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SELF-STUDY TEST

Pulmonary Nuclear Medicine

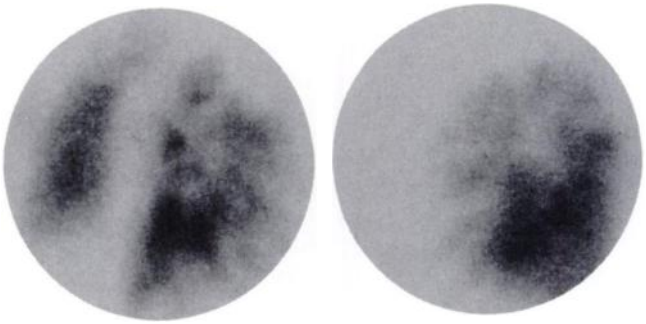
Questions are taken from the *Nuclear Medicine Self-Study Program I,* published by The Society of Nuclear Medicine

DIRECTIONS

The following items consist of a heading followed by numbered options related to that heading. Select those options you think are true and those that you think are false. Answers may be found on page xxxx.

Figure 1 shows the ventilation-perfusion images in a 54-yr-old woman with suspected pulmonary embolism. True statements concerning this clinical situation include:

1. The findings are consistent with pulmonary lymphangitic carcinomatosis.
2. The changes, if due to pulmonary lymphangitic carcinomatosis, would be primarily caused by spread of tumor through the lymphatic system of the lungs.
3. A normal chest radiograph would be very unusual in a patient with these findings on perfusion imaging.
4. Diffuse vasculitis occasionally produces similar findings.



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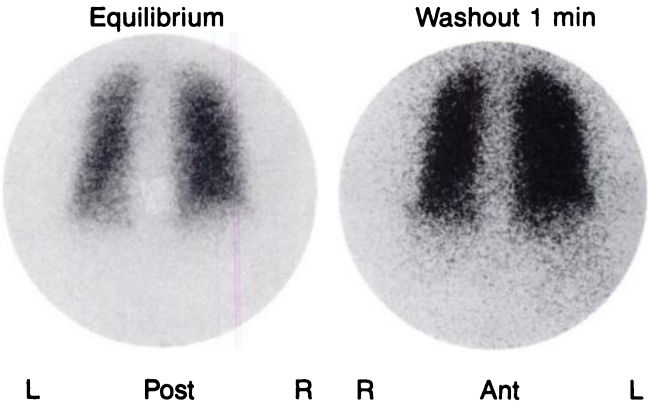

True statements concerning pulmonary ventilation and perfusion include:

5. Patient position is an important determinant of regional ventilation because of gravitational effects on intrapleural pressure gradients.
6. In the upright patient, airflow is greatest in alveoli at the apex.
7. Both ventilation and perfusion increase from apex to base in the upright lung, but the ventilation-perfusion ratio decreases.
8. Xenon gas clears most quickly from regions of lung having high alveolar compliance.
9. Gas exchange is best in regions where perfusion is less than ventilation.

True statements concerning pathologic conditions affecting pulmonary function include:

10. Pneumoconstriction following pulmonary embolization is rarely observed in xenon ventilation studies.
11. Pulmonary infarction frequently occurs (over 40% of cases) as a result of pulmonary embolism.
12. Alveolar hypoxia is often associated with obstructive pulmonary disease.
13. Precapillary arteriolar sphincters normally respond to alveolar hypoxia by dilating.
14. Airways collapsing from loss of normal alveolar structure is a hallmark of both obstructive and restrictive lung disease.

(continued on page 1336)

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SELF-STUDY TEST
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True statements concerning evaluation of regional ventilation by ^{133}Xe scintigraphy include:

15. Regions of compromised ventilation are indicated either by slow tracer entry noted on washin images or by delayed clearance on washout images.
16. Tracer concentration and chest wall thickness affect count rate during xenon washout studies, but these factors have no effect on regional xenon clearance rates.
17. The time required to clear xenon from the lungs is largely unaffected by local alveolar volume and air flow.
18. Depth and frequency of respiration affect global rates of tracer clearance but have little influence on relative clearance patterns from individual lung regions.
19. Alveolar compliance and airways resistance are important determinants of the rate of regional xenon clearance.

A 76-yr-old man with a 60 pack-yr smoking history presents with a 3-cm right lower lobe mass. Prior to right pneumonectomy an $FEV_{1.0}$ of 1.5 liters is measured. Quantitative perfusion scintigraphy shows 330,000 counts in the right lung and 270,000 counts in the left lung (geometric means from anterior and posterior views). There is no evidence of a hilar defect, there is no fissure sign, and the costophrenic angle is not blunted. True statements concerning the preoperative assessment of this patient include:

20. The scintigraphic findings indicate that the tumor is resectable.
21. The scintigraphic findings favor a particular type of tumor histology.
22. Differential bronchospirometry with temporary catheter occlusion of the pulmonary arteries would provide accurate information concerning this patient's operability.
23. The postoperative $FEV_{1.0}$ is predicted by multiplying the measured preoperative $FEV_{1.0}$ by the ratio of total pulmonary counts to the counts in the left lung.
24. Based on the $FEV_{1.0}$ and perfusion distribution, this patient will probably suffer from chronic ventilatory insufficiency after pneumonectomy.

True statements concerning the mechanisms of ^{67}Ga uptake in pulmonary disease include:

25. The gallium ion is similar to the ferric ion in atomic charge and radius.
26. Gallium-67 localizes in pulmonary tissues primarily within the first 6 hr after administration.
27. Gallium-67 uptake at sites of inflammation is almost always due to the presence of lactoferrin-containing polymorphonuclear leukocytes.
28. The primary serum transport protein for ^{67}Ga is albumin.
29. Large extracellular fluid compartments and increased capillary permeability are both important factors contributing to the localization of ^{67}Ga.

True statements regarding technical aspects of ^{67}Ga scintigraphy of the chest include:

30. Sensitivity for detection of malignant pulmonary lesions falls when the size of the lesions is less than 1.5 cm.
31. Twenty-four-hour images are optimal for quantitative assessments of pulmonary disease activity.
32. Factors improving sensitivity of ^{67}Ga imaging for tumor screening include *all* of the following: triple peak acquisition, 72-hr imaging, 10-mCi (370-MBq) dose, and tomography.
33. Bronchoscopy within the 24-hr period prior to ^{67}Ga administration frequently causes false-positive scintigrams.
34. Gallium-67 scans are less sensitive for detection of sites of pulmonary neoplasia occurring near the mediastinum than those involving peripheral lung.

True statements regarding the use of ^{67}Ga scintigraphy in evaluation of patients with lung cancer include:

35. Gallium scintigraphy is positive in 85%-95% of patients with carcinoma of the lung.
36. Chest radiography, either alone or in combination with laminography or computed tomography, is the procedure of choice in lung cancer screening.
37. If a peripheral, primary lung cancer localizes gallium but the mediastinum is free of uptake, there is still better than an 80% likelihood that the mediastinal lymph nodes will be positive by mediastinoscopy.
38. Uptake of ^{67}Ga by primary lung cancers is correlated with the frequency of metastasis and survival.
39. If the primary tumor accumulates ^{67}Ga, the likelihood that an extrapulmonary focus of gallium uptake in a metastasis is less than 70%.

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versibility of cardiac wall-motion abnormalities predicted by positron tomography. *N Engl J Med* 1986;314:884–888.
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SELF-STUDY TEST
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True statements concerning hemoptysis include:

40. The major cause is bronchial inflammatory disease (chronic bronchitis or bronchiectasis).
41. It is rarely caused by carcinoma metastatic to lung.
42. The site of bleeding can be detected noninvasively by scintigraphy with either ^{99m}Tc sulfur colloid or ^{99m}Tc-labeled red blood cells.
43. Scintigrams in patients with hemoptysis usually show abnormal pulmonary activity within the first hour after injection of the radiopharmaceutical.
44. A bleeding rate of at least 100 ml/day is needed for localization of bleeding sites by scintigraphy.

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ANSWERS

ITEMS 1-4: Pulmonary Lymphangitic Carcinomatosis

ANSWERS: 1, T; 2, F; 3, F; 4, T

The ventilation images in Figure 10 are normal; the perfusion images show many small and medium-size defects scattered throughout both lungs. Many of the defects appear to outline bronchopulmonary segments. This scintigraphic pattern is unusual for acute pulmonary embolism and has been described in patients with cancer who have autopsy evidence of tumor microembolism and lymphangitic carcinomatosis. The patient shown here had a history of metastatic rectal carcinoma with diffuse interstitial infiltrates. No pulmonary emboli were found at angiography.

Pulmonary lymphangitic carcinomatosis is usually caused by tumor microemboli with subsequent spread of tumor to the pulmonary parenchyma and lymphatics. The cause of the characteristic pattern of perfusion defects in which the perfusion abnormalities appear to outline the segments ("contour mapping") is controversial. Some investigators believe the findings are due entirely to small tumor microemboli that lodge in the smaller peripheral vessels with sparing of the larger, more central segmental and subsegmental arteries. Others hold that there must be interstitial or parenchymal disease in addition to the pulmonary microemboli.

A normal chest radiograph is seen in approximately 20% of patients with lymphangitic carcinomatosis. Other causes of similar perfusion abnormalities include pulmonary vasculitis, primary pulmonary hypertension, and nonthrombotic emboli (fat, oil, or septic).

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ITEMS 5-9: Distribution of Pulmonary Ventilation and Perfusion

ANSWERS: 5, T; 6, F; 7, T; 8, F; 9, F

In upright subjects, there is increasing ventilation from the apex to the base of the lung. Similarly, dependent lung regions ventilate best in supine patients. This dependence on gravity is mediated by the effect of lung weight on the size of alveoli at end-expiration. The smaller distending intrapleural pressure in the dependent lung zones results in smaller alveoli at end-expiration and a larger change in alveolar volume with inspiration. Thus, airflow is lowest in the apical portion of an upright patient's lung. Gravity causes increasing air and blood flow from apex to base in upright individuals, but because the bloodflow gradient is steeper than the airflow gradient, the ratio of ventilation to perfusion decreases. The effects of gravity are modified by the local influences of airways resistance and alveolar compliance. More compliant alveoli generate a smaller recoil force to empty the alveolus of gas and, hence, are slower to clear their content of xenon during washout. Optimum gas exchange takes place when the flow of air and blood is matched. In obstructive pulmonary disease, alveolar hypoxia causes precapillary vasoconstriction to reduce blood flow to poorly ventilated lung regions. This is a protective mechanism, which tends to compensate for reduced airflow by reducing blood flow, thereby improving regional gas exchange.

References

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ITEMS 10-14: Pathologic Conditions Affecting Pulmonary Function

ANSWERS: 10, T; 11, F; 12, T; 13, F; 14, F

Three significant respiratory events follow embolic obstruction of pulmonary arteries: (1) addition of a large alveolar dead space; (2) pneumoconstriction; and (3) loss of alveolar surfactant. Pneumoconstriction involves the terminal airways and is caused by several factors. Reduction in the carbon dioxide tension in the embolized lung causes constriction that can be overcome by deep inhalation. In addition, humoral agents, such as serotonin and histamine, which presumably are released from platelets adhering to the embolus may also promote pneumo-

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and complex glycoproteins. *Proc Natl Acad Sci USA* 1982;78:4540–4544.
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constriction. Evidence for pneumoconstriction is rarely seen clinically on xenon ventilation images in patients with pulmonary embolism, and is uncommon even in experimental studies.

Pulmonary infarction is an uncommon complication of pulmonary embolism for several reasons. First, the lung is supplied with three sources of oxygen: pulmonary arterial blood, bronchial arterial blood, and the airways. Experimentally, compromise of at least two of the three sources is necessary to promote infarction. Second, the total occlusion of a vessel by an embolus is uncommon. In the great majority of instances some blood flows around the embolus and reaches the peripheral zones of the affected lung region. Clinically, infarction is more often seen with peripheral, rather than with central, embolization and in patients with underlying heart disease. Frank infarction, which is rare, must be distinguished from transient radiographic opacities, which are common, and are most likely due to hemorrhage associated with embolism.

Alveolar hypoxia is not generally associated with pulmonary embolization. The limitation of blood flow in the face of relatively minor effects on airflow tends to keep alveolar oxygen tension high and carbon dioxide tension low. In obstructive pulmonary disease, where alveolar hypoxia is common, precapillary sphincters react by constricting, rather than dilating, as is the response in peripheral tissues. This constriction reduces the flow of blood past poorly oxygenated alveoli and protects against shunting of large amounts of venous blood into the systemic circulation.

Airway collapse generally occurs where there is disruption of the surrounding lung by destructive alveolar processes. This is one of the causes of airway compromise in chronic obstructive pulmonary disease. Restrictive lung disease, on the other hand, is characterized by increased amounts of collagen and elastin in the alveolar walls. This tends to increase the elastic recoil of the lungs and keep the airways open.

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ITEMS 15-19: Evaluation of Regional Ventilation with ^{133}Xe

ANSWERS: 15, T; 16, T; 17, F; 18, T; 19, T

Clearly, the factors responsible for ventilatory compromise are not affected by the quantity of tracer gas used in xenon studies. Tracer concentration and chest wall thickness influence the number of counts detected by the camera, but they do not affect the kinetics of tracer elimination from the lung. Total lung volume, respiratory depth, and breathing frequency may affect the global rate of tracer clearance, but they have no effect on the relative rates of clearance in individual lung zones. Regional kinetics are influenced by both airway and alveolar morphology. Structural changes may affect airways resistance or alveolar compliance, which are two important factors in xenon clearance time, because they strongly influence local lung volume and airflow rates. The regional flow per unit lung volume is inversely related to clearance time.

References

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ITEMS 20-24: Preoperative Perfusion Scintigraphy in Bronchogenic Carcinoma

ANSWERS: 20, F; 21, F; 22, T; 23, F; 24, T

Despite early reports indicating that the size of perfusion abnormalities could help determine resectability, subsequent studies have shown that perfusion imaging criteria are unreliable for evaluating the extent of hilar and mediastinal involvement, which is the primary determinant of resectability. Chest radiography, laminography, and computed tomography are much more reliable in assessing resectability. The presence of pleural fluid is often considered a contraindication for pneumonectomy, but the perfusion scan is much less sensitive in detecting pleural effusion than chest radiography. Scintigraphic procedures do not yield patterns that are predictive of specific tumor histology. Differential bronchospirometry and temporary arterial occlusion were used as the "gold standards" that validated the accuracy of differential scintigraphic assessments. They are the most direct and accurate means of determining differential function, but they are rarely used today because of the simplicity of noninvasive, quantitative scintigraphic methods.

In this patient, the differential perfusion scan reveals that the left lung receives 45% of total lung blood flow (270,000 left lung counts ÷ 600,000 total lung counts). The predicted postoperative $FEV_{1.0}$ may be calculated as: 45% × 1500 ml = 675 ml. This is less than 800 ml, the $FEV_{1.0}$ threshold below which the risk of chronic ventilatory insufficiency is unacceptably high.

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ITEMS 25-29: Mechanisms of Pulmonary ^{67}Ga Localization

ANSWERS: 25, T; 26, T; 27, F; 28, F; 29, T

Gallium is a Group IIIb transition metal. The Ga^{+3} ion resembles the ferric ion in atomic radius and charge, and in the types of inorganic complexes these two ions form. A major difference between gallium and iron is the inability of gallium to be reduced in vivo. Whereas ferric ion is easily reduced to the ferrous state and interacts with a variety of intracellular proteins, gallium remains bound to transport proteins. The fraction not bound to protein is either cleared by the kidney or passes into extravascular spaces. Most of the accumulation in the extravascular compartment occurs when the intravascular-extravascular gradient is the highest (i.e., during the first 6 hr after administration). The degree of accumulation at a site of inflammation or in tumors is significantly affected by the size of the extravascular fluid space and the degree of vascular permeability.

Leukocytes are rich in lactoferrin, which binds the majority of ^{67}Ga taken up by the leukocytes. However, it is unlikely that this is the main explanation for localization in inflammatory sites. Neutrophils are clearly not essential for uptake, because ^{67}Ga localization can be seen in patients without circulating neutrophils. Furthermore, analysis of abscess contents, either sterile or bacterial in origin, reveals that most of the ^{67}Ga is in the noncellular fraction. Other mechanisms, such as increased capillary fluid exchange, increased extravascular fluid, bacterial uptake, and extracellular lactoferrin binding, are probably more important.

Although several serum proteins can bind ^{67}Ga, affinity

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chromatography and ultrafiltration studies of human serum demonstrate that virtually all of bound gallium is associated with transferrin.

ITEMS 30-34: Technical Aspects of ^{67}Ga Scintigraphy of the Chest

ANSWERS: 30, T; 31, F; 32, T; 33, F; 34, T

The sensitivity for scintigraphic detection of gallium-avid tumors and sites of inflammation is improved by factors that either increase the lesion photon density or the target-to-nontarget ratio. Photon flux is improved by increasing the administered activity or by maximizing the number of detected photons by using more than one ^{67}Ga photopeak. The target-to-nontarget ratio is improved by tomographic imaging, and by 48- to 72-hr delayed imaging, which takes advantage of physiologic clearance of background activity. Lesions smaller than 1.5 cm in diameter are difficult to detect, presumably because of smaller gallium content and smaller target-to-nontarget ratio. Scatter from neighboring structures reduces the detection rate of lesions near the mediastinum and those at the right lung base near the liver.

Although studies have failed to demonstrate increased gallium uptake after bronchoscopy, 50% of patients have diffuse patterns of gallium localization following lymphangiography with ethiodan (Lipiodol).

Gallium-67 pulmonary images performed at 24 hr demonstrate increased levels of nonspecific gallium uptake, presumably due to circulating bound tracer. Despite lower counting statistics, 48-hr images are used for quantitative studies because they provide a significant improvement in specificity for diagnosis of active pulmonary parenchymal disease.

Reference

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ITEMS 35-39: ^{67}Ga Scintigraphy in Lung Cancer

ANSWERS: 35, T; 36, T; 37, F; 38, T; 39, F

Gallium-67 scintigrams show a high frequency of positive studies in patients with carcinoma of the lung, ranging between 85% and 95% in several series. Although most tumor cell types show similar degrees of gallium localization, the highest detection rates are found with epidermoid carcinoma and the lowest rates with adenocarcinoma. In a large series reported by DeMeester et al, whole-body ^{67}Ga scintigraphy was found to be sufficient for initial screening for extrapulmonary metastatic disease in patients with lung cancer. If the primary tumor localizes gallium, there is more than a 90% probability that an extrapulmonary site of ^{67}Ga uptake represents a metastatic lesion; however, this generally should be confirmed by biopsy.

Radiographic procedures remain the method of choice for screening for primary lung cancer; they have been shown to be at least as sensitive as gallium imaging and they are both simple and cost-effective.

Although there is disagreement about the predictive value of the absence of mediastinal gallium uptake in gallium-avid primary lung tumors, there is agreement that the likelihood of mediastinal disease is less than 50% in such circumstances. Peripheral tumors are even less likely to be associated with mediastinal disease in this setting. Uptake of ^{67}Ga by primary lung cancers is correlated with the frequency of metastasis and patient survival as shown in reported series, where indices of ^{67}Ga uptake have been derived from scintigraphic and autoradiographic studies.

ITEMS 40-44: Hemoptysis

ANSWERS: 40, T; 41, T; 42, T; 43, F; 44, F

Chronic bronchitis and bronchiectasis are the major disorders causing hemoptysis in adults and children. In adults, hemoptysis is most closely related to common conditions, such as chronic bronchitis; in children, cystic fibrosis with bronchiesctasis is a more common cause. Hemoptysis also is frequently associated with primary lung carcinoma, but it is only rarely seen in association with metastatic disease to the lung from extrapulmonary primary tumors. Even when hemoptysis recurs in the setting of a chronic disease with which it is known to be associated, an attempt to localize the site of bleeding and evaluate its cause may be justified. Important lesions, such as primary carcinoma, frequently are overlooked in patients with chronic inflammatory bronchial diseases simply because the hemoptysis is assumed to be secondary to the preexisting disorder.

Hemoptysis can be detected scintigraphically with either ^{99m}Tc sulfur colloid or ^{99m}Tc-labeled red blood cells. Both agents have been used successfully, but many scans become positive only several hours after injection of the radiopharmaceutical. Because ^{99m}Tc sulfur colloid is extracted rapidly from the circulating blood, positive studies are less likely with this agent than with labeled red blood cells. Regardless of which agent is used, investigators have demonstrated that the site of bleeding can be visualized in only about 50% of patients. In patients with positive studies, however, estimated bleeding rates have been as low as 50 ml/day.

For further in-depth information, refer to the syllabus pages in Nuclear Medicine Self-Study I.