Gallium-67 Scans of the Chest in Patients with Acquired Immunodeficiency Syndrome

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Eighty-six [^{67}Ga]citrate chest scans were performed in 71 adult patients with the acquired immunodeficiency syndrome. Forty-five of these patients also had Kaposi's sarcoma. Only 29 of 57 abnormal scans were correlated with abnormal chest radiographs. Chest radiographs were negative for 27 scans and unavailable for one. Several scan patterns were seen. Diffusely increased lung uptake was seen most commonly with *Pneumocystis carinii* pneumonia, but also other infections and noninfectious inflammatory conditions. Focal uptake corresponding to regional lymph node groups occurred most often with *Mycobacterium avium-intracellulare* but also with lymphoma. Localized intrapulmonary uptake was seen in bacterial pneumonias. Perihilar activity occurred in two cases. When chest radiographs were abnormal and ^{67}Ga scans negative, the most common diagnosis was pulmonary Kaposi's sarcoma.

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Patients with the acquired immunodeficiency syndrome (AIDS) present with a variety of infections. The most common of these is *Pneumocystis carinii* pneumonia (PCP); candida esophagitis, cytomegalovirus (CMV), cryptococcus, herpes simplex, toxoplasmosis, *Mycobacterium avium-intracellulare* (MAI), and other infections occur with less frequency (*14*). Symptoms may be subtle and protean (*5*) and conventional diagnostic approaches unhelpful (*5,6*). In addition those AIDS patients with Kaposi's sarcoma (KS), of which there is an increased incidence in AIDS, may have fever or respiratory complaints. Patients with KS may have pulmonary involvement by KS with or without superimposed infection (*2*). It is generally believed that the early diagnosis of infection and institution of appropriate therapy may improve the clinical outcome in AIDS patients. The role of noninvasive testing such as pulmonary function tests (*7*), arterial blood gases (*8*), chest radiographs (*9*), and gallium scanning (*6,8,10*) in pulmonary infections have been examined primarily vis a vis PCP. Fiberoptic bronchoscopic biopsy, bronchial brushings or washings, or even open lung biopsy may be necessary to make a specific diagnosis (*8,11*).

We reviewed our experience with gallium scanning in patients suspected of having pulmonary complications of AIDS to assess the value of gallium scan results not only in PCP, but also in other opportunistic infections and neoplasms which occur in this population.

PATIENTS AND METHODS

Eighty-six gallium-67 (^{67}Ga) citrate scans of the chest were performed on 71 patients suspected of having AIDS presenting with fever and/or respiratory symptoms. The scans represent consecutive referrals over a 20-mo period from a group of clinicians who see the majority of AIDS and KS patients in our institution. Seventy patients were homosexual males. One was a woman with Von Willebrand's disease who had received multiple cryoprecipitate transfusions. There were no intravenous drug abusers. The mean age was 34 yr old (range 25–54 yr old). Forty-five of these patients had a diagnosis of KS.

Gallium scans were performed 48–96 hr after the intravenous administration of 5 mCi (185 MBq) of [^{67}Ga]citrate using a large field-of-view camera fitted with a medium-energy collimator and using 20% energy windows set at 93, 184, and 296 keV photopeaks. Anterior and posterior views of the chest

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TABLE 1
Final Diagnoses Based on Clinical Outcome

Diagnostic basis	No. of cases	Final diagnosis	Finding/outcome
Physical examination	1	Herpes zoster	Skin lesions
Radiographic examination	4	Disseminated extrapulmonary Kaposi's sarcoma	Adenopathy on CT Submucosal lesions on small bowel series
	1	Candidiasis	Plaques on esophagram (positive blood cultures)
	1	Colitis	Barium enema
Response to medical therapy	14	PCP	Treated with pentamidine, trimethoprim-sulfamethoxazole
	1	Herpes simplex	Treated with acyclovir
No source found	2	Spontaneous resolution of symptoms	
	1	Negative cultures; no source found	

were obtained for a total of 500,000 counts per view. Whenever possible, views of the abdomen and pelvis were also obtained.

Activity in the lungs was considered increased when it exceeded activity in the adjacent chest wall soft tissues. Abnormal accumulation was characterized as diffuse, localized and intrapulmonary, focal and corresponding to a regional lymph node group(s), or perihilar.

The gallium scans were compared retrospectively with chest radiographs. All chest radiographs were obtained within 1 wk of the ^{67}Ga injection and most within 3 days. Final diagnosis was based on results of biopsy and/or culture (61 scans) or clinical outcome (25 scans) (Table 1).

RESULTS

Fifty-seven of 86 scans demonstrated abnormalities (Table 2). In 29 of these scans the abnormal radiogallium accumulation and the chest radiograph abnormality were congruent in distribution. Twenty-seven scans were abnormal without corresponding chest radiograph abnormalities. For one positive scan there was no available concurrent chest radiograph.

Of the 29 negative gallium scans, chest radiographs were normal in 20 and abnormal in eight. In one case, no radiograph was available.

Positive Chest Gallium Scans

Forty of the 57 abnormal gallium scans showed a diffuse pattern of increased lung uptake. The most common infection associated with this diffuse pattern (29 cases) was *Pneumocystis carinii* pneumonia (PCP) (Fig. 1). Only 15 of these scans with abnormalities due to PCP had positive correlative chest radiographs. In one of these patients, cytomegalovirus (CMV) and KS were documented along with PCP on lung biopsy. In another, the scan was initially read as negative, but retrospective evaluation suggested very faint diffuse accumulation and transbronchial biopsy demonstrated PCP.

Eleven other scans showed diffuse uptake. Of these, three patients had evidence of CMV pneumonitis: in one cytologic analysis of bronchial washings demonstrated CMV, in the second rising viral titers were

TABLE 2
Positive Gallium Scans by Diagnosis and Chest Radiograph Findings

Gallium uptake pattern	Diagnosis	Radiograph +	Radiograph −	Radiograph not available
Diffuse	PCP	15	13	1
	CMV	2	1	
	CMV & Cryptococcus	2		
	Chronic inflammation, fibrosis	1	1	
	?Toxoplasmosis	1	1	
	Bleomycin toxicity	1		
	Histoplasmosis	1		
Perihilar uptake	PCP		1	
	Legionella		1	
Localized, intrapulmonary	Bacterial pneumonia	5		
Focal	MAI	1	8	
	Lymphoma		1	
		29	27	1

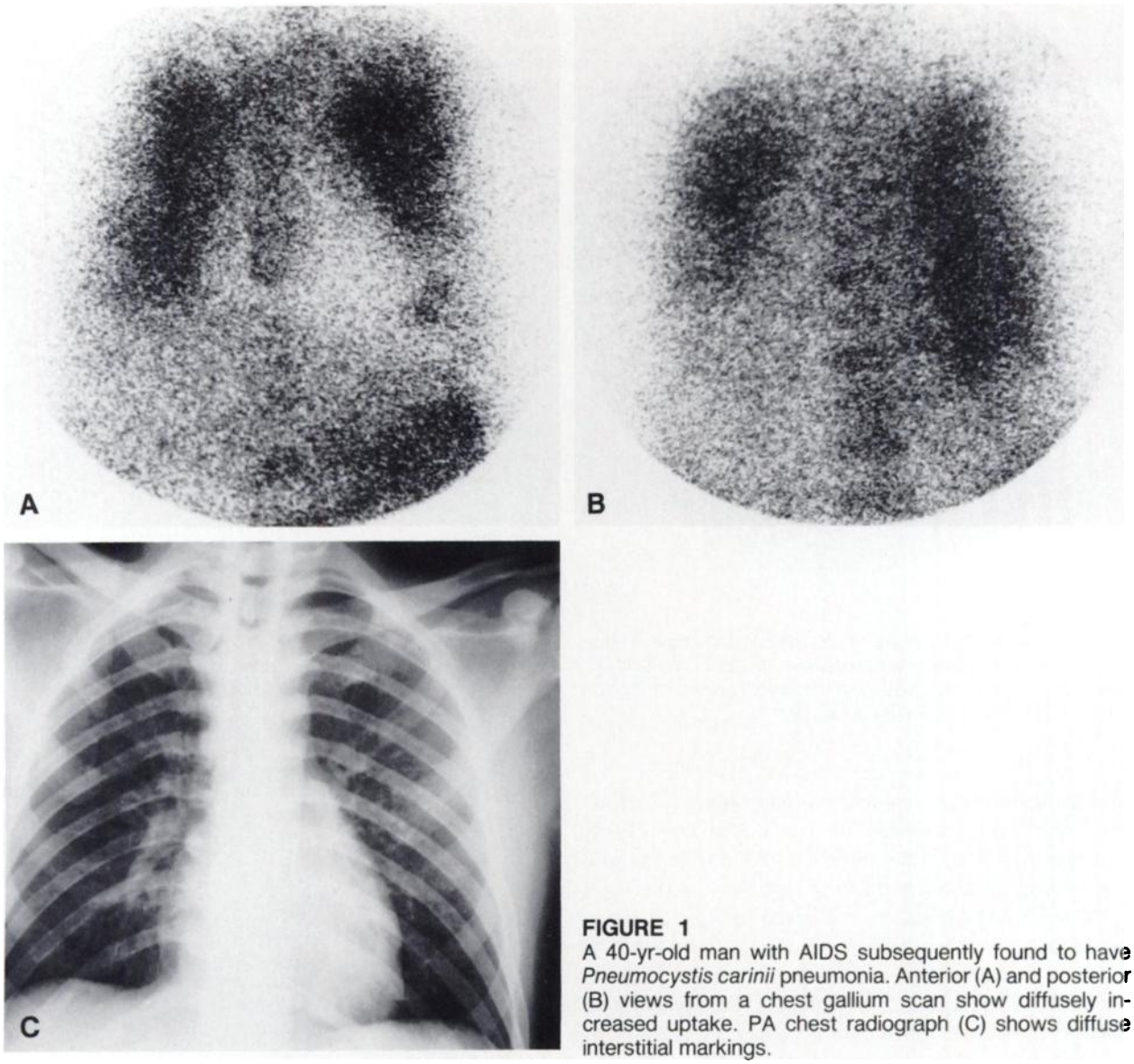

FIGURE 1
A 40-yr-old man with AIDS subsequently found to have *Pneumocystis carinii* pneumonia. Anterior (A) and posterior (B) views from a chest gallium scan show diffusely increased uptake. PA chest radiograph (C) shows diffuse interstitial markings.

found, and in the third transbronchial biopsy showed CMV pneumonitis. Two of three chest radiographs in these cases of CMV were positive. In two other patients with positive chest radiographs concurrent CMV and cryptococcus infections were documented on transbronchial biopsies. In another patient with a positive chest radiograph, biopsy revealed nonspecific chronic inflammation with fibrosis. A second patient showed interstitial fibrosis on biopsy; chest radiograph was normal. In two other patients with evidence of extrapulmonary toxoplasmosis and diffuse uptake on scan, no definite etiology could be identified in the lungs; one patient had increased interstitial markings on a chest radiograph and known central nervous system toxoplasmosis; in the other in whom chest radiographs were negative, elevated titers to toxoplasmosis were documented. In a single patient with extrapulmonary KS, chest radiograph revealed diffuse interstitial infiltrates. Transbronchial biopsy suggested bleomycin toxicity but no evidence of pulmonary KS. Finally, the patient with Von Willebrand's disease showed faint diffuse uptake on scan and minimally increased interstitial markings on chest film. Disseminated histoplasmosis was documented by blood cultures but lung biopsy was not performed because of the patient's bleeding diathesis.

In two patients a perihilar, but intrapulmonary distribution of increased ^{67}Ga uptake was seen (Fig. 2). Radiographs were normal in both patients. One was due to PCP diagnosed on bronchoscopic biopsy; the other to legionella.

In five scans, gallium accumulation was localized and intrapulmonary (Fig. 3). A congruent radiographic abnormality was present in all five. In each of these cases, bacterial pneumonia, either *Klebsiella spp.* or *Staphylococcus aureus* was found in sputum, bronchial washings, or open lung biopsy. One of these patients

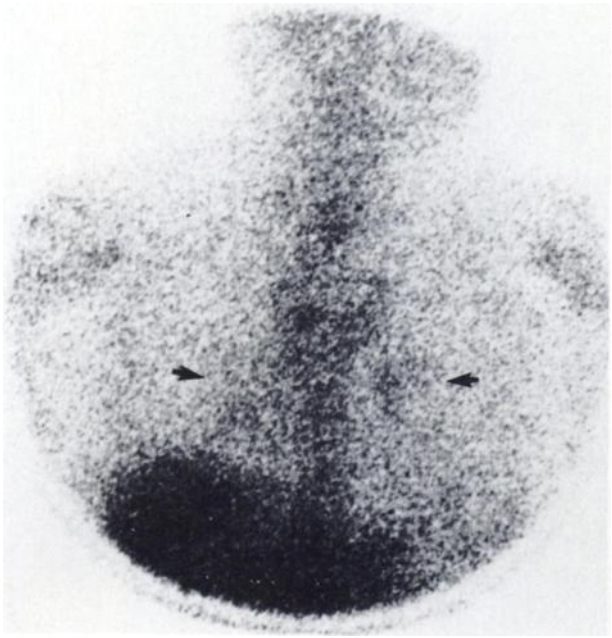

FIGURE 2
53-yr-old patient with AIDS, PCP, and normal chest radiographs. Anterior gallium scan shows bilateral perihilar uptake (arrows) less discrete than usually seen in association with lymph node uptake (see Fig. 3).

also had radiographic evidence of pulmonary KS. However, the KS appreciated on plain film was clearly distinguishable from the patient's pneumonia and did not correspond in location to the gallium uptake.

Of ten scans with abnormal focal gallium accumulation (Fig. 4), nine were seen in association with *Mycobacterium avium-intracellulare*. The foci of uptake occurred in parahilar, mediastinal, supraclavicular, and/or cervical locations. In only one case did a chest radiograph suggest the presence of lymphadenopathy. MAI infections were documented by lymph node biopsy in six cases and bone marrow and/or liver biopsy in three. Focal uptake on gallium scan in the supraclavicular region was also seen in one patient with lymphoma.

Negative Chest Gallium Scans

Twenty-nine chest gallium scans were negative. Of these, eight had positive correlative radiographs (Table 3). All eight of these patients had documented extrapulmonary KS. In five, lung biopsies showed pulmonary KS, but no infection. The chest radiograph presentation in these five was variable: nodules in two, diffuse interstitial infiltrates in two, and both nodules and interstitial infiltrate in one (Fig. 5).

In two additional patients the chest radiograph showed mildly increased interstitial markings: one patient with biopsy proven CMV pneumonitis and another with disseminated herpes. In the eighth patient, chest radiograph revealed both increased interstitial markings and consolidation. Biopsy showed acute and chronic inflammation but no organisms. The patient had a history of bleomycin therapy.

In 20 patients with negative gallium scans there were negative correlative chest films. For one negative scan no chest radiograph was available (Table 4). An extra-

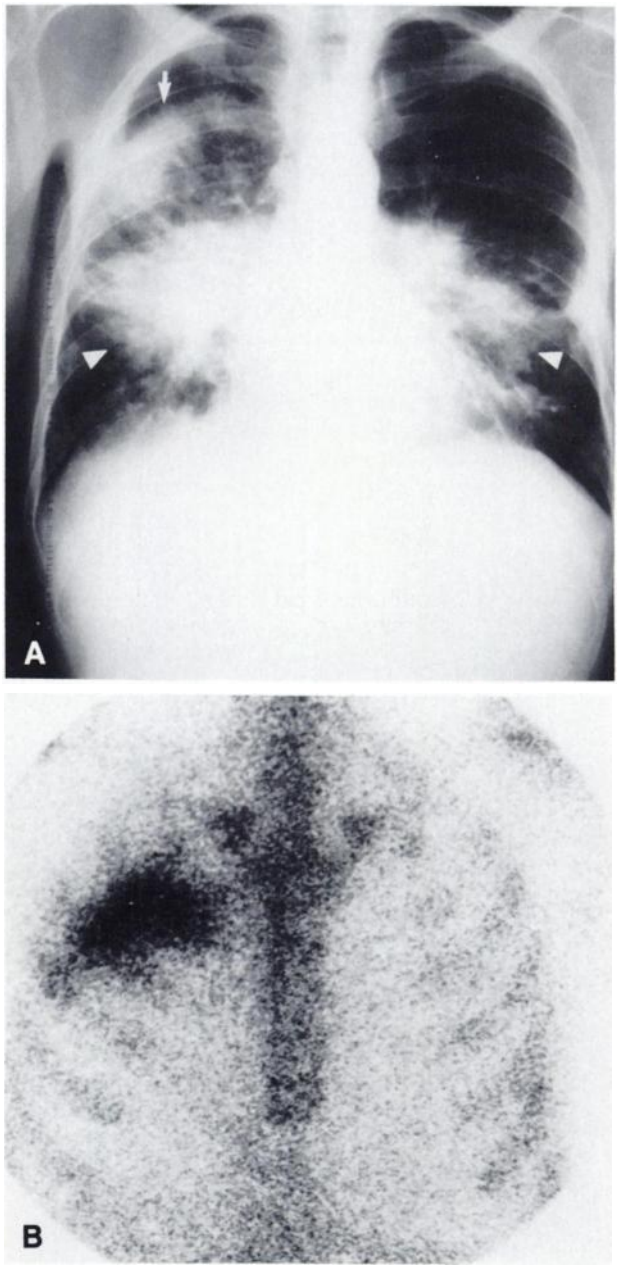

FIGURE 3
42-yr-old man with known pulmonary Kaposi's sarcoma (KS) and new onset of fever. PA chest radiograph (A) shows perihilar densities (arrowheads), which had been present for several months and were found on biopsy to be pulmonary KS. A new right upper lobe infiltrate is also seen (arrow). Anterior (B) view from a gallium scan shows accumulation of radiogallium in a distribution corresponding to the new infiltrate. Open lung biopsy of this infiltrate showed *Klebsiella* pneumonia.

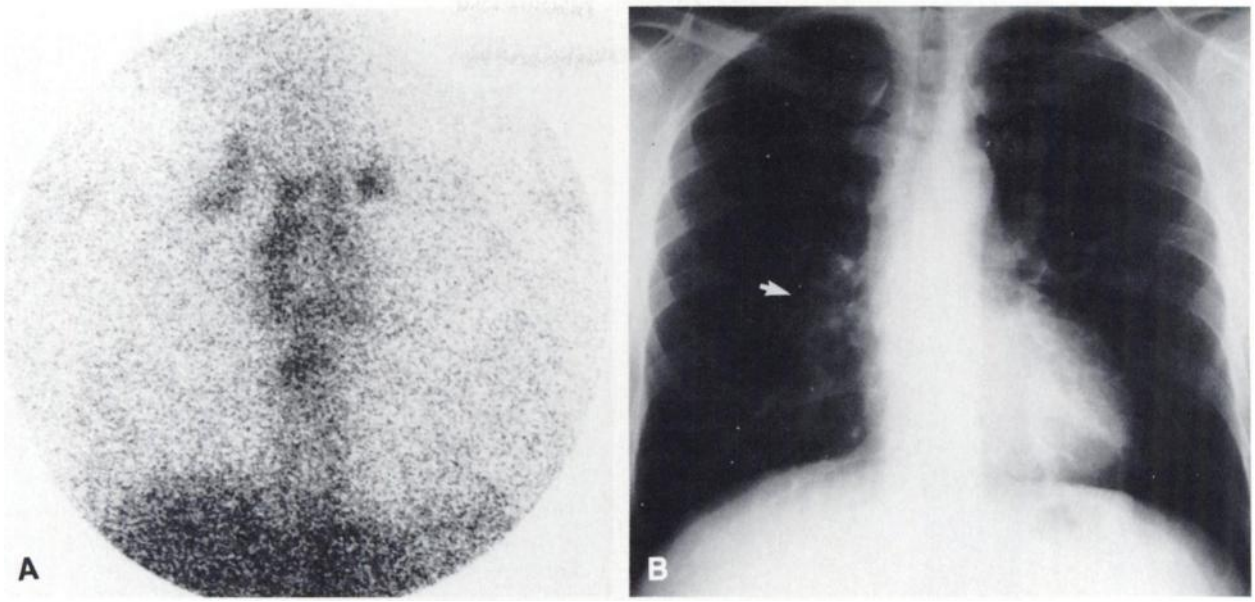

FIGURE 4
29-yr-old man with AIDS and biopsy proven *Mycobacterium avium-intracellulare* lymphadenitis. Anterior chest gallium scan (A) with focal gallium accumulation in supraclavicular, paratracheal and mediastinal or parahilar lymph nodes. PA chest film (B) with subtle hilar lymphadenopathy (arrow).

thoracic source of fever could be identified in all but three of these cases. In six, fever was ascribed to extrapulmonary KS. Four others had colitis or enteritis. Four had documented CNS infections including toxoplasmosis, histoplasmosis, CMV and cryptococcus. Single cases of disseminated candidiasis, herpes simplex, and herpes zoster occurred. One patient had streptococcal pharyngitis. In three patients, the cause of the symptoms remained unidentified.

Abdominal and Pelvic Findings

Attempts were made to scan the abdomen and pelvis whenever possible. However, because the patients were primarily referred for evaluation of pulmonary symptoms or findings, they frequently were unwilling to undergo these additional views. Of the 23 abdominal-pelvic scans obtained, 15 were negative. Two showed focal activity in the midline consistent with para-aortic lymphadenopathy. Both occurred in patients with MAI. Four scans suggested diffusely increased bowel uptake. In one case this was associated with proven bacterial enteritis. In two, increased gastric uptake was noted. Endoscopic biopsy of gastric mucosa in one of these patients failed to reveal an abnormality.

TABLE 3
Negative Gallium Scans with Positive Chest Radiographs by Diagnosis

Pulmonary KS	5
CMV	1
Disseminated herpes	1
Inflammation (?Bleomycin toxicity)	1
	8

DISCUSSION

A high incidence of *Pneumocystis carinii* pneumonia in AIDS patients has been identified consistently in studies of the AIDS population (*1,2,12*). PCP was the single most common infection in the series reported here. Sensitivity for PCP infections on gallium scans was high (29 of 30 were initially read as positive) and similar to the findings of Barron and others who reported >90% sensitivity over all scans regardless of chest radiograph findings and 86% sensitivity with negative chest radiographs.

In our series the overall specificity of a positive gallium scan for PCP was 51%. This is lower than the overall specificity reported by Barron and co-workers (74%) and may reflect the use of gallium scanning in our institution very early in the evaluation of a symptomatic AIDS patient.

More selective criteria for evaluating gallium scans in the setting of AIDS may increase the specificity for PCP. When only a diffuse pattern is considered, the specificity in our series increased to 83% for PCP. Coleman and others found that utilization of a grading system based on intensity of uptake increased the specificity of gallium scanning for PCP to greater that 90% (*8*). The specificity of positive gallium scans in Barron's series increased to 85% when chest radiographs were negative (*6*).

The diffuse pattern of gallium uptake occurred in entities other than PCP, particularly CMV or CMV in combination with cryptococcus (five cases). Mild to moderately positive scans with CMV infections have

been reported previously in both AIDS patients (*8*) and other immunosuppressed patients (*13*). Within our series there was also a false-negative scan in a patient with biopsy proven CMV pneumonitis.

Diffuse pulmonary uptake also was seen in patients with disseminated histoplasmosis and toxoplasmosis but without definite documentation of pulmonary involvement. This pattern also occurred in patients with nonspecific inflammatory changes in the lung such as bleomycin toxicity.

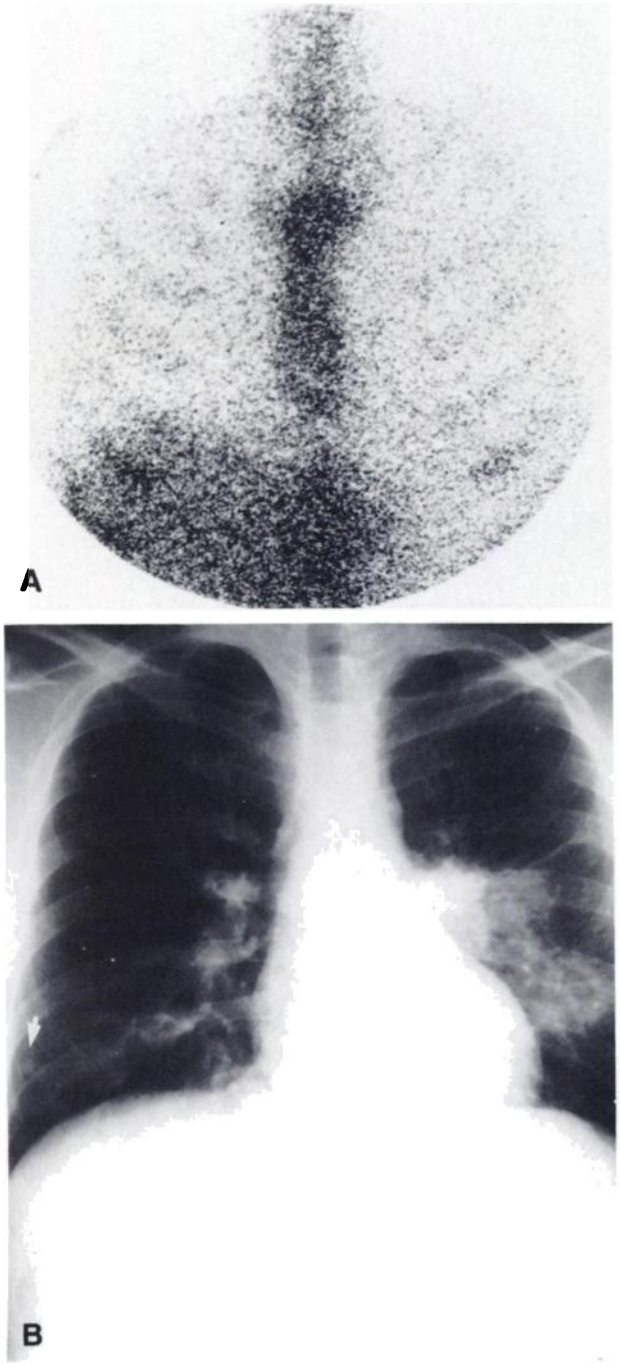

FIGURE 5
38-yr-old man with known extrapulmonary KS and new onset of dyspnea. Although gallium scan of the chest (A) is within normal limits, the PA chest film shows both interstitial infiltrates and nodules (arrow) found on biopsy to be pulmonary KS.

TABLE 4
Negative Gallium Scans with Negative Chest Radiographs by Diagnosis

Extrapulmonary KS	6
Colitis &/or enteritis	4
CNS infections	4
Disseminated candidiasis	1
Disseminated herpes simplex	1
Disseminated herpes zoster	1
Streptococcal pharyngitis	1
Unknown	3*
	21

* One without correlative chest radiograph.

Another pattern of gallium uptake seen was more localized intrapulmonary activity often corresponding in distribution to a pulmonary segment or lobe. In all scans with this finding, radiographs demonstrated an infiltrate in the same distribution. In each, a bacterial pneumonia was diagnosed.

The only case of bacterial pneumonia in this series that deviated from this pattern occurred in a patient with a negative chest radiograph, bilateral nonfocal perihilar gallium uptake, and legionella.

The positive predictive value of gallium accumulation in intrathoracic regional lymph nodes for MAI infections was 90%. Only one patient had lymphadenopathy appreciated on plain film. Because MAI is an extremely common infection in AIDS patients (*3,4*), these results indicate that the gallium finding of focal lymph nodes uptake in an AIDS patient should suggest MAI lymphadenitis. However, lymphoma may present with a similar scan pattern, making tissue diagnosis imperative.

A negative gallium scan with positive chest radiograph was often associated with pulmonary KS (five of eight patients) in this series. In an additional patient with pulmonary KS and bacterial pneumonia, gallium accumulation was confined to the segmental pneumonia. Often, the chest radiograph in AIDS patients with KS is nonspecific revealing bilateral interstitial infiltrates indistinguishable from opportunistic infection (*14*). The absence of accumulation of gallium in KS lesions, recognized in non-AIDS patients previously (*15*) suggests gallium scanning may be used to differentiate between pulmonary KS and infection in AIDS patients with KS.

Because of the high prevalence of PCP in the AIDS population and the high sensitivity of gallium for PCP, gallium scanning has been advocated for screening in symptomatic AIDS patients, especially when radiographs are negative (*6,8,10*). Our findings support this use of gallium (Fig. 6). However, the overall specificity

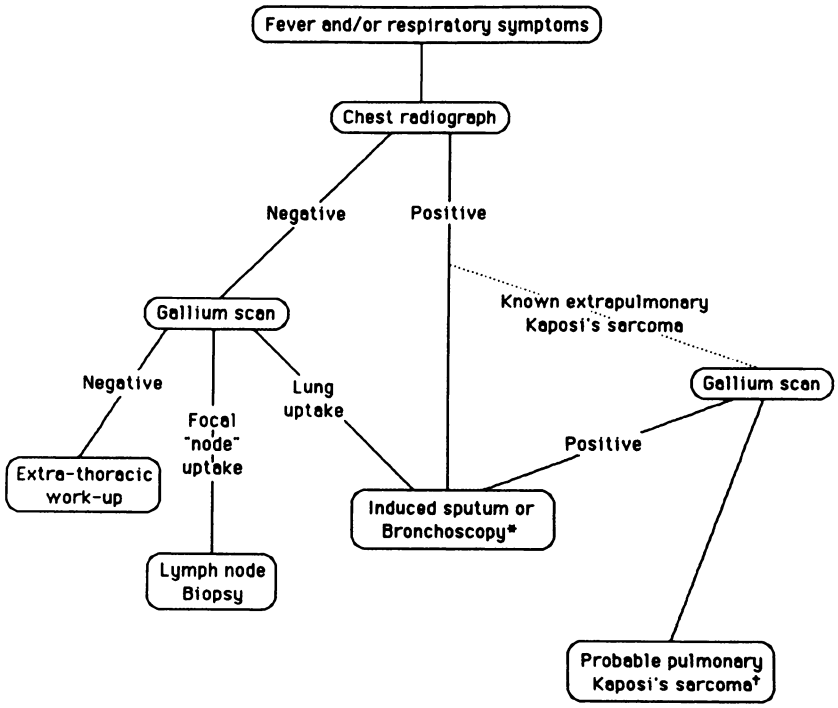

FIGURE 6
Diagnostic algorithm for the evaluation of AIDS patients with fever and/or respiratory symptoms. *Bronchoscopy includes alveolar lavage and transbronchial biopsy. †A patient with known extrapulmonary Kaposi's sarcoma, positive radiograph, and negative gallium scan may go on to bronchoscopy depending on the particular clinical situation.

of a positive chest gallium scan for PCP in this series was less than reported elsewhere. Similarly, the pattern of focal lymph node uptake, although highly predictive for MAI infection in this series, was also seen in association with lymphoma. This emphasizes the need for tissue diagnosis in the setting of a positive gallium scan before the institution of potentially toxic therapy (*5,8*). The pattern of gallium uptake (focal lymph node versus localized intrapulmonary versus diffuse pulmonary uptake) can be extremely useful in directing clinicians to an appropriate site for biopsy, i.e., lung versus lymph node.

A negative chest radiograph combined with a normal chest gallium scan had a high negative predictive value for intrathoracic pathology. This constellation of findings in a symptomatic AIDS patient should direct the search for infection away from the chest. Even with a positive chest radiograph, a negative gallium scan points to noninflammatory pathology. In AIDS patients with these findings, KS should be considered strongly.

REFERENCES

1. Update: acquired immunodeficiency syndrome—United States. *Morbid Mortal Week Rep* 1986; 35:17–21.
2. Murray JF, Felton CP, Garay SM, et al. Pulmonary complications of the acquired immunodeficiency syndrome. Report of a national heart, lung, and blood institute workshop. *NEJM* 1984; 310:1682–1688.
3. Greene JB, Sidhu GS, Lewin S, et al. *Mycobacterium avium-intracellulare*: a cause of disseminated life-threatening infection in homosexuals and drug abusers. *Ann Intern Med* 1982; 97:539–546.
4. Zakowski P, Fligiel S, Berlin OGW, et al. Disseminated *Mycobacterium avium-intracellulare* infection in homosexual men dying of acquired immunodeficiency. *JAMA* 1982; 248:2980–2982.
5. Kovacs JA, Hiemenz JW, Macher AM, et al. *Pneumocystis carinii* pneumonia: a comparison between patients with the acquired immunodeficiency syndrome and patients with other immunodeficiencies. *Ann Intern Med* 1984; 100:663–671.
6. Barron TF, Birnbaum NS, Shane LB, et al. *Pneumocystis Carinii* pneumonia studied by gallium-67 scanning. *Radiology* 1985;154:791–793.
7. Stover DE, White DA, Romano PA, et al. Spectrum of pulmonary diseases associated with the acquired immunodeficiency syndrome. *Am J Med* 1985; 78:429–437.
8. Coleman DL, Hattner RS, Luce JM, et al. Correlation between gallium lung scans and fiberoptic bronchoscopy in patients with suspected *Pneumocystis carinii* pneumonia and the acquired immunodeficiency syndrome. *Am Rev Respir Dis* 1984; 130:1166–1169.
9. McCauley DI, Naidich DP, Leitman BS, et al. Radiographic patterns of opportunistic lung infections and Kaposi's sarcoma in homosexual men. *Am J Roentgenol* 1982; 139:653–658.
10. Tuazon CU, Delaney MD, Simon GL, et al. Utility of gallium^{67} scintigraphy and bronchial washings in the diagnosis and treatment of *Pneumocystis Carinii* pneumonia in patients with the acquired immunodeficiency syndrome. *Am Rev Respir Dis* 1985; 132:1087–1992.
11. Broaddus C, Dake MD, Stulbarg MS, et al. Bronchoalveolar lavage and transbronchial biopsy for the diagnosis of pulmonary infection in the acquired immunodeficiency syndrome. *Ann Intern Med* 1985; 102:747–752.
12. Centers for Disease Control. *Pneumocystis* pneumonia—Los Angeles. *Morbid Mortal Week Rep* 1981;

30:250–252.
13. Isam AH, Wenzl JE, Leonard JC, et al. Pulmonary cytomegalovirus infection, detection by gallium-67 imaging in the transplant patient. *Arch Intern Med* 1979; 139:286–288.
14. Garay SM, Belenko M, Fazzini E, et al. Pulmonary manifestations of Kaposi's sarcoma. *Chest*: in press.
15. Krishnamurthy GT, Singhi V, Taylor RD, et al. Radionuclide scanning in the evaluation of Kaposi sarcoma. *Arch Intern Med* 1976; 136:400–403.