages is related to the particle size and the airway patency.

Using a Bird respirator and micronebulizer, at a pressure of 10 cm H_2O and a flow rate of seven, 2-7 μ has been stated as being the particle size range. The mist is administered at room temperature. There is a resultant humidity deficit in the tracheo-bronchial tree as the mist enters. This results in evaporation reducing the particle size to 0.5–3 μ allowing them to proceed farther out toward the alveoli. If the mist were administered at body temperature there would be no humidity deficit and the particles would coalesce and precipitate out in the

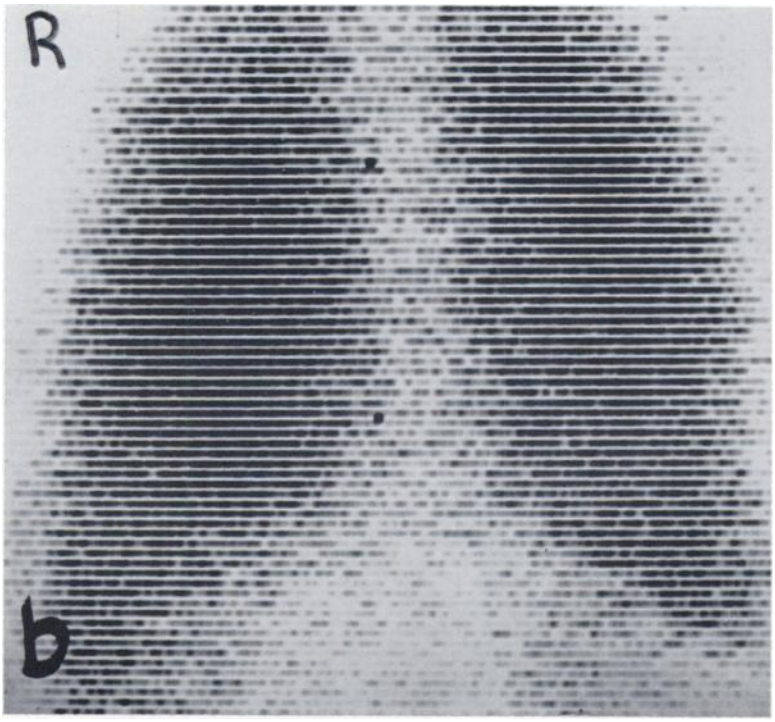

Fig. 1b. Shows a normal vascular lung scan done posteriorly on the same patient as (1a) after heating the material at 80° for 15 minutes.

trachea and main stem bronchi. The amount and site of deposition of an aerosol containing a heterogenous mixture of particle sizes is dependent on many factors. Perhaps the greatest of these are particle size and airway patency (11). The

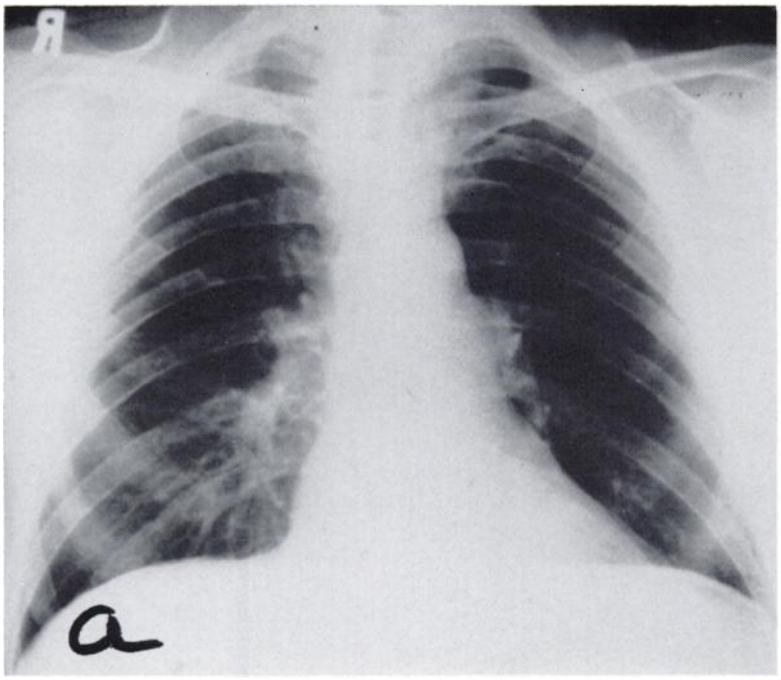

Fig. 2a. Normal chest film from a patient with previous history of pulmonary emboli.

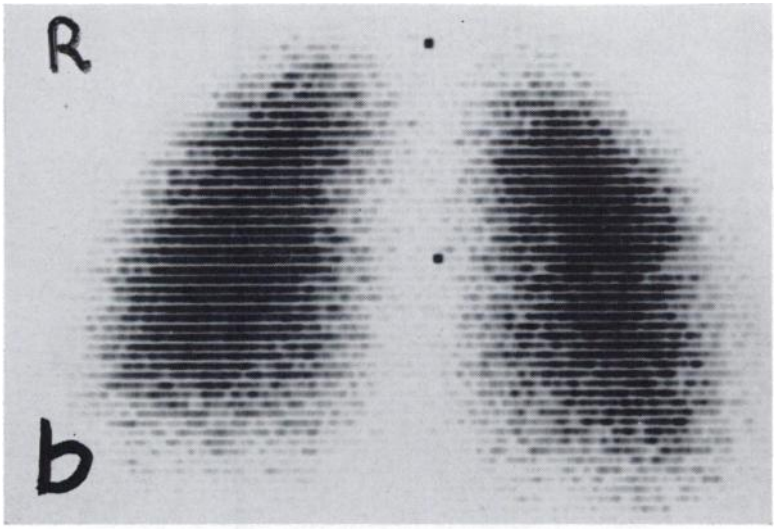

Fig. 2b. Posterior lung scan using ^{131}I albumin aggregates on the day of the chest x-ray showing slight residual scar in the left mid lung laterally, but otherwise normal.

spectrum of particle sizes of the aerosol described herein was not measured. In a study involving a similar aerosol (12), the deposition of particles relative to their size was reported as:

Particle Size	*Deposition*
30 μ	Trachea and larynx
10-30 μ	Bronchial tree
3-10 μ	Bronchioles and alveolar ducts
1- 3 μ	Alveoli (deposited)
0.5 μ	Easily reach alveoli but many are exhaled without being deposited

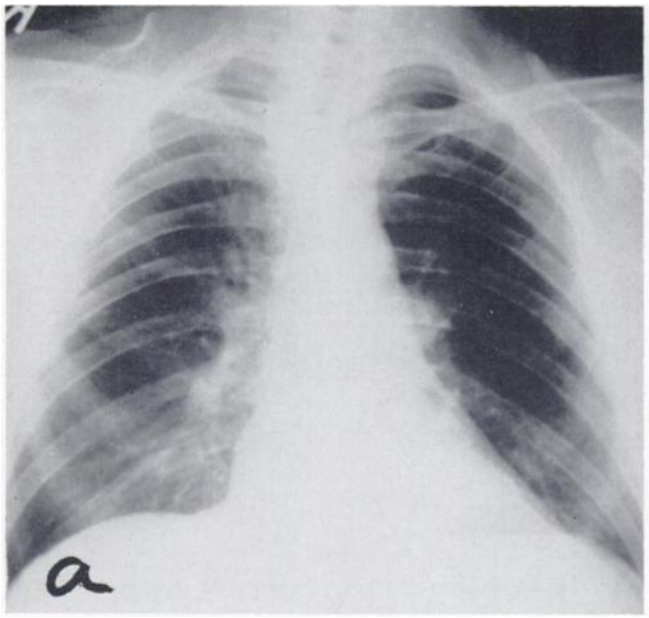

Fig. 3a. Chest film on the same patient as Figure 2 but two months later, showing a small pleural scar on the left hemidiaphragm; otherwise unremarkable.

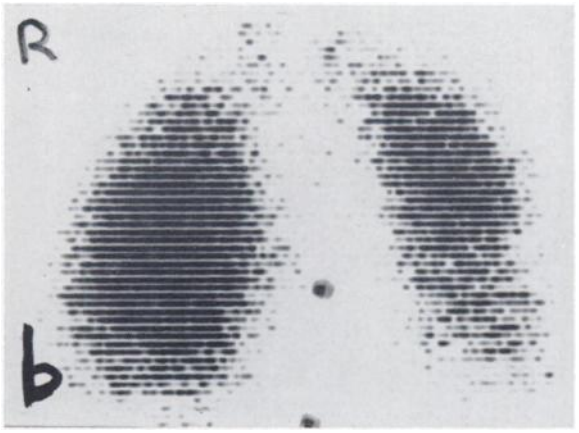

Fig. 3b. Anterior vascular lung scan done at the same time as Fig. 3c showing slight decrease in activity in the left lower lobe laterally. This illustrates the importance of doing a posterior scan when lower lobe emboli are suspected, as there may be very little representation on the anterior scan.

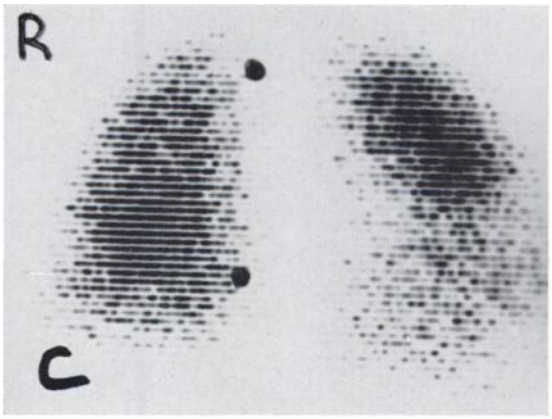

Fig. 3c. Posterior lung scan on this patient at this time showing considerable decrease of radioisotope distribution in the left lower lobe compatible with the pulmonary emboli suspected clinically.

Other factors which may affect particle deposition include the rate and volume of air flow to a section of the lung and electrostatic charges on the particles. Assuming a spectrum of particle sizes similar to the aforementioned aerosol, probably less than ten per cent of the nebulized particles reach the alveoli and are deposited. More may reach the alveoli but then be exhaled again and be deposited elsewhere in the tracheo-bronchial tree. Because of these many factors affecting aerosol particle deposition, we cannot refer to this procedure as a *ventilatory* lung scan even though we can demonstrate the presence of "material" deposited in the alveoli.

Material: One mC of ^{197}Hg Chlormerodrin, ^{131}I human serum albumin or ^{198}Au colloid is placed in the nebulizer, and administered under positive pres-

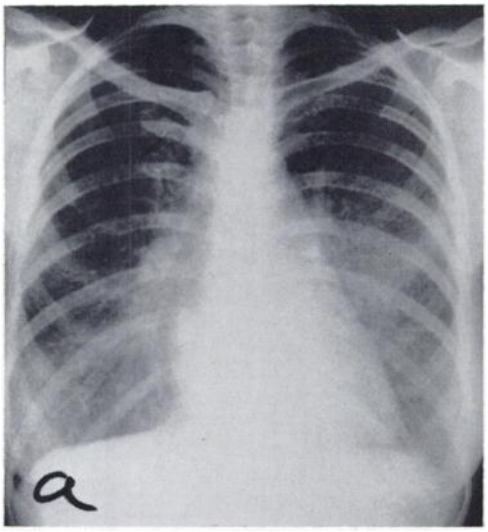

Fig. 4a. Chest film on a patient with mitral stenosis and lower lobe hemosiderosis with an infiltrate seen in the left lower lobes, at approximately pulmonary artery level.

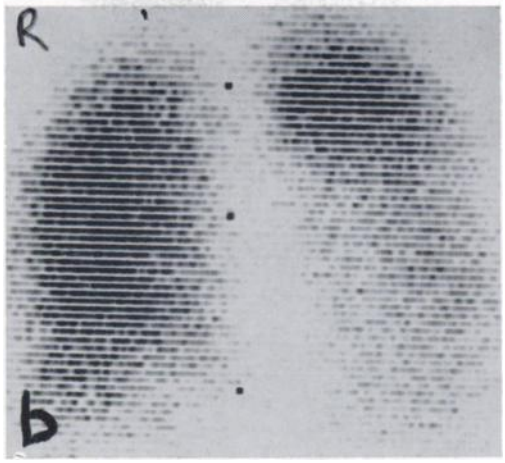

Fig. 4b. Posterior vascular lung scan showing marked decrease in radioisotope distribution in the left lower lobe, patient as in 4a.

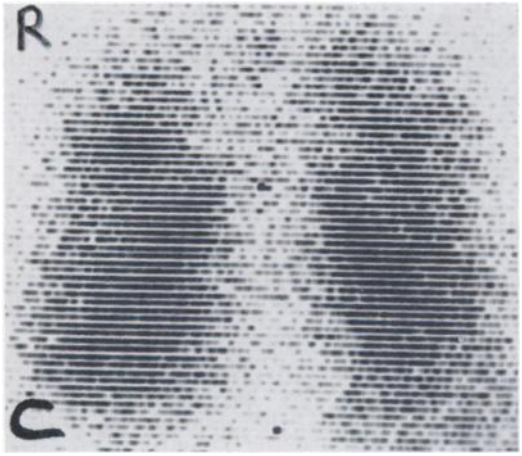

Fig. 4c. Inhalatory lung scan, showing equal deposition in both lower lobes. (Patient as in 4a and b.) The near-normal darkening in the inhalatory scan, in spite of defective darkening in the vascular scan, indicates that the diseased region, though physiologically dead, continues to ventilate.

sure; ^{99m}Tc sulfur colloid is being tried and appears satisfactory. We prefer the ^{198}Au or ^{99m}Tc colloids because there is less gut absorption. For several reasons, ^{99m}Tc-S is preferred. First, patient irradiation is reduced and second, it is possible to separate the gamma energy of ^{99m}Tc (140 KeV) from ^{131}I (364 KeV), and, therefore, obtain a perfusion and inhalatory scan at the same sitting by changing the detector's spectrometer settings and rescanning. Less than 15% of activity at ^{99m}Tc spectrometer settings is due to ^{131}I scatter with equivalent counting rates.

Internal Dose Calculation: The approximate lung dosage from 1 mc of ^{198}Au nebulized with the assumption of 20% deposited in the tracheo-bronchial tree and an effective half-life of the material from 4 to 12 hours varies from 0.6 to 1.8 rads. With ^{99m}Tc-S this would be reduced by a factor of approximately one-hundred. A laxative should be administered after the scan to ensure rapid removal of swallowed activity. The patient is encouraged to expectorate rather than swallow. This will help to reduce the hypopharyngeal, esophageal and gastric cardia activity which is seen on the scans.

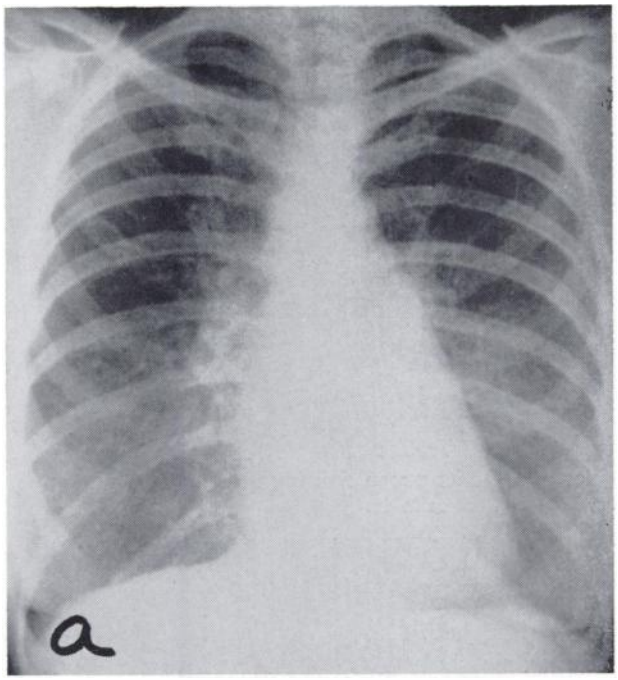

Fig. 5a. Chest film on the same patient as Figure 4 taken 5 days later, showing clearing of the infiltrate in the left lower lobe.

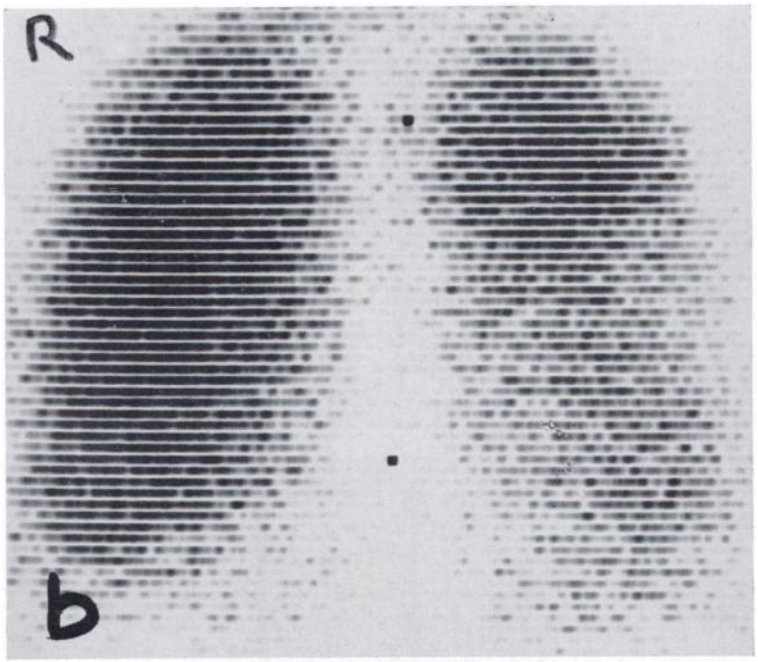

Fig. 5b. Posterior vascular lung scan showing improved deposition in the left lower lobe compatible with recanalization of the pulmonary embolus.

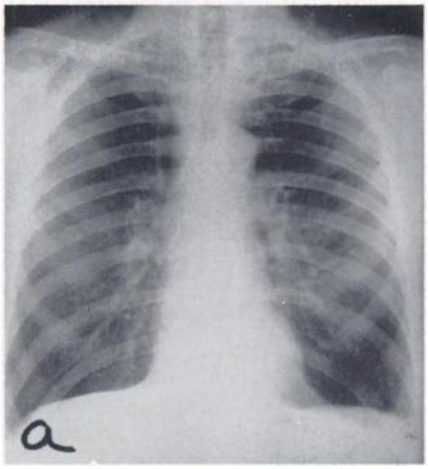

Fig. 6a. Chest film in a 60-year-old man with emphysema, showing increased apical and basal radiolucency.

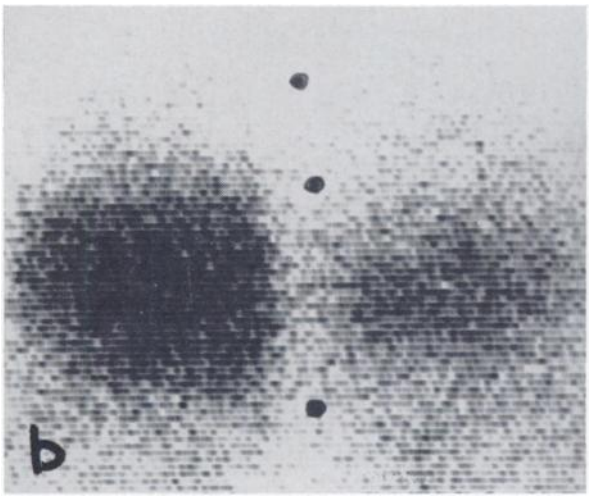

Fig. 6b. Vascular lung scan shows marked diminution of activity in apices and bases.

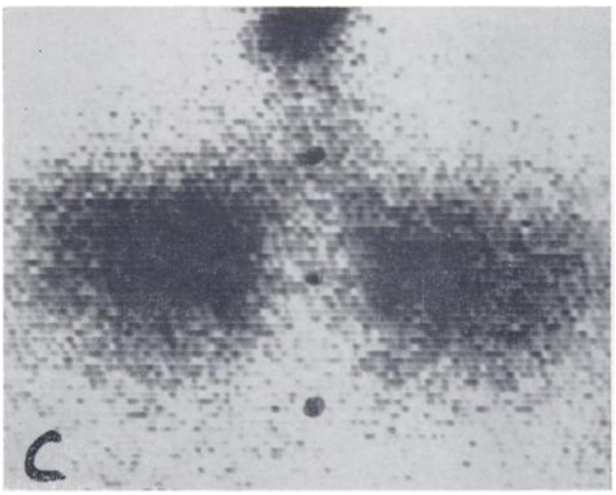

Fig. 6c. Inhalatory lung scan shows marked diminution of activity in apices and bases.

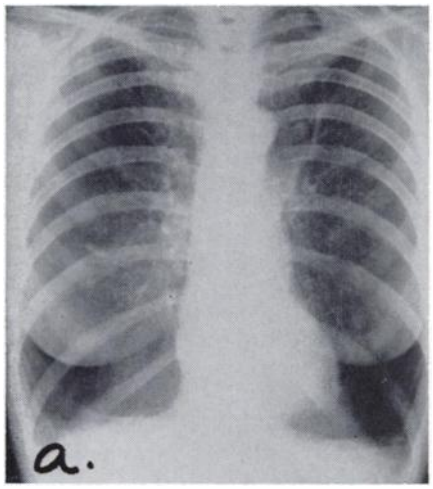

Fig. 7a. Posterior chest film on a patient showing large bullae in both lower lobes.

The mechanism of removal of the inhaled particles varies depending on the area where they are deposited, *viz.*, on ciliated epithelium, or in the deep respiratory tract where several different mechanisms to remove the particles are available (13).

APPLICATIONS

It should be understood that lung scanning techniques, as new scanning procedures, are undergoing changes of technique and interpretation. That is not to say these techniques have no established areas of usefulness, but rather we do not know: (1) all the mechanisms of radionuclide distribution which may be occurring, and; (2) all the disease states in which these lung scans would make a major contribution to the management of the patient.

Some causes of nonuniform pulmonary blood flow, other than gravity, are (14):

1. Blockage of the pulmonary circulation by blood clot, fat, gas, oil or tumor cells.
2. Partial or complete occlusion of a pulmonary artery by congenital anomaly.
3. Compression of pulmonary vessels by masses or pneumo- or hydrothorax.
4. Reduction of pulmonary vascular bed by lung tissue destruction.
5. Regional congestion of vessels in heart failure.
6. Anatomic venous-to-arterial shunts as in pulmonary hemangioma.
7. Regional differences in the alveolar pressure transmitted to the pulmonary capillaries because some alveoli are air filled and some fluid filled.
8. Overexpansion of some alveoli and collapse of others.
9. Unilateral bronchial hypoxia (15).

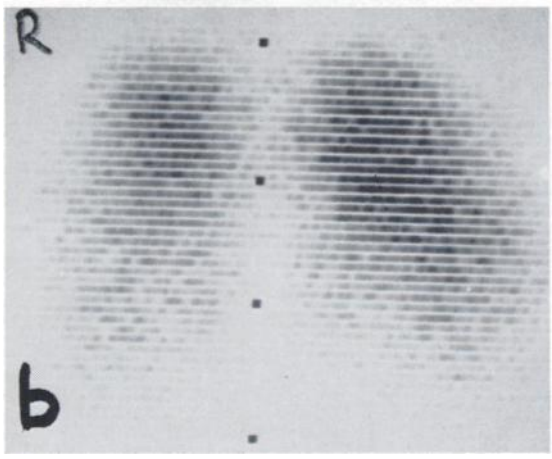

Fig. 7b. Posterior vascular scan of the lungs showing a poor deposition in both lower lobes with some diminished deposition throughout the entire right lung.

Pulmonary Embolus: As was shown experimentally (16,17), the pulmonary vascular scan is positive immediately after a pulmonary embolus. There are subtle microscopic changes by one hour, gross changes by four hours and changes on chest x-ray by 24 to 48 hours, if at all. Enzyme studies require serial determinations over a two to three day period. Electrocardiographic changes may be nonspecific and misleading. The three tests which are positive immediately after pulmonary embolus are: (1) the vascular lung scan: (2) the pulmonary angiogram, and; (3) measurement of the physiologic dead space, characteristically increased in pulmonary embolus. The vascular lung scan is the simplest of these to perform.

As pulmonary emboli without infarct may be dissolved in as short a time as three to four days, it is important to do the vascular lung scan as soon after the suspected pulmonary artery embolus as possible. We have seen scans return to normal while the serum lactic dehydrogenase activity was still elevated.

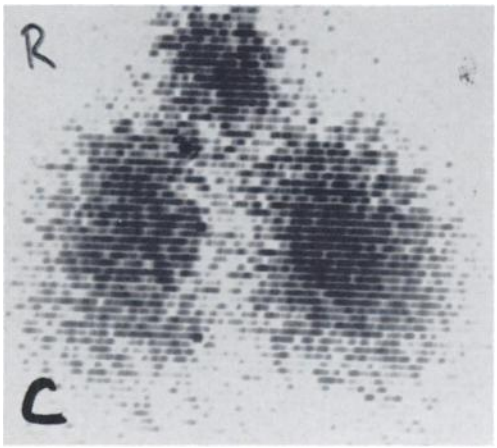

Fig. 7c. Inhalatory scan showing poor deposition in the lower lobes in the area of the bullae. The large concentration high in the mid-line is in the hypopharynx of the patient.

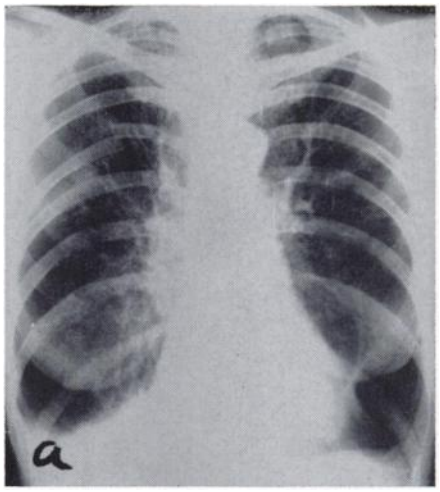

Fig. 8a. Post-operative chest film showing the surgical trauma to the right sixth rib, and also reaction at the right base.

The major application of lung vascular scanning in pulmonary embolus is in the early evaluation of the patient, especially if there are no obvious roentgen findings. If there is a positive lung scan, and a positive chest film, the differential diagnosis becomes near legion with pneumonia, abscess, atelectasis, infected bullae, carcinoma, and loculated empyema, being among the considerations.

Such a case in point is that of a 62-year-old physician with recurrent calf swelling and a history of previous pulmonary emboli. During a follow-up evaluation, a chest film and posterior vascular lung scan were performed, both being normal (Fig. 2a,b). Two months later, he had a recurrence of a left chest pain. A chest film (Fig. 3a) was normal, except for a small pleural scar along the left hemidiaphragm. A posterior vascular lung scan showed a marked decrease in

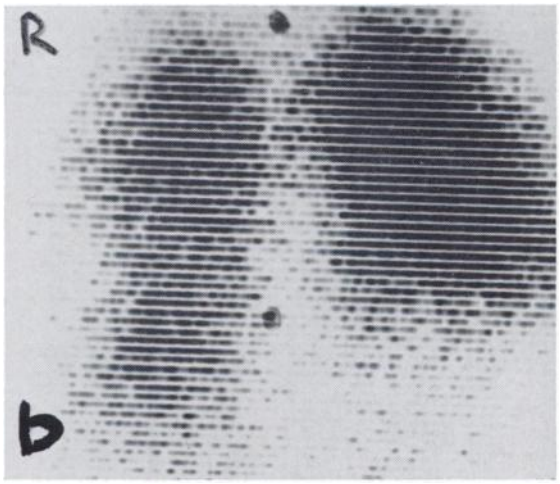

Fig. 8b. Posterior vascular scan, postoperatively, showing improved filling in the right lower lobe region compared to the preoperative scan.

filling in the left lower lobe (Fig. 3c). An anterior scan done at the same time (Fig. 3b) does not portray the extent of his compromised pulmonary vasculature nearly as well as the posterior scan. This is because the focusing depth of the collimator, two to four inches, portrays the upper lobe and lingula in the anterior scan and the lower lobe and posterior segment of the upper lobe in the posterior scan. The most suspect region of the lung should be scanned first. Since the lower lobes are most commonly involved in pulmonary emboli, the posterior scan is preferred and is done as a routine. The anterior or lateral vascular lung scans are reserved for special instances of suspected upper lobe disease or in patients who cannot lie prone.

A representation of the increased physiologic dead space in pulmonary embolus may be obtained by performing both the vascular and the inhalatory lung scans. Such a case was a 40-year-old woman with mitral stenosis and lower lobe hemosiderosis. She had an episode of a sudden left chest pain, and 24 hours later a density in the left lower lobe was seen on chest x-ray (Fig. 4a). The clinical problem was whether the x-ray finding represented pneumonia, localized pulmonary edema, or pulmonary embolus. A posterior vascular lung scan showed decreased filling in the left lower lobe (Fig. 4b). This did not exclude the possibility of pneumonia or pulmonary edema. An inhalatory lung scan was done (Fig. 4c) showing equal filling of the bases. This would not have occurred in either pulmonary edema or pneumonia, so the presumption was that this was a pulmonary embolus, and the inhalatory vascular lung scan difference in left lower lobe filling was the representation of the increased physiologic dead space seen in pulmonary embolus. A repeat chest film and lung scan five days later (Fig. 5a,b) showed the area to have cleared on x-ray and improved on lung scan suggesting pulmonary embolus with recanalization of the vessel.

Emphysema: The inhalatory lung scan demonstrates the patency of the pulmonary airway and communication, or lack of communication, between blebs or

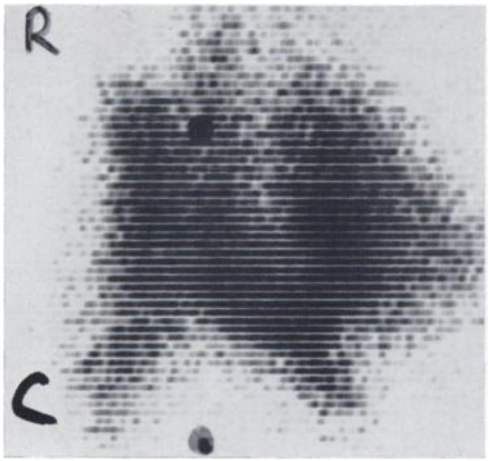

Fig. 8c. Inhalatory scan showing improved filling in the right lower lobe. The decreased activity laterally in the right lung on the inhalatory scan is thought to represent reaction from the placement of the thoracotomy tube. The activity increase in the mid-line and in the lower margin of the left lobe is thought to be in the esophagus and stomach.

bullae and the major bronchial tree. Blebs and bullae are better demonstrated with the inhalatory than the vascular lung scan. In patients with emphysema, there is diminished deposition of radioactivity in the periphery of the lung in association with blebs and bullae. The scan findings are frequently more striking than the roentgen findings (Fig. 6). The decrease in activity in these regions, as seen in the vascular lung scan, is thought to be due to poor regional perfusion. Pulmonary artery shunting may also be contributory (18).

The lung scan may be used in evaluating patients after surgical resection of blebs or bullae. A 42-year-old woman had marked bullous emphysema of both

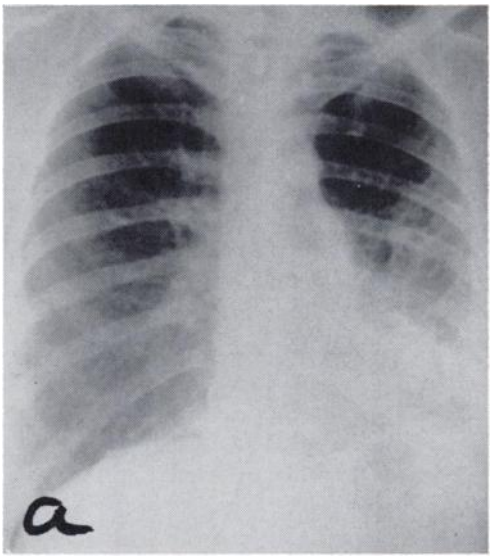

Fig. 9a. Chest film showing multiple cysts in the left lung with increased density.

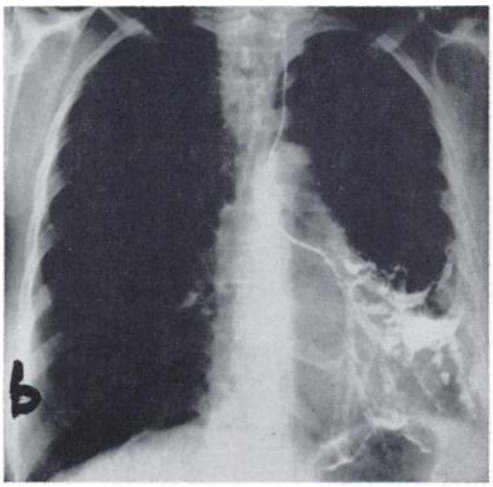

Fig. 9b. Left bronchogram showing the dye collecting in large saccular dilatations in the lower lobe.

lung bases. Her chest film (Fig. 7a) shows the increased radiolucency at the lung bases. The vascular (Fig. 7b), and inhalatory (Fig. 7c) lung scans show absence of radioactivity in the lung bases. Her right lung base bullae were resected and she improved considerably. The postoperative chest film (Fig. 8a) shows little change. The lung scans (Fig. 8b,c) show better perfusion and deposition in the right lung base as the compressed lung expands into the space previously occupied by bullae. The defect in the right lateral border coincides with the area where the thoracotomy tube was placed and this may represent residual reaction in that area.

Congenital Cystic Lung with a hypoplastic pulmonary artery was found in a 34-year-old woman. A routine chest film showed multiple cysts in the left lower

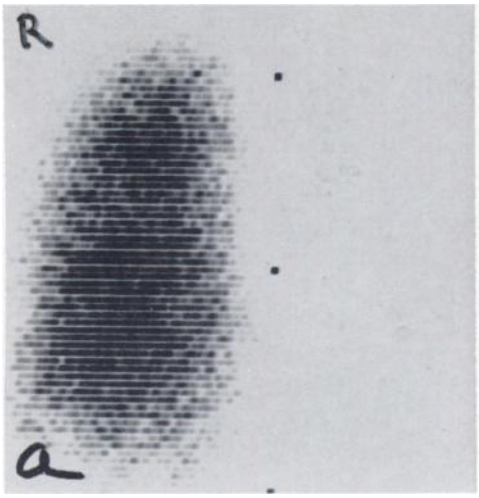

Fig. 10a. Posterior vascular scan showing normal activity throughout the right lung with absent activity on the left.

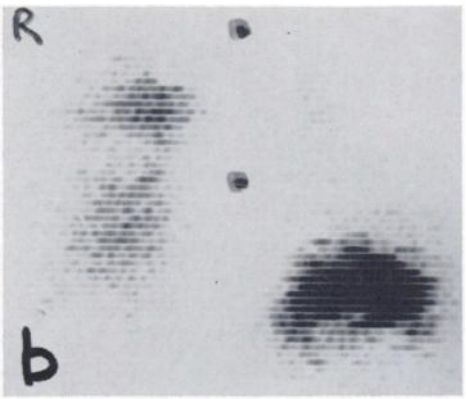

Fig. 10b. Posterior inhalatory scan showing activity deposited throughout the right lung, with a wedge of inactivity of undetermined significance in the right mid-lung region. There is no activity seen in the left lung. The large activity seen in the lower border on the left side is in the cardia of the stomach.

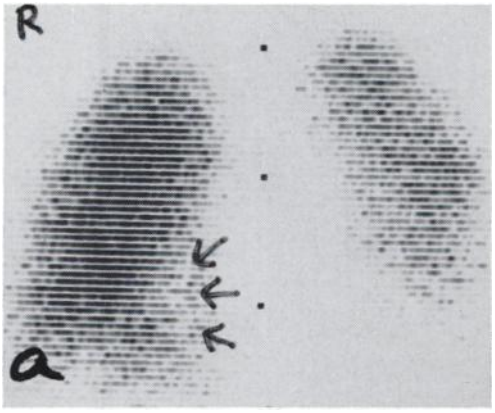

Fig. 11a. Posterior vascular scan showing general decreased activity on the left side with a definitely decreased area of activity in the right medial basal segment, where a cavity was seen by x-ray.

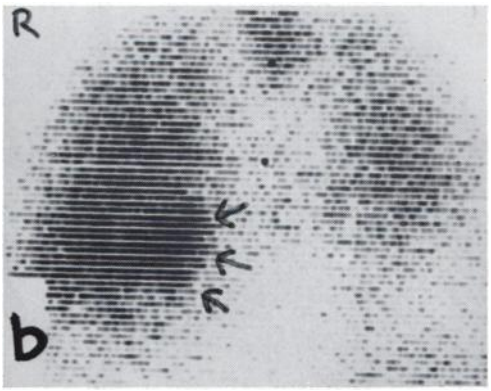

Fig. 11b. Posterior inhalatory scan showing decreased activity on the left with increased activity in the area of the cavity in the right medial basal segment. The activity seen in the mid portion of the scan above the apices is in the hypopharynx.

lobe (Fig. 9a). A bronchogram (Fig. 9b) showed multiple cysts filling with the contrast material. The vascular and inhalatory lung scans (Fig. 10a,b) showed almost no activity in the left lung. Her pulmonary function studies were normal and a left pneumonectomy was performed. At that time a hypoplastic left pulmonary artery was found. Pulmonary function studies postoperatively were unchanged from her preoperative values.

Acquired Cavitary Disease: A 55-year-old man with pulmonary fibrosis and an alveolar capillary block was found to have a *cavity* in the right lower lobe's medial basal segment. A vascular lung scan (Fig. 11a) showed diminished activity in the region of the cavity, presumed to be an area of poor perfusion. The inhalatory lung scan (Fig. 11b) showed increased activity in the cavity, demonstrating its communication with the tracheo-bronchial tree and the patency of this connection. In bronchiectasis we have noted that even the large saccules which fill with the oily contrast medium do not fill on the inhalatory lung scan. This may be due to a functional rather than an anatomic obstruction to air flow in the bronchiectatic segment.

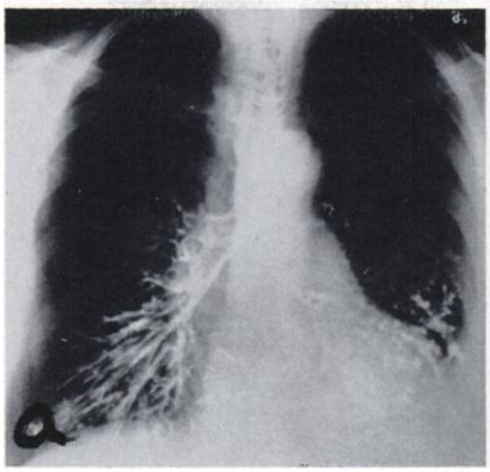

Fig. 12a. Bronchogram showing advanced saccular bronchiectasis in the left lower lobe.

Bronchiectasis: Both the vascular and the inhalatory lung scans show a decreased to absent deposition of radioactivity in the diseased lung. It is not known whether the decreased vascular bed representation is due to decreased pulmonary artery perfusion to the hypoxic bronchiectatic segment, or because of pulmonary arterio-venous shunting, allowing the particles to pass through without lodging in normal sized pulmonary capillaries. The lack of deposition of the radio-colloid in these patients, as seen in the inhalatory lung scan, probably represents a functional rather than an anatomic obstruction, since the bronchographic contrast material usually fills the involved segments. Such a case was a 47-year-old woman with severe saccular bronchiectasis in the left lower lobe. Her bronchogram

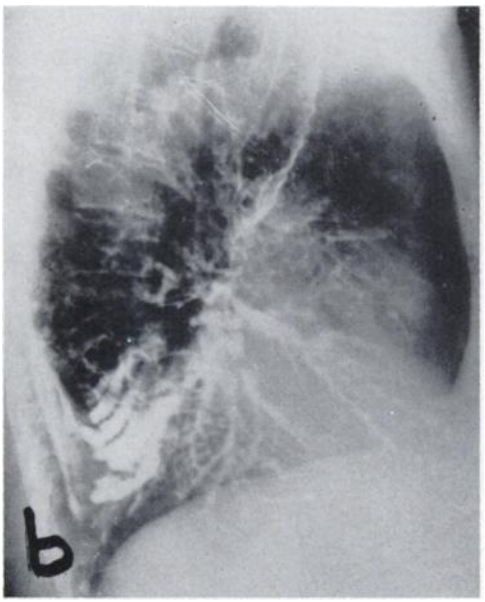

Fig. 12b. Bronchogram showing advanced saccular bronchiectasis in the left lower lobe.

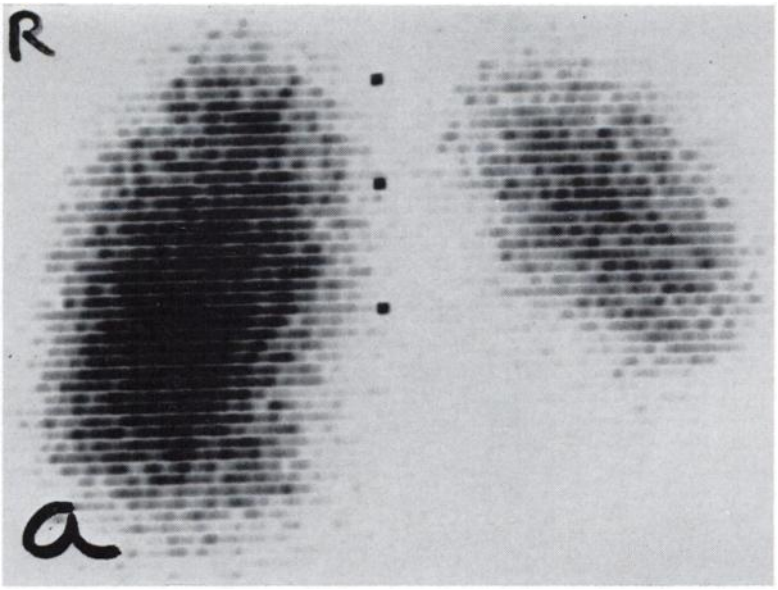

Fig. 13a. Posterior vascular scan showing absent activity in the left lower lobe.

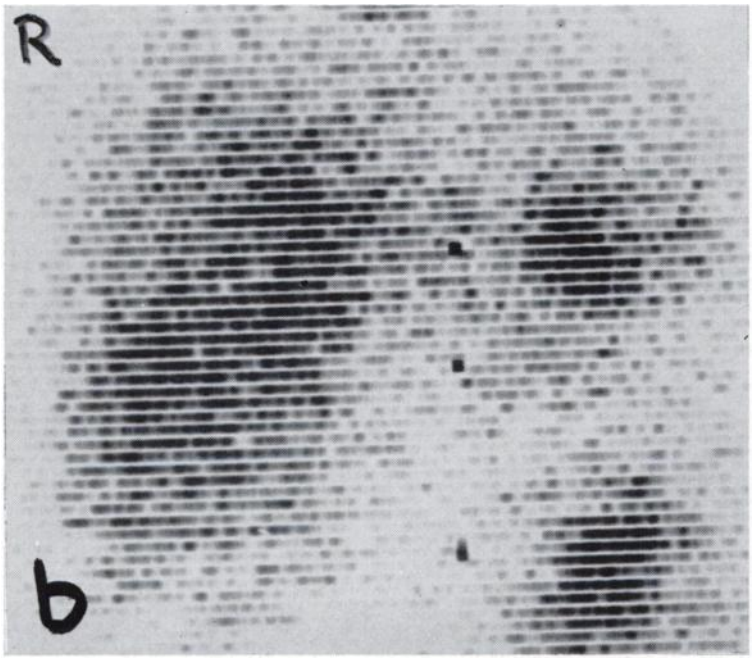

Fig. 13b. Posterior inhalatory lung scan showing absent deposition on activity in the left lower lobe. The activity at the inferior margin on the left is in the cardia of the stomach.

(Fig. 12a, b) demonstrates the extent of the disease, and her lung scans (Fig. 13a, b) show the decrease in deposition of the aggregate in the vascular scan and of the colloid in the inhalatory scan; characteristic of bronchiectasis in our experience.

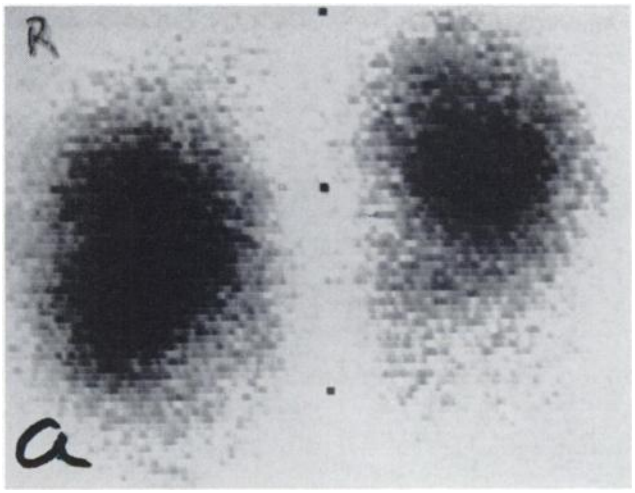

Fig. 14a. Posterior vascular scan showing decreased activity in the left apex and in the right lower lobe with scattered areas of suggestive decreased activity in the right lobe medially as well as laterally.

Asthma: A markedly abnormal inhalatory scan is seen in patients with acute asthma. A 62-year-old man with long-standing emphysema was seen in an acute asthmatic state. His vascular lung scan (Fig. 14a) shows several areas of decreased radioactivity throughout both lungs, presumably in areas of bleb formation. The inhalatory scan (Fig. 14b) showed markedly decreased deposition throughout both lungs, disproportionate to the changes seen in the vascular lung scan. At bronchoscopy the bronchi were seen to be markedly narrowed, almost in spastic contraction, but would dilate after washing with normal saline solution. Several days after his initial inhalatory lung scan, and after his acute asthmatic attack had subsided, a repeat inhalatory lung scan (Fig. 14c) showed considerably

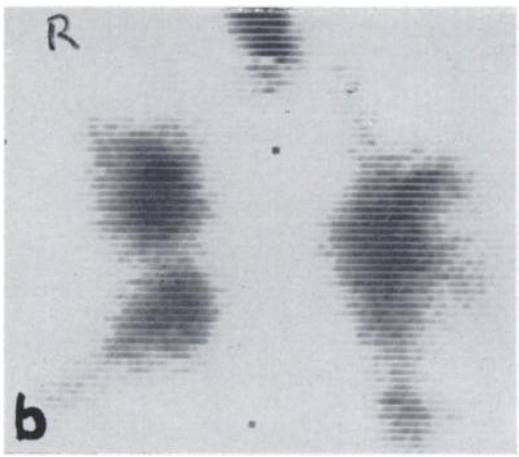

Fig. 14b. An inhalatory lung scan done after the vascular lung scan showing marked decrease in deposition of the colloid throughout both lungs in the upper mid and lower portions.

improved distribution peripherally. We have not performed inhalatory scans on simple uncomplicated acute asthmatics, but we feel this case demonstrates the functional airway obstruction and relatively normal perfusion seen in acute asthma (19).

Carcinoma: There is decreased deposition of the aggregate in areas of primary bronchogenic carcinoma. The reason for this may be due to: (1) pulmonary artery compression from hilar metastases; (2) predominately bronchial artery supply to the tumor, or; (3) reflex decreased pulmonary artery perfusion secondary to lobar hypoxia as a result of bronchial obstruction by the tumor.

If there are hilar metastases or extrabronchial extension of the carcinoma, the pulmonary artery is more vulnerable to compression than is the cartilagenous bronchus. Such an example was a 57-year-old man with carcinoma arising in the right main stem bronchus with extrabronchial extension (Fig. 15). At thoracotomy, the tumor was seen compressing the pulmonary artery and flow was markedly diminished. Once the occluding tumor was dissected away, the pulmonary artery flow returned to near normal, even though nearly complete obstruction of the right bronchus, caused by the tumor mass, remained. A pneumonectomy was performed.

SUMMARY

The current status of lung scanning is difficult to define as it is undergoing change continually. This is the usual pattern of new radioisotope scanning procedures.

It does appear that lung scanning will offer a real contribution to the evaluation of patients with pulmonary parenchymal and vascular diseases.

The usefulness of the vascular and inhalatory lung scans in pulmonary

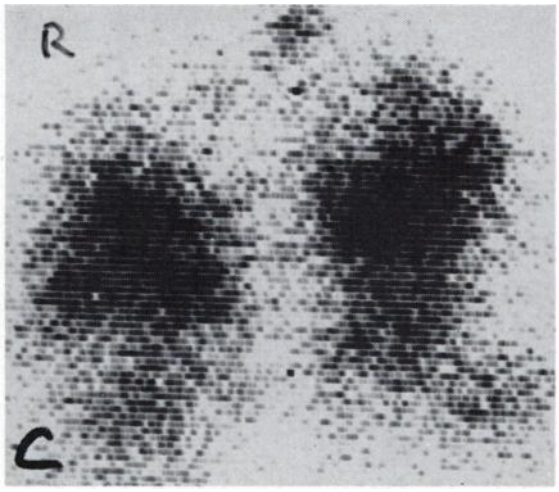

Fig. 14c. Posterior inhalatory scan done several days after the first acute asthmatic episode and subsided, showing improved deposition throughout both lung fields with poor deposition remaining in the right apex and lower lobe, and in the area of suspected blebs in the left lower lobe laterally.

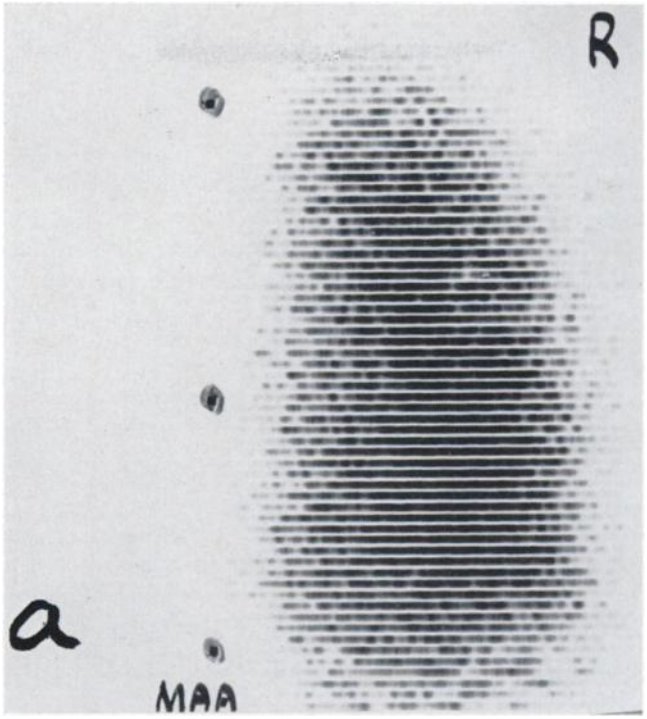

Fig. 15a. Vascular and lung scan in a 57-year-old man with carcinoma of the right main stem bronchus showing almost complete absence of activity in the right lung.

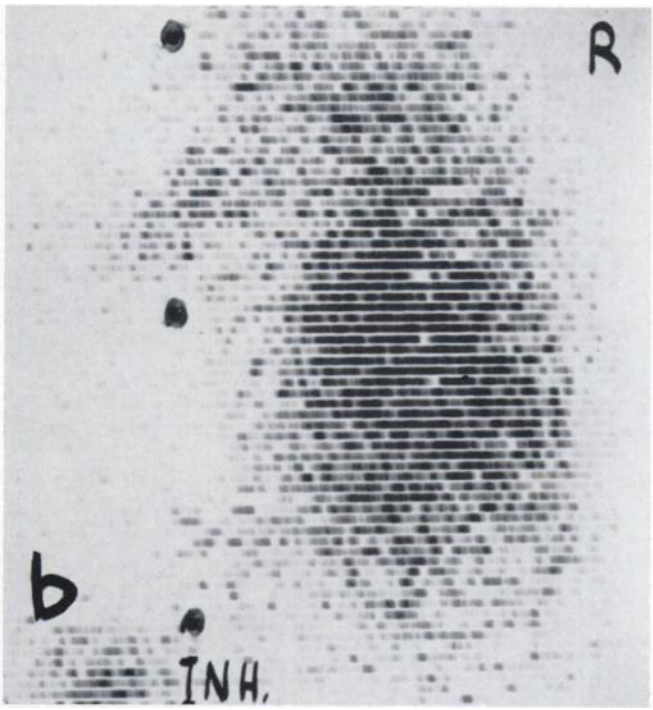

Fig. 15b. Inhalatory lung scan in a 57-year-old man with carcinoma of the right main stem bronchus showing almost complete absence of activity in the right lung.

embolus diagnosis is proven; in bronchiectasis and emphysema is promising; and in neoplastic disease is unclear.

ACKNOWLEDGMENT

The ^{131}I human serum albumin aggregates were graciously supplied by Dr. Gordon Lindenblad of E. R. Squibb Company, New Brunswick, New Jersey.

The Bird Respirator used to perform these studies was loaned to us by the Bird Corporation.

REFERENCES

1. Taplin, G. V., Dore, E. K., Johnson, D. E. and Kaplan, H. S.: Suspension of Radioalbumin Aggregates for Photoscanning the Liver, Spleen, Lung and Other Organs. *J. Nuc. Med.* **5**:259-275, (1964).

2. Quinn, J. L. III, Whitley, J. E. Hudspeth, A. S., and Prichard, R. W.: Early Clinical Applications of Lung Scintiscanning. *Radiology* **82**:315-317, Feb., 1964.

3. Wagner, Jr., H. N., Sabiston, Jr., D. C., Iio, M. McAfee, J. G., Meyer, J. K. and Langan, J. K.: Regional Pulmonary Blood Flow in Man by Radioisotope Scanning. *J.A.M.A.* **187**:601-603, Feb. 22, 1964.

4. Quinn, J. L. III, Whitley, J. E.: Lung Scintiscanning. *Radiology* **83**:937-943, Nov. 1964.

5. Altenerun, H. J.: The Isotope Thoracograph After Inhalation of Radioactive Aerosols. Radioaktive Isotope in Klinik Und Forschung, *Band VI*, Urban & Schwarzenburg, Munich, **6**:396-402, 1965.

6. Taplin, G. V.: *Personal Communication.*

7. Temple, J., Pircher, F., and Sieker, H.: Evaluation of Pulmonary Ventilation and Perfusion by Isotope Scanning. *Clinical Res.* **13**:76, Jan., 1965.

8. Temple, J., Pircher, F., Kirsch, W. and Sieker, H.: Study of Pulmonary Ventilation by Isotope Scanning, *Clin. Res.* **13**:352, Apr., 1965.

9. Taplin, G. V., et al: *Human Lungscanning with Macro-radioalbumin Aggregates,* Scientific Exhibit, 11th Annual Meeting, Soc. of Nuc. Med. Berkeley, Calif. June, 1964.

10. Furth, E. D., Okinaka, A. J., Focht, E. F., and Becker, D. V.: The Distribution Metabolic Fate and Radiation Dosimetry of ^{131}I Labeled Macroaggregated Albumin, *J. Nuc. Med.,* In Press.

11. Mitchell, R. I.: Retention of Aerosol Particles in the Respiratory Tract: A Review. *Am.Rev.Resp.Dis.* **82**:627-639, 1960.

12. Nelson, S. W. and Christofordis, A. J.: An Automatic Inhalation-Actuated Aerosol Anesthesia Unit, *Radiology* **82**:226-234, 1964.

13. Casarett, L. J., and Miller, P. S.: Alveolar Reactivity Following Inhalation of Particles. *Health Physics* **10**:1003-1011, Dec. 1964.

14. Comroe, J. H.: Physiology of Respiration, *Year Book Med.,* Pub. Chicago, p. 151, 1965.

15. Fishman, A. P.: Respiratory Gases in the Regulation of the Pulmonary Circulation, *Physiol. Rev.* **41**:214-280, 1961.

16. Whitley, J. E., Quinn, J. L. III, Hudspeth, A. S. and Prichard, R. W.: The Scintiscanning of Experimentally Produced Pulmonary Infarcts, *Radiology* **81**:884-885, 1963.

17. Quinn, J. L. III, Whitley, J. E., Hudspeth, A. S., and Watts, F. D.: An Approach to the Scanning of Pulmonary Infarcts, *J. Nuc. Med.* **5**:1-8, Jan., 1964.

18. Jacobson, G., Turner, A. F., Balchum, O. and Jones, C.: Pulmonary Arteriovenous Shunts in Emphysema Demonstrated by Wedge Arteriography: *Amer.J.Roent.Rad.Ther.* and *Nuc. Med.* 93:868-878, Apr., 1965.

19. Ledbetter, M. K., Bruch, E., and Farki, L. E.: Perfusion of the Underventilated Compartment of the Lungs in Asthmatic Children, *J.Clin.Invest.* **43**:2233-2240, Dec., 1964.