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# Detection of Extrapulmonary Tuberculosis with Gallium-67 Scan and Computed Tomography

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We evaluated 23 patients with extrapulmonary tuberculosis (TB) with  $^{67}\text{Ga}$  imaging to assess its usefulness in the diagnosis of this condition. We performed computed tomography (CT) in 17 patients to assess CT features of extrapulmonary TB in comparison with findings from  $^{67}\text{Ga}$  scans. Nineteen of 23 patients (83%) had positive findings on  $^{67}\text{Ga}$  scans. One of five patients with tuberculous mediastinal lymphadenopathy, two patients with cervical lymphadenitis and a patient with renal TB had negative  $^{67}\text{Ga}$  scans. It was observed that the detection of previously unrecognized primary foci of TB, without concomitant pulmonary TB, was possible using  $^{67}\text{Ga}$  imaging in five patients (22%). The  $^{67}\text{Ga}$  scan was relatively sensitive for the localization of extrapulmonary TB. It is suggested that the  $^{67}\text{Ga}$  scan could serve as a screening method, when followed by CT and ultrasonography, for the initial detection of occult tuberculous lesions, especially in patients with prolonged fever.

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**G**allium-67 is useful in the detection of active inflammatory lesions and certain tumors (1). It has been used widely in the evaluation of various pulmonary diseases including tuberculosis (TB) (2-7). Siemsen et al. (8) reported pulmonary uptake of radiogallium in 97% of patients with active TB. There have been, however, very few reports on the evaluation of extrapulmonary TB using the  $^{67}\text{Ga}$  scan (9,10). Thus, further exploration is needed to validate its clinical role in the diagnosis of extrapulmonary TB.

In the present study, we attempt to demonstrate the utility of  $^{67}\text{Ga}$  imaging for detecting extrapulmonary TB in patients with prolonged fever. We performed  $^{67}\text{Ga}$  scanning on all 23 patients and computed tomography (CT) on 17. The comparative roles of  $^{67}\text{Ga}$  and CT scanning in the diagnosis of extrapulmonary TB are discussed.

## MATERIALS AND METHODS

The study group consisted of 23 patients with histologically (biopsies in 18, bacilli culture in 3) or response-to-medication proven extrapulmonary TB. The age of the patients ranged from 22 to 67 yr, with a mean age of 42 yr. There were 13 males and 10 females. Fourteen patients had various sites of lymphadenopathy: three had peritonitis; three had spinal TB; two had intestinal TB; and one had renal TB. Concurrent active pulmonary TB was found in seven patients (32%) by a sputum culture and old tuberculous lung lesions in two patients on a chest radiography. Acquired immunodeficiency syndrome (AIDS), myelodysplastic syndrome and diabetes mellitus were identified in one patient each. Tuberculous pleural effusions were seen in two patients and pericardial effusion in one patient.

Each patient received 185 MBq (5 mCi) of gallium citrate intravenously. Scanning was performed with a 7500 Orbiter gamma camera (Siemens Medical Systems, Iselin, NJ) using a large field of view and a medium-energy parallel-hole collimator, with a 20% window centered on the 93, 185 and 300 keV photopeaks, at 24, 48, and 72 hr after injection of gallium citrate. Anterior and posterior views of the whole body were obtained as well as spot views of suspicious areas. Two radiologists were involved in the interpretation of the  $^{67}\text{Ga}$  images. Care was taken to differentiate physiologic gallium accumulations in the spine, sternum, ribs and colon from pathologic uptake by analyzing the pattern of distribution and temporal course.

Of the 23 patients, 17 (11 patients had tuberculous lymphadenopathy; three patients had spinal TB; two patients had tuberculous peritonitis; one patient had intestinal TB) also underwent CT to assess the extent of the abnormality. The CT scans were obtained on a GE CT/T 9800 scanner (General Electric Medical Systems, Milwaukee, WI). CT scans were obtained before and after the intravenous bolus administration of 100-150 ml of water-soluble contrast media (Rayvist, Schering; Conray, Mallinckrodt) with a contiguous 10 mm slice thickness and 10-mm interval. All abdominal CT scans were taken after oral ingestion of dilute methylglucamine diatrizoate (Gastrografin, Squibb). The CT images were analyzed for the attenuation, enhancement pattern and extent of lesions.

## RESULTS

### Sensitivity of the $^{67}\text{Ga}$ Scan

As shown in Table 1, the sensitivity of the  $^{67}\text{Ga}$  scan in detecting extrapulmonary TB was 83%. Nineteen of 23 patients showed positive accumulation of radiogallium.

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**TABLE 1**  
Comparative Results of <sup>67</sup>Ga and CT Scans in Extrapulmonary TB (n = 23)

Patient no.	Chief complaint	Site of TB	<sup>67</sup> Ga scan*	CT	Methods of confirmation	Remarks
1	Neck mass	Cervical L/N	Negative	NA	Biopsy	
2	Weight loss	Cervical L/N	Negative	NA	Biopsy	
3	Cough, Fever	Mediastinal L/N	Positive	Carinal L/N	Biopsy	
4	Fever	Mediastinal L/N	Negative	Hilar L/N	Biopsy	Leukopenia <sup>†</sup>
5	Weight loss	Mediastinal L/N	Positive	Mediastinal L/N	Biopsy	AIDS
6	Fever	Mediastinal L/N	Positive	NA	Biopsy	
7	Fever	Mediastinal L/N	Positive	Mediastinal L/N	Biopsy	Diabetes mellitus
8	Fever	Abdominal L/N	Positive	Multiple L/N	Operation	
9	Weight loss	Abdominal L/N	Positive	Multiple L/N	Biopsy	
10	Fever	Abdominal L/N	Positive	Mesenteric L/N	Operation	
11	Fever	Abdominal L/N	Positive	Multiple L/N	Biopsy	
12	Mass, Fever	Abdominal L/N	Positive	Mesenteric L/N	Operation	
13	Fever	Abdominal L/N	Positive	Multiple L/N	Biopsy	
14	Fever	Pelvic L/N	Positive	Obturator L/N	Operation	
15	Pain, Fever	Peritoneum	Positive	NA	Biopsy	
16	Fever	Peritoneum	Positive	Ascites	AFB culture	
17	Fever	Peritoneum	Positive	Ascites	Anti-TB therapy	
18	Back pain	Spine	Positive	Bony destruction	Operation	
19	Back pain	Spine	Positive	Bony destruction	Operation	
20	Fever	Spine	Positive	Bony destruction	Operation	
21	Diarrhea	Intestine	Positive	Wall thickening	AFB culture	Fistula
22	Fever	Intestine	Positive	NA	Anti-TB therapy	
23	Weight loss	Kidney	Negative	NA	AFB culture	

\* Overall positive rate of <sup>67</sup>Ga scan in extrapulmonary TB was 19/23 (83%).

<sup>†</sup> Leukopenia (leukocyte count:  $1.6 \times 10^9$ /liter) because of myelodysplastic syndrome.

L/N = lymph nodes and NA = not applicable.

One patient with myelodysplastic syndrome (Patient 4) had a negative <sup>67</sup>Ga scan but was shown to have tuberculous mediastinal lymphadenopathy by mediastinoscopic biopsy. He was the only patient with leukopenia (leukocyte count:  $1.6 \times 10^9$ /liter) in the present study. One patient with renal TB (Patient 23), who had a positive urine culture for acid-fast bacilli (AFB), had no discernible abnormality on 48- and 72-hr images of the <sup>67</sup>Ga scan. The patient data and results of the <sup>67</sup>Ga and CT scanning according to lesion location are summarized in Table 1.

#### Findings of the <sup>67</sup>Ga Scan and CT

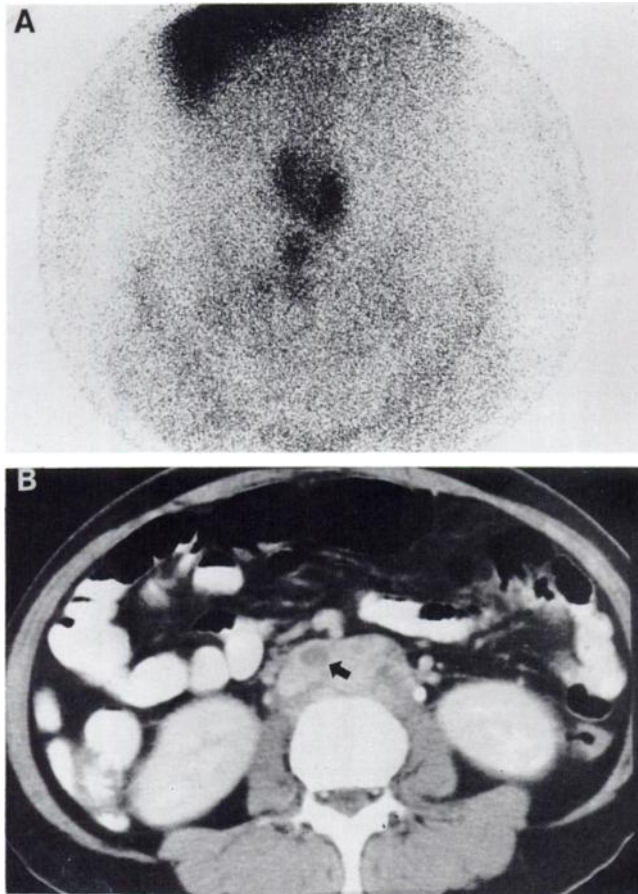
Gallium-67 scanning in extrapulmonary TB demonstrated focal or diffuse increased uptake which persisted at 72 hr after injection of gallium (Fig. 1A). The images obtained at 48 hr after injection were sufficient to localize the lesion in all except one case with intestinal TB which was detectable only on 72-hr image of the <sup>67</sup>Ga scan. Enlargement of lymph nodes with central low attenuation and rim enhancement at CT was the most common finding in four patients with tuberculous abdominal lymphadenopathy and four patients with mediastinal lymphadenitis (Fig. 1B). In three patients with spinal TB (Patients 18, 19, 20), <sup>67</sup>Ga images showed focal areas of increased radioactivity in the vertebrae, while CT scans revealed bone destruction in the vertebral body delineated by marginal sclerosis (Fig. 2).

#### Comparative Roles of the <sup>67</sup>Ga Scan and CT

Table 1 shows the order of diagnostic protocols employed to obtain the final diagnosis of extrapulmonary TB. In five patients (Patients 10, 11, 13, 14, 22), there were no apparent clinical manifestations when observed by conventional radiography (chest PA) and laboratory tests. One patient with unsuspected pelvic lymphadenitis (Patient 14) showed positive <sup>67</sup>Ga scan and also a subsequent CT exhibited presence of left pelvic lymphadenopathy (Fig. 3). The use of anti-tuberculous agents resulted in clinical improvement in all five.

In another patient with mesenteric lymphadenopathy (Patient 12), the <sup>67</sup>Ga scan showed a distinct radioactivity along the mesenteric root, and the CT scan revealed inhomogeneous, low-attenuation mesenteric lymph nodes (Fig. 4). Gallium-67 scans of three patients with tuberculous peritonitis (Patients 15, 16, 17) showed diffuse abnormal abdominal activity (Fig. 5A), although the CT scan failed to give specific information about active inflammation. In one patient with intestinal TB and colcutaneous fistula (Patient 21), the <sup>67</sup>Ga scan showed focal uptake along the fistulous tract and distal ileum (Fig. 5B).

On the basis of above results, CT seemed to be effective in delineating the anatomy and extent of lesions prior to biopsy, especially in lymphadenopathy of the mediastinum and abdomen. Rather specific diagnosis of extrapulmonary TB was made in eight patients (Patients 3, 4, 5, 7, 9,

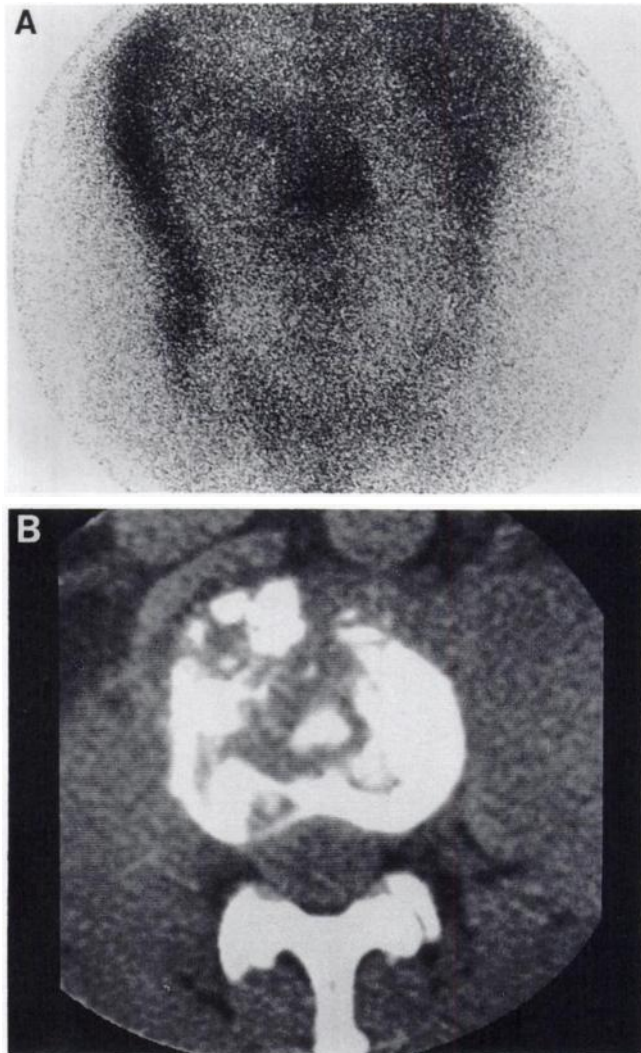


**FIGURE 1.** A 42-yr-old woman with fever (Patient 8) confirmed surgically as abdominal TB. (A) Gallium-67 scan taken at 48 hr after injection shows a focal area of increased radioactivity in the mid-abdominal region. (B) CT scan shows conglomerated multiple para-aortic lymph nodes with central low attenuation (arrow) and peripheral rim enhancement.

10, 12, 13) with lymphadenopathy, characterized by central low-attenuation and rim enhancement in CT (11-13). In contrast, in the five patients (Patients 10, 11, 13, 14, 22) of previously unlocalized extrapulmonary TB, it is clear that the  $^{67}\text{Ga}$  scan was a valuable screening method.

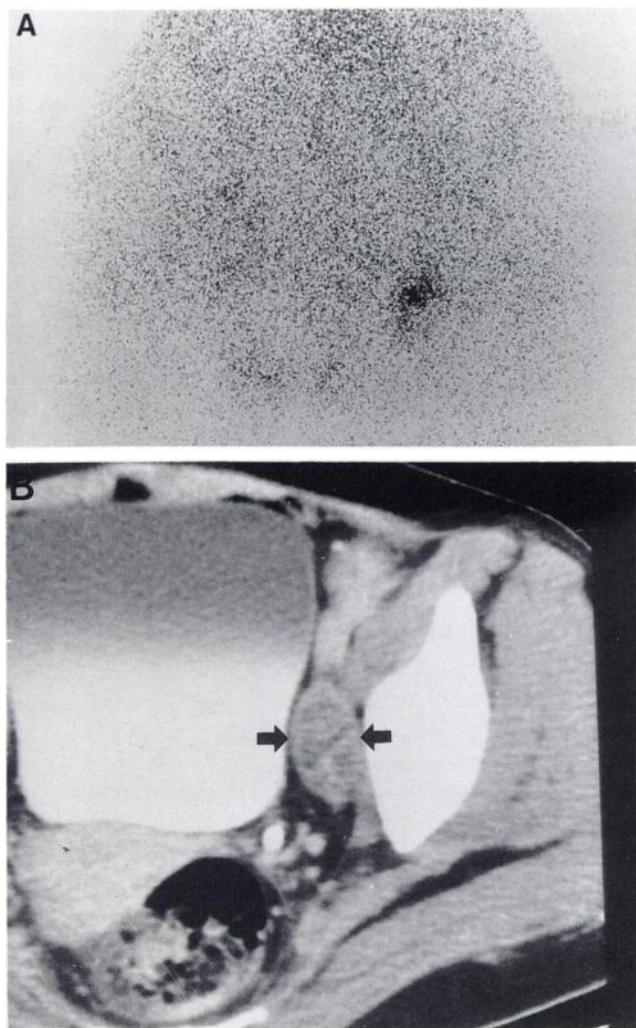
## DISCUSSION

Extrapulmonary TB (skeletal, mediastinal, peritoneal, renal TB and others) is often overlooked and its diagnosis is delayed because of nonspecific symptoms and frequent lack of concomitant pulmonary involvement (9,14-16). Radioactive gallium scanning was first introduced by Edwards and Hayes in patients with Hodgkin's disease (17). The  $^{67}\text{Ga}$  scan has been very useful in the diagnosis of certain malignant neoplasms, acute inflammatory disease, diffuse interstitial lung disease, sarcoidosis, and active TB (4-8). Since the initial observations, gallium has been widely used in the workup of patients with unexplainable prolonged fever or fever of unknown origin (FUO). It was demonstrated by Habibian et al. and Kissin and Williamson that a  $^{67}\text{Ga}$  scan in patients with FUO can show a high



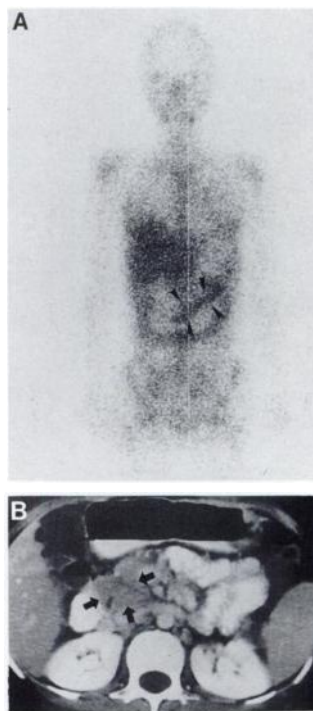
**FIGURE 2.** A 31-yr-old man with back pain (Patient 18) confirmed as spinal TB by spinal fusion surgery. (A) Gallium-67 scan taken 72 hr after injection shows a dense focal area of increased radioactivity at the lumbar region (L 1-2). (B) CT scan of the corresponding L-2 vertebra shows multifocal lytic bony destruction of the anterior vertebral body delineated by irregular sclerotic change.

diagnostic sensitivity (18,19). For detecting acute infections,  $^{111}\text{In}$ -WBC scanning is preferred, whereas  $^{67}\text{Ga}$  scan has higher sensitivity for diagnosis of chronic and granulomatous inflammation (20,21). A comparative study using  $^{111}\text{In}$ -WBCs and  $^{67}\text{Ga}$  scanning in tuberculous enteritis revealed a slight advantage of  $^{67}\text{Ga}$  scan over  $^{111}\text{In}$ -WBC scan (22). Palestro et al. concluded that while  $^{67}\text{Ga}$  scan is more useful for detecting TB and *Pneumocystis carinii* pneumonia, the  $^{111}\text{In}$ -WBC scan is superior to the  $^{67}\text{Ga}$  scan in the detection of other nonpulmonary infections in 101 patients with AIDS (23). With developments in other imaging modalities, including ultrasonography (US), CT and magnetic resonance imaging (MRI), the role of the  $^{67}\text{Ga}$  scan has changed considerably (24-26). McNeil et al., in a prospective study of patients with fever



**FIGURE 3.** A 45-yr-old woman with fever, weight loss and no localizing area of inflammation (Patient 14) confirmed surgically as TB. (A) Gallium-67 scan taken 24 hr after injection shows a focal area of the increased radioactivity in the left pelvic cavity. (B) Corresponding contrast-enhanced CT scan shows the left pelvic lymphadenopathy with internal inhomogeneous low density and peripheral enhancing rim (arrows).

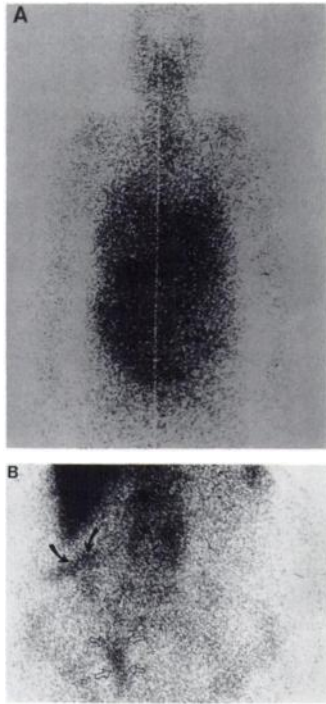
using receiver operating characteristic analysis, reported that CT, US and  $^{67}\text{Ga}$  scans have similar capabilities in detecting septic foci and that sensitivity can be increased by using any two of them (10). However, there have been few reports on the evaluation of extrapulmonary TB using the  $^{67}\text{Ga}$  scan. Our results showed a high sensitivity of the  $^{67}\text{Ga}$  scan in the detection of extrapulmonary TB. It is noteworthy that the sensitivity would have been 90% (19/21), if two patients with small sized (less than 2 cm in diameter) cervical lymphadenopathy (Patients 1 and 2) with negative  $^{67}\text{Ga}$  scans were excluded. One leukopenic patient with mediastinal TB and underlying myelodysplastic syndrome was negative on the  $^{67}\text{Ga}$  scan. This false-negative result may have been due in part to leukopenia (27), but the exact cause of the negative result was not determined.



**FIGURE 4.** A 42-yr-old man with fever and palpable abdominal mass (Patient 12) confirmed surgically as mesenteric TB. (A) Gallium-67 scan taken 48 hr after injection shows the increased radioactivity in the mid-abdomen along the mesenteric root (arrowheads). (B) Contrast-enhanced CT scan shows lymphadenopathy in the mesentery around the superior mesenteric vessels as multifocal inhomogeneous low-attenuation areas (arrows).

In addition to the detection of focal inflammatory lesions, the  $^{67}\text{Ga}$  scan may often contribute to an early diagnosis of unsuspected systemic disease (28). Another advantage of the  $^{67}\text{Ga}$  scan is that the whole body is evaluated at once; serendipitous findings in 12% of patients were reported on the  $^{67}\text{Ga}$  scan (10,28). One of the most important problems in the application of the  $^{67}\text{Ga}$  scan is its low specificity. Therefore, correlation with the CT scan and the biopsy of positive lesions on the  $^{67}\text{Ga}$  scan are mandatory to diagnose extrapulmonary TB. In the patient with extrapulmonary TB and underlying systemic disease, early detection of a primary focus is important to avoid delay in proper management. In recent years, the incidence of TB has actually been increasing in contrast to the steady decline of previous years (14,16,29). Recent reports have emphasized that TB may develop during the course of human immunodeficiency virus (HIV) infection before the development of other illnesses suggestive of AIDS (30). It has been observed that many extrapulmonary manifestations of TB developed in patients with AIDS (31).

On contrast-enhanced CT scans, tuberculous mediastinal and abdominal lymphadenopathy typically show lymph nodes with central low-attenuation and peripheral rim enhancement representing caseating necrosis and hyperemic granulation tissue, respectively (11-13). Typical



**FIGURE 5.** (A) A 53-yr-old woman with fever and progressive abdominal distension (Patient 16) confirmed as tuberculous peritonitis by AFB culture from ascitic fluid. Gallium-67 scan taken at 48 hr after injection shows increased homogeneous radioactivity in the whole abdomen. CT scan failed to give information about active inflammation. (B) A 31-yr-old woman with diarrhea (Patient 21) confirmed as intestinal TB. Colocutaneous fistula was present clinically. Gallium-67 scan taken 72 hr after injection shows hot uptake along the fistulous tract (curved arrows) and ileum (open arrows).

CT findings of tuberculous spondylitis are calcified paraspinal masses with thick, irregular rim and anterior vertebral body destruction (32).

In patients with FUO and no localizing symptoms, the  $^{67}\text{Ga}$  scan and other inflammatory imaging methods such as  $^{111}\text{In}$ -WBC (21,23),  $^{99\text{m}}\text{Tc}$ -HMPAO leukocyte (33,34), and  $^{111}\text{In}$ -labeled IgG scan (35,36) should be considered in the diagnostic workup before administering drugs that may mask the site of infection. Selective application of the  $^{67}\text{Ga}$  scan in unlocalized FUO as early as possible to detect a primary lesion and then CT (or US) for anatomical and pathological specificity are recommended. This can be followed by a biopsy or culture. It would be also appropriate to perform a  $^{67}\text{Ga}$  scan in patients with documented extrapulmonary TB as a follow-up procedure, as there are few other methods for determining disease activity like sputum AFB in pulmonary TB.

In conclusion, the  $^{67}\text{Ga}$  scan is sensitive in the localization of extrapulmonary TB, particularly in patients with suspected inflammatory lesions. The  $^{67}\text{Ga}$  scan may play an important role in the detection of occult tuberculous lesions, and CT can be helpful for more exact localization and specific diagnosis.

## ACKNOWLEDGMENTS

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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.

True statements concerning <sup>99m</sup>Tc DTPA aerosol inhalation studies include:

1. The normal effective pulmonary clearance half-time is approximately 3 hr.
2. The size of the aerosol droplets ranges from 2-4 μM in diameter.
3. The radiation dose to the lung is about the same as that for a typical <sup>133</sup>Xe ventilation study.
4. There normally is a substantial amount of focal, central airways deposition.
5. They must be performed before perfusion scintigraphy.

The pulmonary clearance of <sup>99m</sup>Tc DTPA aerosol is accelerated by which of the following conditions?

6. pulmonary embolism

7. cigarette smoking
8. adult respiratory distress syndrome
9. idiopathic pulmonary fibrosis
10. hyaline membrane disease

True statements concerning the pulmonary accumulation of radioiodinated propanediamine (HIPDM) include:

11. It is inhibited by oabain.
12. It is diminished in the presence of chlorpromazine.
13. It is saturable.
14. It is Na<sup>+</sup>/K<sup>+</sup> ATPase-dependent.
15. It is increased in the presence of propranolol.

## **SELF-STUDY TEST**

# **Pulmonary Medicine**

### **ANSWERS**

#### **ITEMS 1-5: <sup>99m</sup>TcDTPA Aerosol**

ANSWERS: 1, F; 2, F; 3, F; 4, F; 5, F

Several of these statements represent common misconceptions about radioaerosol scintigraphy. After inhalation, the aerosolized <sup>99m</sup>Tc activity clears from the lung by direct absorption into the bloodstream across the alveolar-capillary membrane with a normal biological half-time of approximately 1 hr. Thus, the overall effective half-time is slightly less than 1 hr, because of the simultaneous decay of <sup>99m</sup>Tc. This pulmonary clearance time can be altered in the presence of various types of pulmonary pathology, as addressed in the next question. The relatively rapid pulmonary clearance of <sup>99m</sup>Tc assures that the radiation dose to the lung will be small. In fact, typical radiation exposure from a conventional preperfusion aerosol inhalation study is less than 100 mrad to the lungs, compared with several hundred millirads from a typical <sup>133</sup>Xe rebreathing ventilation study.

Current radioaerosol preparations achieve relatively uniform peripheral deposition of activity because the size of the aerosol particles generated by the nebulizer is in the submicronic range. Aerosol particle diameters are in the 0.5-0.8 micron range, rather than the 2-4 micron range. Aerosol generators that produce 2-4 micron radioaerosols yield substantial de-

grees of focal, central airways deposition, even in the presence of normal breathing or with only relatively mild central airflow turbulence. Although central deposition of submicronic radioaerosols may occur in patients with excessive bronchial secretions or those with active bronchospasm, only mild degrees of central deposition are seen in smokers and patients with mild to moderate degrees of obstructive airways disease. Thus, adequate peripheral deposition is obtained to permit accurate evaluation of ventilation-perfusion match and mismatch.

Radioaerosol studies with <sup>99m</sup>Tc DTPA can be performed either before or after the perfusion dose is administered. When the studies are performed prior to perfusion scanning, the radioaerosol nebulizer is loaded with approximately 30 mCi of activity. After several minutes of breathing the radioaerosol, approximately 750 μCi of activity is actually deposited in the lungs. This amount of activity would be insufficient to evaluate the distribution of ventilation if a usual dose (3-5 mCi) of <sup>99m</sup>Tc particles had already been given for perfusion scintigraphy. Consequently, if a post-perfusion aerosol inhalation study is desired, the administered activity of <sup>99m</sup>Tc particles should be reduced to no more than 1 mCi, and this should be followed by radioaerosol inhalation from a nebulizer

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