Regional Ventilation in the Differential Diagnosis of Pulmonary Embolism

By Jose R. Medina, M.D., Philippe L’Heureux, M.D., James P. Lillehei, M.D., and Merle K. Loken, M.D., Ph.D.

With the technical assistance of Richard Ponto, B.A.

SUMMARY

In the diagnosis of pulmonary embolism by lung scanning, clinical errors of interpretation may arise. Diseases that affect the distribution of pulmonary blood flow, such as pulmonary emphysema and bronchial asthma, may be confused with pulmonary embolism.

With the addition of ventilation studies with $^{133}$Xenon to the perfusion scans, distinct differences appear between patients with emboli and those with obstructive lung disease. In patients with pulmonary emboli, ventilation is preserved in the areas of decreased perfusion, whereas patients with obstructive lung disease show both decreased ventilation and perfusion in the affected areas.

Additional Indexing Words:

$^{133}$Xenon Ventilation-perfusion Pulmonary embolism Lung scans

LUNG SCANNING with macroaggregates of albumin labelled with radioactive isotopes is widely used in the diagnosis of pulmonary emboli. Errors in the interpretation of defects evidenced in lung scans may be due to technical or clinical factors. Technical errors are related to the particle size, to the equipment used, and to the resolution achieved. Clinical errors of interpretation arise when other diseases altering the distribution of pulmonary blood flow are confused with pulmonary embolism. Such entities include pulmonary emphysema, bronchial asthma, and cystic lesions of the lung.

The purpose of this paper is to report our experience with the clinical application of a $^{133}$Xenon and Anger scintillation camera technic, with emphasis on the contribution which regional ventilation studies can make in the differential diagnosis of abnormalities of pulmonary perfusion.

Methods

Twelve normal volunteers, ages 25 to 32 years, nine patients with pulmonary emboli without infarction, and 20 patients with obstructive lung disease underwent ventilation and perfusion studies with $^{133}$Xenon and the Anger scintillation camera. The diagnosis of pulmonary embolism was confirmed by pulmonary arteriograms in seven of the nine patients and thought to be almost certain on the basis of clinical findings in the other two. Six of these patients were studied within 24 to 48 hours after the onset of symptoms. The emboli occurred 3 weeks prior to the xenon study in one patient, and 3 months prior to the study in two others. In the latter three patients, the lung regions showing perfusion defects by the xenon study corresponded to the defects on the original scans and arteriograms.

The 20 patients with obstructive lung disease were selected from a larger group of such patients because they showed localized defects in distribution of pulmonary blood flow on the xenon studies. The clinical diagnosis in these patients was pulmonary emphysema in 19 and bronchial asthma in one. All the patients had severe obstructive lung disease as evidenced by mean values for FEV$_1$/VC* of 39 ± 13%, for vital

*Forced expiratory volume in 1 sec/vital capacity.

From the Departments of Medicine and Radiology, the University of Minnesota Medical School, Minneapolis, Minnesota.

This investigation was supported by grants from the Minnesota Respiratory Health Association, the Picker Foundation, and the Graduate School of Medicine of the University of Minnesota, Minneapolis, Minnesota.

Circulation, Volume XXXIX, June 1969
capacity of 60 ± 14% of predicted value, and for RV/TLC* of 62 ± 10%.

The xenon studies were done with the subjects seated and with the camera crystal positioned over the posterior surface of the chest. The Anger camera has a crystal, 11 inches in diameter, that encompasses most of the lungs. In patients with large chests, a portion of the bases was excluded.

Assessment of pulmonary perfusion was made by the intravenous injection of a bolus of 3 to 5 millicuries of 133Xenon dissolved in saline solution. Xenon is carried to the pulmonary circulation and diffuses immediately into the alveoli. If the subject holds his breath, there is no redistribution of radioactivity. A scintiphotograph obtained during breath-holding, therefore, represents regional perfusion. Once the patient resumes breathing, xenon washes out of the lungs and serial scintiphotographs are obtained. These photographs demonstrate regional clearance of xenon from the lung.

Ventilation was studied separately by having the patient breathe 3 to 5 mc of 133Xenon gas from a closed-circuit spirometer. After the first inhalation of 133Xenon, the patient held his breath and a single breath scintiphotograph was obtained. Then the patient rebreathed the xenon-air mixture to attain a uniform distribution of xenon within the lung. The spirometer was then removed and the subject was allowed to breathe room air while xenon cleared from the lungs. Scintiphotographs were obtained during rebreathing and clearance.

All scintiphotographs were obtained with 30,000 counts.

Results

After intravenous injection of 133Xenon, the scintiphotographs of normal subjects (fig. 1) showed uniform distribution of radioactivity throughout both lungs. Patients with pulmonary emboli and patients with pulmonary emphysema showed filling defects on the perfusion scintiphotographs (figs. 2 and 3). On the clearance scintiphotographs, marked differences became apparent. Patients with emphysema retained radioactivity in the areas of decreased perfusion, indicating that ventilation was impaired in these areas as well. Normal subjects and patients with pulmonary emboli showed uniform clearance of the injected xenon.

After a single inhalation of 133Xenon gas, radioactivity was uniformly distributed in normal subjects and in patients with pulmonary emboli. After rebreathing, the clearance of 133Xenon also was uniform and rapid. All patients with pulmonary emphysema demonstrated decreased radioactivity after a single breath of 133Xenon in the region where perfusion was decreased. Prolonged rebreathing of 133Xenon was necessary to visualize these areas. During clearance, these same areas showed marked retention of radioactivity.

*Residual volume/total lung capacity.
The correlation of lung scanning with macroaggregates with the perfusion scintiphoto-}

graphs and the pulmonary arteriograms was good (fig. 4A and B).

**Discussion**

Lung scans with labelled macroaggregates of albumin have proved to be useful in the
diagnosis of pulmonary emboli. In the presence of a normal chest roentgenogram,
concave- or triangular-shaped defects at the periphery of the lung are strongly suggestive
of pulmonary emboli. Such patterns are not specific for emboli, however, since patients
with chronic obstructive pulmonary disease can show similar defects.

By adding ventilation studies to the perfusion scans, we have found distinct
differences between patients with emboli and
Figure 4

(A) The macroaggregate scan shows a large perfusion defect at the right base and smaller defects at the left base in a patient with pulmonary embolism. The pulmonary arteriogram, which is reversed to correspond to the scan, shows complete occlusion (arrow) of the right lower lobe pulmonary artery and pruning of the left lower lobe arteries.

(B) The scintiphotographs show a large area of decreased radioactivity at the right base during perfusion similar to the defects shown in figure 4A. The ventilation photograph (single breath) shows uniform distribution of radioactivity.
those with obstructive lung disease. The scintiphotographs of patients with pulmonary emboli showed preserved ventilation in the areas of decreased perfusion, while patients with obstructive lung disease showed both decreased ventilation and perfusion in the affected areas.

Our patients with pulmonary emboli were studied 24 hours or more after the onset of symptoms, and the hypoperfused areas were well ventilated. Similar findings were reported by Bass and associates.7 Experimental work in dogs8 suggests that during the first 24 hours after acute embolization ventilation and perfusion are both decreased in the affected region; thereafter, ventilation returns while perfusion is still decreased. No studies of regional ventilation have been reported on human beings during the first 24 hours after embolization.

Our initial studies with 133-xenon and the scintillation camera indicate that this technic will have considerable practical usefulness in the differential diagnosis of pulmonary emboli. The speed and resolution achieved permit performance of the entire study in only a few minutes, and it can be done on seriously ill patients. Where a scintillation camera is not available, lung areas showing abnormal perfusion on a macroaggregate scan can be evaluated for ventilation 24 hours later by means of 133-xenon and small scintillation detectors.9

Although xenon injection, inhalation, and rebreathing were performed separately in our study, we now feel that the necessary information for the differential diagnosis of pulmonary emboli can be obtained from the intravenous injection alone.10 Scintiphotographs made during breath-holding after injection of 133-Xe depict perfusion, and those made during clearance represent regional ventilation.

Acknowledgment
We wish to express our appreciation to Richard V. Ebert, M.D. for his encouragement and comments in reviewing this manuscript.

References
Regional Ventilation in the Differential Diagnosis of Pulmonary Embolism
JOSE R. MEDINA, PHILIPPE L'HEUREUX, JAMES P. LILLEHEI, MERLE K. LOKEN and Richard Ponto

Circulation. 1969;39:831-835
doi: 10.1161/01.CIR.39.6.831
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1969 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/39/6/831

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/