The Diagnostic Role of Nuclear Medicine in the Acquired Immunodeficiency Syndrome

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This paper is a review of (a) the pathophysiology of the autoimmune deficiency syndrome (AIDS), and (b) the diagnostic procedures nuclear medicine has to evaluate human immunodeficiency virus related disorders. This article is organized in an organ system approach to AIDS pathology. The application of [^{67}Ga]citrate, ^{111}In-labeled white blood cells, [^{201}Tl]chloride, single photon emission computed tomographic, and positron emission tomographic brain agents, [^{99m}Tc]sulfur colloid and [^{99m}Tc]methylene diphosphonate to the pulmonary, nervous, gastrointestinal, dermatologic, musculoskeletal, and renal systems is discussed. These radioisotopes allow earlier diagnosis than routine radiographic studies, and can monitor the effect of therapy on disease activity. In this review an attempt is made to provide clinically useful algorithms to suggest a specific pathogen based on the pattern of radionuclidic uptake.

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Understanding the acquired immunodeficiency syndrome (AIDS) and the diagnostic role nuclear medicine plays in this entity has become increasingly important. Approximately 10 million individuals are estimated to be infected worldwide with the human immunodeficiency virus (HIV) which induces AIDS. In the next decade, up to 50% of these individuals will present with maladies related to the HIV infection. The fatality rate is close to 100% for individuals with AIDS.

This review will focus on the diagnostic methods nuclear medicine provides to detect HIV-infectious diseases, HIV-induced tumors, and HIV related systemic disorders. The advantage provided by nuclear medicine is that nuclear scintigraphy detects early functional and physiologic alterations that occur before structural changes can be detected by other radiologic imaging modalities.

The acquired immunodeficiency syndrome is induced by integration of the human immunodeficiency virus into the cellular immune system (*1*). The initial event appears to require exposure to a body fluid containing the HIV by an individual with macrophage immune stimulation (*2,3*). Macrophage activation can be detected by in vivo tests (*2,3*) and can be visualized by increased splenic sulfur colloid uptake on a liver-spleen scintigram (Fig. 1) in pre-AIDS patients (*4*). Immune stimulation of macrophages can occur in a variety of disorders, the most common being infections. An immune stimulated status has been noted in many of the high risk population who develop AIDS (*2*). This population includes the following categories of individuals: (a) individuals involved in homosexual practices; (b) i.v. drug abusers; (c) prostitutes; (d) individuals receiving multiple blood transfusions; (e) individuals with sexual contact with groups 1, 2, 3, and 4 above; and (f) children of the above five groups with in utero contact with the HIV virus.

With regards to health workers caring for the AIDS victim the risk of HIV conversion is low unless they themselves are in one of the above categories. Evaluation of health workers exposed to HIV containing fluids and not known to have a high risk background were felt to have the presence of associated macrophage stimulation in the few who converted (*5*). The routine use of precautions such as disposable gloves, avoiding unneeded contact with bodily fluids, and appropriate sterile and needle precautions is suggested to avoid the rare HIV conversion in health personnel. Also, avoiding AIDS fluid exposure during an immune stimulated illness is desirable.

The HIV infected individuals have been categorized into three pre-AIDS groups, as well as an AIDS group (Table 1). The acutely HIV infected individual, who is

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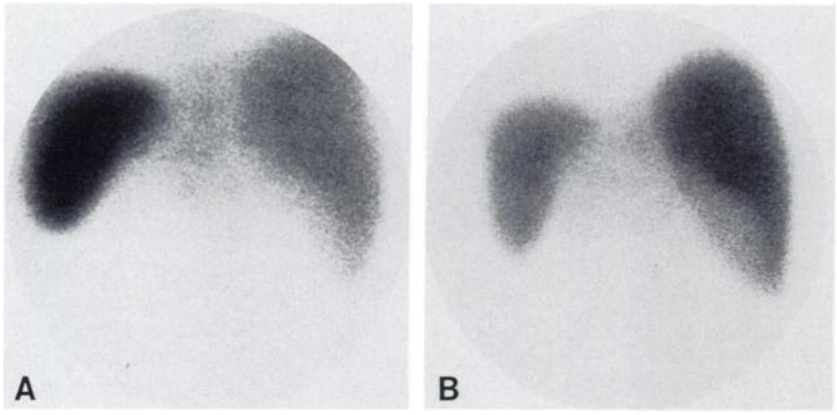

FIGURE 1
The progression of the [^{99m}Tc]sulfur colloid scan (posterior view) from an increased splenic uptake pattern in the pre AIDS state (A) to a decreased splenic uptake pattern when the patient converted to AIDS status (B).

immune stimulated, may or may not manifest clinically with a viral syndrome, is classified in group I. They may remain negative on conventional HIV serology tests for up to 36 mo and may remain asymptomatic (group II) for many years. Subsequently the cellular immune system becomes defective, and patients are less likely to remain asymptomatic in a pre-AIDS status. The HIV positive individual is only classified to have AIDS when he fulfills the criteria established by the Center of Disease Control (*6*). This includes evidence of HIV dementia, a wasting syndrome, certain opportunistic infections or specific tumors (*6*). The HIV positive individual with persistent lymphadenopathy who does not fulfill AIDS criteria is classified as having group III status with AIDS related complex (ARC).

NUCLEAR MEDICINE APPLICATIONS

A number of nuclear medicine imaging procedures are currently known to be useful in the patient in whom AIDS is suspected (*7*).

These radioisotopic methods may be used for the early detection of opportunistic infections and tumors, to assess disease activity pre- or post-therapy, and to evaluate the total extent of disease involvement. The early diagnosis provided by nuclear medicine is important because of the poor prognosis of delayed treatment of AIDS related infection and tumors. Also, nuclear medicine studies are helpful to assess the immunologic status of the individual, to classify HIV exposed individuals, to suggest the type of underlying pathology noninvasively and to prognosticate the outcome of the patient.

Although altered T helper to T suppressor cell is a helpful test suggesting AIDS in HIV+ patients who are not on immunosuppressive therapy, the critical step needed to alter an HIV infected system to AIDS may be defective chemotaxis (*8*). Defective chemotaxis is reflected by reduced splenic macrophage uptake on technetium-99m (^{99m}Tc) sulfur colloid on liver spleen scans (Fig. 1) (*4*). This immune dysfunction and reversal of colloid shift seen on liver spleen scintigraphy can be transiently reversed with azidothymidine (*4*).

The role nuclear scintigraphy plays in the evaluation of the AIDS patient can be approached from the standpoint of the organ involved and the potential pathologic entities that may affect that organ system.

Lung Pathogens

Pneumocystis carinii. In two of every three AIDS patients *Pneumocystis carinii* infections is the initial presentation of conversion of pre-AIDS to AIDS status (*9–11*). Although fever, tachypnea, dyspnea, mild nonproductive cough and diffuse interstitial infiltrates on

TABLE 1
Human Immunodeficiency Virus Infection Status

Group	HIV status	Clinical status
Pre-AIDS—Group I	Acutely HIV infected	May or may not develop viral infection symptoms
Pre-AIDS—Group II	Asymptomatic HIV carrier	May remain negative on standard serology tests for up to 36 mo Lasts for many years
Pre-AIDS—Group III	AIDS related complex	Persistent lymphadenopathy Does not fulfill AIDS criteria
AIDS	Autoimmune deficiency syndrome	Fulfill AIDS criteria of HIV dementia, wasting syndrome, certain opportunistic infections or specific tumors

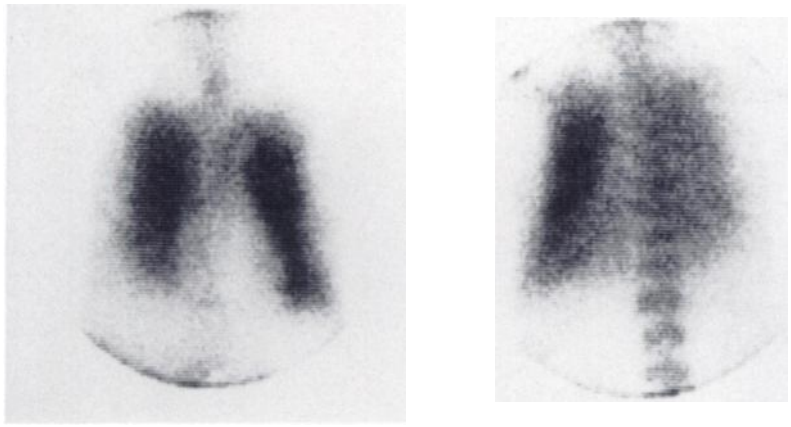

FIGURE 2
In a patient with normal chest radiograph, diffuse bilaterally increased lung activity without hila uptake is well seen on the oblique gallium-67 scintiphotos in this patient with *Pneumocystis carinii* pneumonia (PCP).

chest radiographs may be present, subtle prolonged minimal symptoms and normal chest x-rays frequently occur in many early cases of *Pneumocystis carinii* pneumonitis (PCP) (*10,12*). Since over 30% of these patients die as a result of lung infections it is important to detect early PCP because PCP therapy when the chest radiograph is normal provides a better prognosis for the AIDS patient (*12*). Gallium scintigraphy is abnormal in 85% to 95% of PCP cases (9,13–15). Gallium scintigraphy can even detect PCP in asymptomatic patients with normal chest x-rays (*16*). Unfortunately, false-positive gallium-67 (^{67}Ga) scan readings of PCP can occur in up to 50% of cases (*9,15*) unless diagnostic patterns of uptake are analyzed (*13,16–18*). The characteristic pattern of diffuse increased bilateral lung uptake of ^{67}Ga of intensity greater than liver (Fig. 2) has a specificity of 90% for PCP (*15*). The presence of heterogeneous diffuse lung uptake may have a higher predictive value than homogeneous uptake (*17*) and when the concurrent chest radiograph is also normal, the specificity approaches 100%. If the intensity of lung uptake is less than liver uptake, the specificity falls to

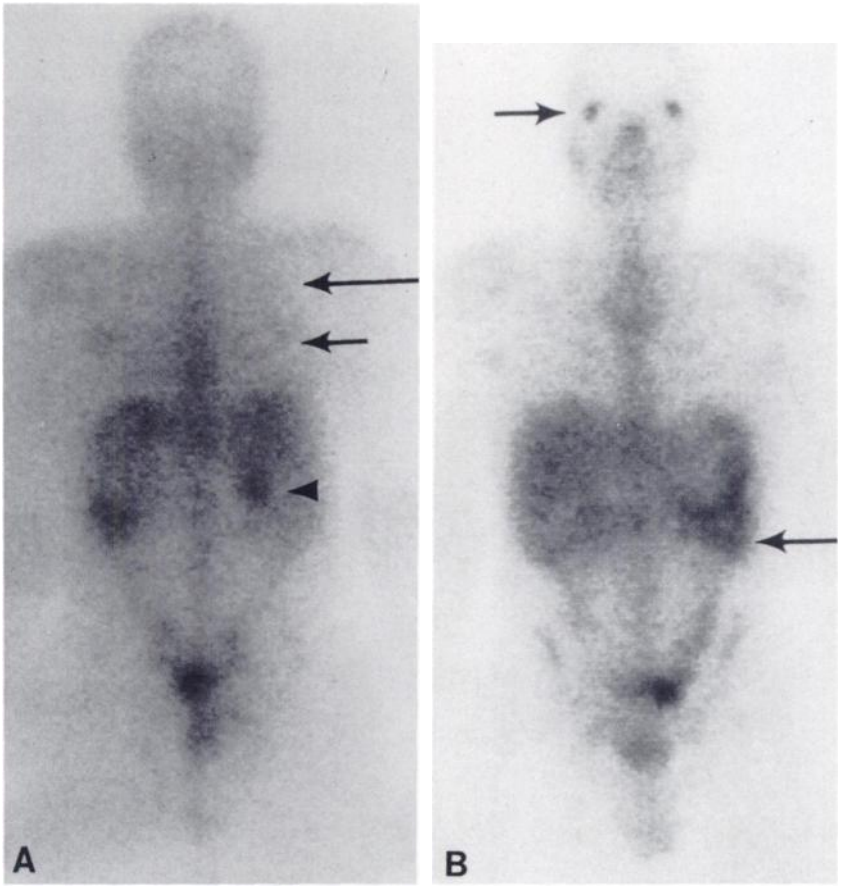

FIGURE 3
A posterior whole-body ^{67}Ga scan (A) in a patient with systemic cytomegalovirus (CMV) infection with perihilar symmetrical low grade lung uptake (double arrows) and intense right adrenal uptake (arrow head). The anterior view (B) shows symmetric bilateral ocular uptake (upper short arrow) and prominent bowel activity (long arrow).

50% since this may reflect the other types of diffuse underlying lung disease including viral infections such as Cytomegalic virus (CMV) (Fig. 3), smokers pneumonitis, lymphocytic interstitial pneumonitis (LIP) (Fig. 4) (*18,19*), postdrug treatment parenchymal pathology and other gallium avid disorders. Although more than 80% of AIDS patients acquire *Pneumocystis carinii* pneumonia, one must be aware of the disease pattern's of other pathogens seen on ^{67}Ga scintigraphy. For example, low grade lung activity with bilateral parotid uptake is characteristic of LIP (Fig. 4); while non-nodal lobar ^{67}Ga lung uptake is suggestive of bacterial pneumonia (Fig. 5); and nodal uptake with patchy asymetric low grade or lobar uptake is associated with granulomatous disease such as histoplasmosis and mycobacterial infections (Figs. 6 and 7). It is important to remember that ^{67}Ga nodal uptake is not normally expected in uncomplicated PCP. Due to the slow response to therapy (*20,21*) and high rate of recurrence (*21*), a baseline and follow-up ^{67}Ga scan may be useful to demonstrate successful response to treatment and to detect early recurrences. Recurrence of PCP occurs in ~66% of patients with PCP followed for up to 15 mo (*22*).

Usually, the initial PCP presentation, has a higher ^{67}Ga avidity, than that seen following treatment and with recurrences (*16*). Also, an almost normal, low grade ^{67}Ga intensity has been described in fatal PCP (*16*). X-rays are important in these fatal cases since chest radiographs are usually markedly abnormal. The low grade almost normal uptake in extremely ill patient may reflect reduction of immune functioning lymphocytes which lack gallium avidity. Only if baseline studies are required, can PCP recurrences with minimal increases be appreciated.

Since therapy for PCP commonly in itself induces fever, evaluation of the patient may require [^{67}Ga] citrate scintigraphy to differentiate between drug induced fever or a secondary infection. Pulmonary pathology is virtually ruled out if gallium chest uptake and chest x-ray are normal (*17*).

More recently, therapy for PCP is being done without invasive histologic invasive procedures. In these cases if a non-PCP infection is suggested by the ^{67}Ga scan pattern it is important to treat the patient with the appropriate medication. Also, since AIDS patients can have multiple infections simultaneously, even with positive PCP sputum, if the chest x-ray and gallium scan pattern does not agree with the diagnosis of PCP one must investigate and treat the other pathologic diagnosis suggested by the pattern of uptake.

We feel whole-body gallium scintigraphy should be acquired in all cases. Evaluation of the total-body scan may detect other sites of infection. Detection of these sites together with the pattern of uptake in the rest of the body may change a nonspecific lung uptake diagnosis to a more specific diagnostic disease pattern (Table 2).

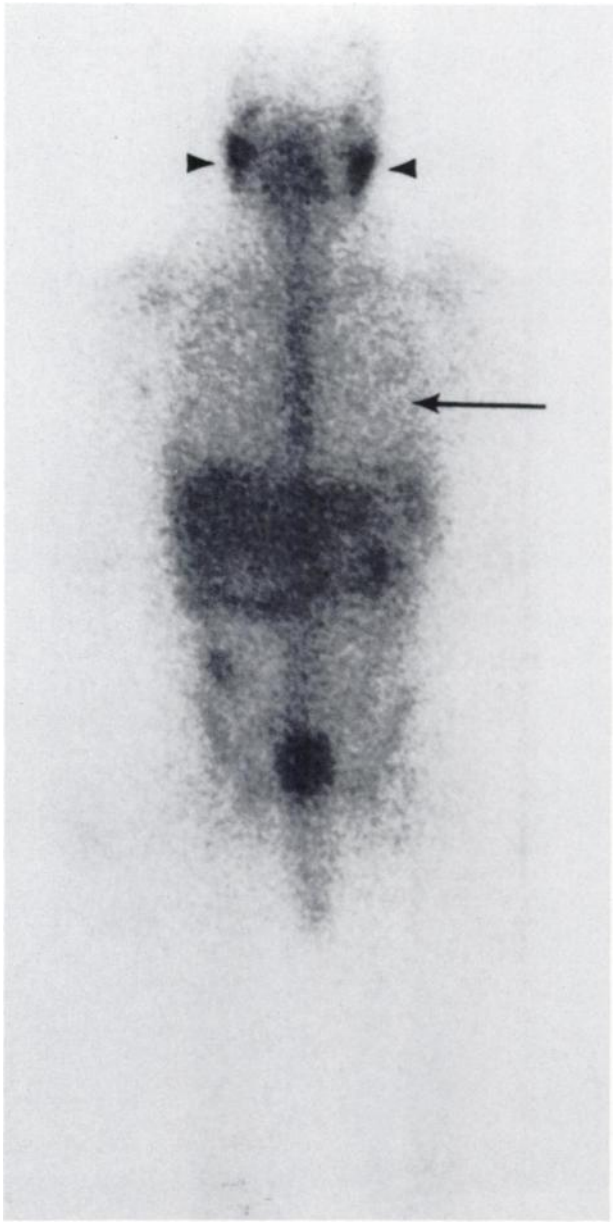

FIGURE 4
The characteristic pattern of lymphocytic interstitial pneumonitis (LIP) with intense bilateral parotid uptake (arrow heads) and low grade lung uptake without hilar uptake (arrow).

Mycobacterium and other granulomatous infections. *Mycobacterium avium-intracellulare* (MAI) causes widespread disease in 25% to 50% of AIDS patients (*23*). Travel history as well as the country or state of origin of the patient is important to suggest granulomatous diseases which may mimic MAI infections (for example with travel in Southwest USA one must exclude coccidiomycosis, with travel in the Ohio basin one must exclude histoplasmosis and with travel outside

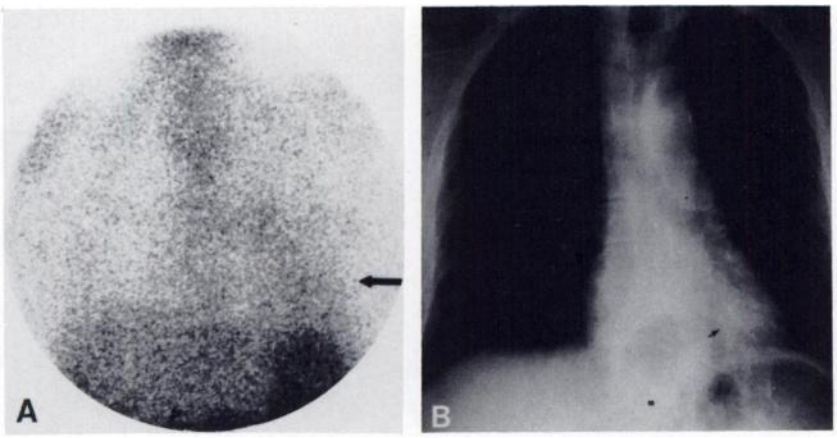

FIGURE 5
The common lobar [^{67}Ga]citrate pattern of bacterial infection where no nodal uptake is present. Lobar uptake is present (arrow) in the left lower lobe on the anterior chest view (A). A subtle infiltrate (arrow) is seen in the same location on the chest x-ray (B).

the USA to countries as Haiti one must exclude tuberculosis). *Mycobacterium tuberculosis* (Tb) is noted with an increased incidence and a high prevalence in Haitians, intravenous drug abusers, and economically disadvantaged groups (*24,25*).

In mycobacterial lung infections, gallium scintigraphy pattern may demonstrate increased activity associated with tuberculosis pleural effusions, tuberculous lobar pneumonias or show patchy low grade lung uptake along with hilar and nonhilar nodal uptake (Fig. 6). The atypical mycobacterial infections present more frequently with extra hilar nodes (Fig. 7) while tuberculosis tends to be more commonly limited to hilar uptake (Fig. 6).

Nodal gallium uptake along with normal lung activity has been seen in lymphoma (*16,17*) and possibly ARC lymphadenopathies (*16*).

Bacterial infections. A wide spectrum of bacterial infections occur in patients with HIV disease. Streptococcal pneumonia is most common, but hemophilus influenza and *Salmonella typhi* are also seen. Clinical and radiographic presentation of these diseases may be difficult to distinguish from other infections. The ^{67}Ga scintigraphic pattern of localized lobar uptake without nodal uptake (Fig. 5) suggests bacterial infection rather than PCP or mycobacterial infection (*17,18*). When gallium scintigraphy shows uptake in multiple pulmonary lobes as well as bone, one must consider aggressive bacterial infections such as actinomycosis (Fig. 8) or nocardia (*19*). In these aggressive bacteria infections needle biopsy often is negative.

Fungal infections. Pulmonary fungal infections can extend beyond the lung parenchyma into adjacent soft tissues or bone similar to aggressive bacterial infections (Fig. 8). Oral and esophageal candidiasis is common but systemic disease with pulmonary involvement is rare. However, if one notes esophageal uptake and localized lung uptake, candidiasis should be considered.

Systemic cryptococcus infection commonly has pulmonary, as well as neurologic involvement, with diffuse

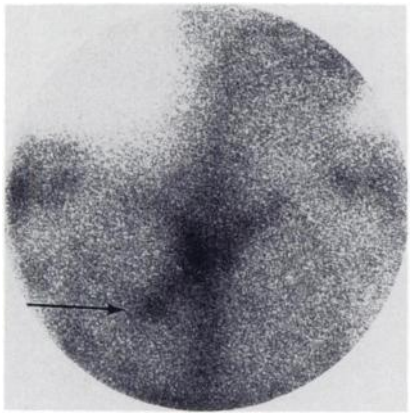

FIGURE 6
Gallium-67 pattern of tuberculosis with intense asymmetric hila uptake seen in the right hila (arrow), with patchy asymmetric lung uptake.

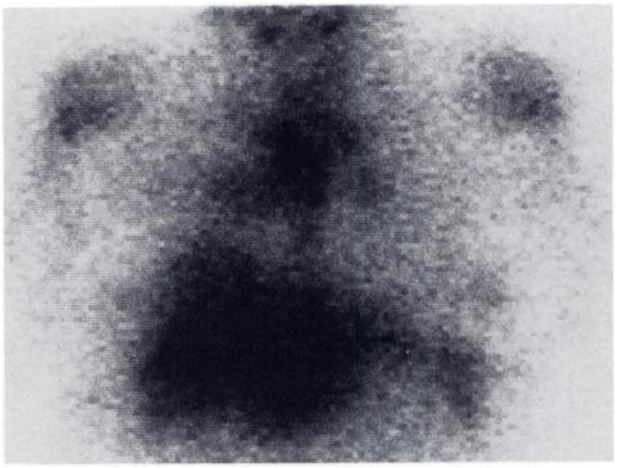

FIGURE 7
The pattern of *Mycobacterium avium-intracellular* (MAI) infection on ^{67}Ga imaging with uptake in nonhilar nodes (axillary, supraclavicular) as well as hilar uptake. The nonhilar uptake is more characteristic of atypical mycobacterium rather than tuberculosis.

TABLE 2
Diagnostic Gallium Scan Patterns Noted in AIDS Patients

Suggested pathology	Lung uptake pattern	Nodal uptake pattern	Characterizing feature
Lymphocytic interstitial pheumonitis	Diffuse low grade	None	Bilateral parotid uptake common
Pneumocystis carinii pneumonia	Diffuse intense early low grade in late stages	None	
Tuberculosis	Patchy or lobar	Common (Hilar)	Unilateral parotid uptake occasional
Atypical mycobacterium	Patchy or lobar	Common (Hilar + extrahilar)	
Bacterial pneumonia	Lobar	None	
Invasive bacterial pneumonias as actinomycosis or fungal infections	Multiple lobar uptake	None	Bone uptake
Kaposi's sarcoma	No uptake	No uptake	[^{201}Tl]chloride uptake at site of mass

lung activity, without hilar uptake on gallium scans. Gallium scintigraphy may not detect infectious brain involvement as well as ^{111}In white blood cell imaging (*26*).

Cytomegalovirus. Infection with cytomegalovirus (CMV) is frequent in individuals with HIV infection risk factors. Disseminated disease occurs in a majority of symptomatic patients but culturing CMV may not be the cause of the pulmonary symptoms since it is so common in the normal population and diagnosis of clinical disease is usually only inferred from histopathologic evidence (*27,28*).

Pulmonary CMV infection detection is uncommon and usually occurs in conjunction with more aggressive PCP (*11*). Due to difficulty in diagnosing CMV the pattern of uptake seen on the whole-body gallium scan may be important. A pattern of low grade lung uptake with perihilar prominence (*17*) associated with eye uptake (due to the frequent presentation of CMV as retinitis), adrenal uptake (due to the most frequent pathological findings of CMV as adrenalitis), renal uptake at 48 hr and/or persistent colon uptake with diarrhea symptoms without other pathogens seen in multiple stool specimens of a patient suggests CMV (Fig. 3). If high grade pulmonary uptake is seen superimposed aggressive PCP must be considered.

Pulmonary tumors. Kaposi's sarcoma is the most common tumor seen in AIDS patients. Pulmonary

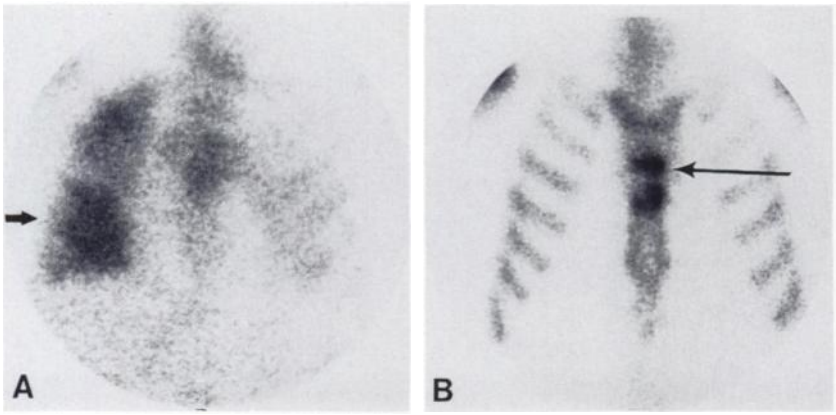

FIGURE 8
The pattern of aggressive infections such as actinomycoses in which osseous as well as soft tissue involvement may be seen. (A) Shows the intense and extensive uptake in ^{67}Ga scintigraphy in the right lung (arrow) and the sternum which is confirmed in the latter on the [^{99m}Tc]methylene diphosphonate bone scan (B).

Kaposi's sarcoma often has no gallium uptake (*15,19*). Thus, an ill-defined lung or mediastinal mass associated with a normal gallium scintigraphy pattern suggests Kaposi's sarcoma (Fig. 9). The diagnosis of Kaposi's sarcoma can be confirmed if uptake of thallium-201 (^{201}Tl) chloride is seen in the mass (*29*). The lack of gallium uptake may distinguish Kaposi's sarcoma from lymphoma which also occurs in AIDS patients and often demonstrates lymph node chain nodal uptakes. The gallium scan's total-body evaluation is helpful to direct lymphoma biopsies in evaluating symptomatic AIDS patients. Normal gallium total-body, head CT, and chest radiographs can be used to exclude infections or tumors in HIV positive patients.

Lymphocytic interstitial pneumonitis. The etiology of lymphocytic interstitial pneumonitis (LIP) is unclear. Various viral and immunological etiologies have been suggested. The x-ray may appear either normal, resemble PCP, mimic viral infections such as cytomegalovirus disease, or miliary tuberculosis. In the late stage of LIP the chest x-ray may show coalesence of multiple alveolar densities.

Steroids that may be beneficial in the treatment of LIP are not beneficial for PCP, tuberculosis, and other opportunistic infections which may mimic LIP on x-ray and clinical grounds. Sputum is not diagnostic for LIP and even lung washings or biopsy may not be able to distinguish LIP from other types of pneumonitis.

Fortunately, ^{67}Ga scintigraphy appears to have a diagnostic pattern of symmetric parotid uptake and low grade diffuse lung uptake without nodal uptake (*19*) which can be distinguished from other causes of lung ^{67}Ga uptake (Table 2).

CNS Pathology

Toxoplasmosis. The most common cause of focal encephalitis in HIV positive individuals is *Toxoplasma gondii* (*10,30*). Serologic tests are of limited use and the most useful test is the CT scan, characteristically with multiple cortical and subcortical ring contrast enhancing lesions associated with edema (*30,31*). Other conditions including lymphoma, fungal infections, progressive multifocal leukodystrophy, tuberculosis, CMV, Kaposi's sarcoma, and hemorrhage can mimic the CT pattern of toxoplasmosis (*31*). Gallium-67 scans are often negative and AIDS CNS infection appears to be better diagnosed by ^{111}In WBC scans (*26*). Although the ^{111}In WBC scan can detect infections, it is not specific and, for definitive diagnosis, a brain biopsy is needed. Because of the invasiveness of brain biopsies, often clinical improvement after 2 wk of therapy, or improvement in the follow-up ^{111}In WBC scans and CT can be used as presumptive evidence of the disease.

Cryptococci. Cryptococcal meningitis occurs in AIDS patients with minimal to fulminant symptoms (*30*). The ^{67}Ga scan often is negative and once again the ^{111}In WBC may be a better scintigraphic test in the CNS (*25*). Both ^{111}In WBC and ^{67}Ga scans can suggest active foci of infection in the lungs, bones, and liver which may be amenable to biopsy for diagnostic purposes instead of an invasive brain biopsy. Indium-111 WBC scintigraphy may detect inflammatory changes before MRI or CT shows structural changes (*26*). If cerebral ^{111}In WBC or CT is positive and no other sites are seen, India ink examination of the CSF or serum for cryptococcal antigen can nearly always make the diagnosis. If this CSF antigen test is negative toxoplasmosis is the most likely diagnosis in AIDS infectious disease.

Cytomegalovirus. CMV encephalitis may also have negative gallium-67 scans and once again ^{111}In WBC scans may be more useful (*26*). As previously described ^{67}Ga uptake in eye, adrenal, colon or esophagus as well as low grade diffuse pulmonary uptake with perihilar prominence (*17*) may be helpful to suggest systemic CMV infection (Fig. 3). At present CMV diagnosis even on tissue specimens may be difficult.

AIDS dementia. A large percentage of AIDS patients may develop HIV virus induced dementia. CT and MRI changes are only seen with far advanced AIDS dementia when structural changes have occurred (*31*). In contrast, AIDS dementia may show early cerebral abnormalities on single photon emission tomography

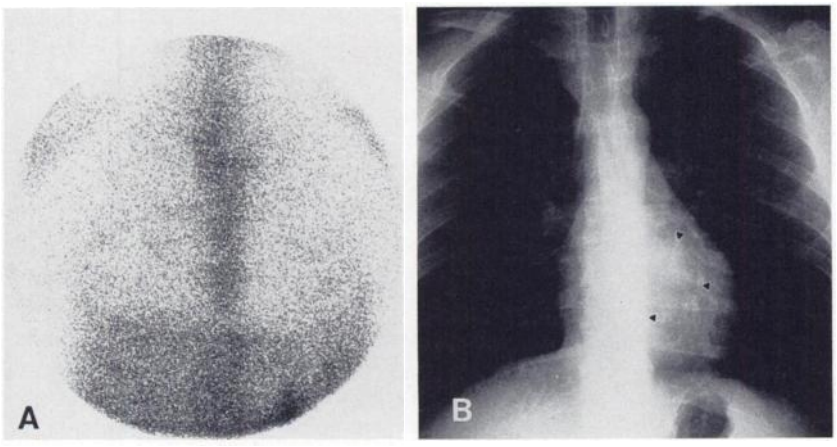

FIGURE 9
The scintigraphic findings characterizing Kaposi's sarcoma with absence of [^{67}Ga]citrate uptake (A) in an ill-defined lung mass (arrow heads) on chest radiograph (B) in one patient with autopsy proven left lower lobe Kaposi's sarcoma.

(SPECT) and positron emission tomography (PET) scans in the thalamus and basal ganglia (*32*). Further work is needed to confirm if characteristic changes are present on SPECT and PET imaging and if nuclear medicine detection occurs before abnormalities are detected on psychologic testing.

CNS tumors. Kaposi's sarcoma and lymphoma are the most common tumors seen in AIDS patients. Gallium-67 scintigraphy often will not detect Kaposi's sarcoma. Technetium-99m-labeled RBC for blood-pool imaging appears to detect this tumor in the skin (Fig. 10). Limited evaluation of ^{99m}Tc-labeled RBC scans in the brain and other organs have been performed. Also tumor specific ^{201}Tl scintigraphy has been shown to have uptake in Kaposi's sarcoma (*29*).

Gallium-67 scintigraphy has a high sensitivity for detecting lymphoma. Whole-body ^{67}Ga scintigraphy is useful since one may detect other sites of lymphoma which may be amenable to biopsy. Since CT or MRI uptake cannot distinguish lymphoma from other inflammatory processes and brain biopsy is invasive locating other biopsy sites can be clinically useful. The ability of detecting distant sites of lymphoma on gallium scintigraphy is also important. However, primary CNS lymphoma in AIDS is common. Since thallium is taken up by tumors thallium scintigraphy may be useful to distinguish tumors from infections and to follow up tumor therapy (*29*). SPECT thallium brain tumor imaging has been performed at our institution (Fig. 11) when correlated to CT and MRI studies demonstrated promising results (*33*). Thallium-201 brain scintigraphy appears to be brain tumor specific and can distinguish active tumor, from edema, post-therapy effects, and infection.

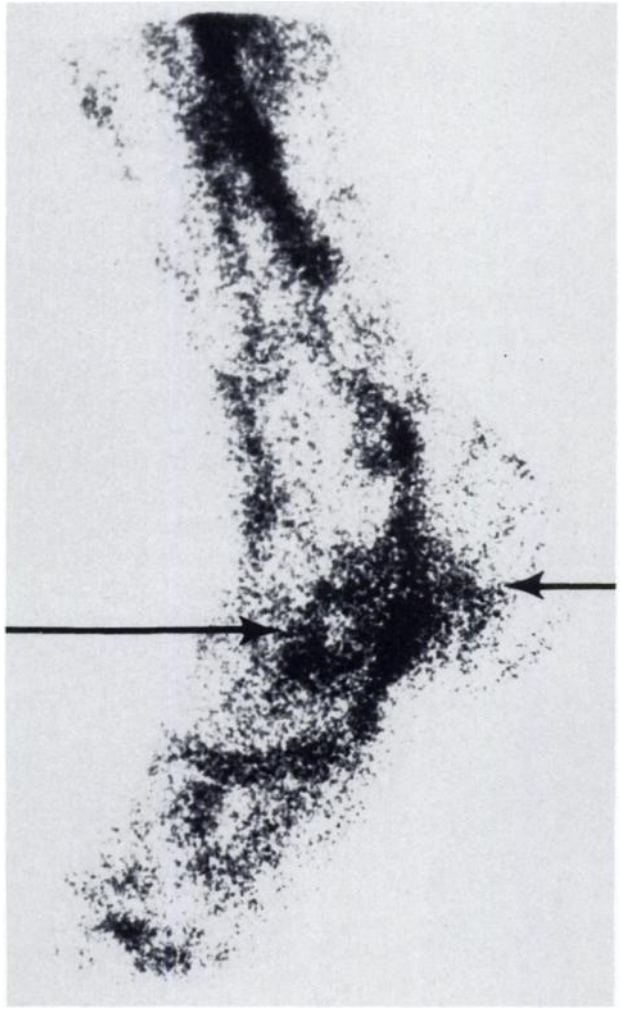

FIGURE 10
A ^{99m}Tc-labeled red cell blood-pool image of the right lower extremity with localization at the site of Kaposi's sarcoma (arrows).

GI Pathology

Infections. Gallium-67 uptake equal or greater than liver uptake, which intensifies over time represents infection in over 50% of patients. However, nonspecific inflammation or tumors may also have this pattern. Indium-111 WBC studies have been shown to have a higher sensitivity and specificity than ^{67}Ga scintigraphy in assessing patients suspected of having GI infections (*26*).

a. Esophageal infections

Oral and esophageal candidiasis is the most common fungal infection in AIDS patients and dysphagia may be the initial presentation of AIDS (*34*). Antibiotic therapy is usually successful in treating candidiasis but recurrence is common. Usually upper GI series and endoscopy are adequate diagnostic tools. Gallium-67 or ^{111}In WBC uptake outside the esophagus can suggest other opportunistic infections if other sites of infection are also seen, since candidiasis is rarely systemic. In 60% of candidiasis cases other opportunistic infections are present (*34*). CMV esophagitis should be suggested when systemic infection occurs and low grade gallium uptake with perihilar prominence is seen in both lungs (*17*) especially when uptake is seen in other sites such as eye, adrenal and colon (Fig. 3) or if the esophagus infection extends to the stomach.

b. Small and large intestine infection

Diarrhea, which is often debilitating, in the immunocompromised individual is usually caused by infections with the protozoan crytosporidium (*35*). Since the organism is shed intermittently multiple stool examinations or bowel biopsies are needed to make the diagnosis. GI contrast studies demonstrate abnormalities in the duodenum and less commonly in segments of the colon. Although less common, isospora should be considered in Haitians and giardiasis should be considered if travel occurs to endemic areas of giardiasis. If no organism is noted on multiple stool exams CMV infection becomes more likely. The presence of abnormal bowel uptake of ^{67}Ga or ^{111}In WBC may be because of a variety of causes. Etiologies to be considered include

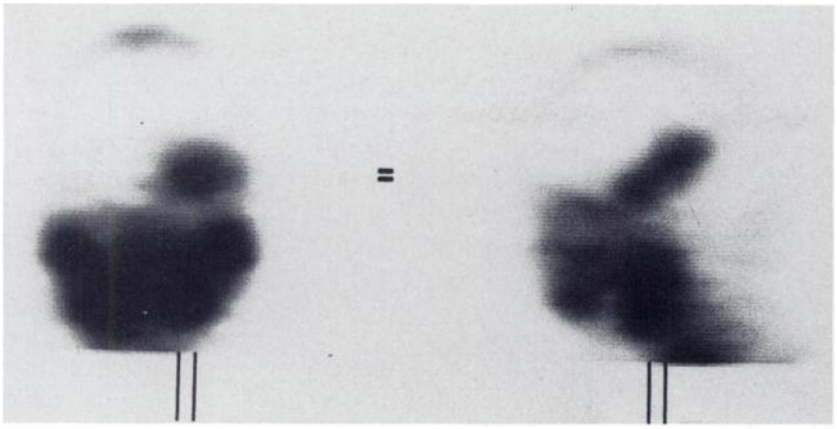

FIGURE 11
The coronal (left) and sagittal (right) reconstruction of a SPECT [^{201}Tl] chloride uptake in an active brain tumor. Thallium imaging occurs in tumors as Kaposi's sarcoma rather than edema, post-therapy necrosis and infections. Thus, thallium SPECT brain images can define the etiology of MRI and CT findings as neoplastic and evaluate tumor therapy in AIDS patients.

normal excretion, crytosporidium, isospora, CMV, giardiasis, granulomatosis infections, GI tumors, bacterial infections such as salmonella or shigella or antibiotic induced colitis. The pattern of uptake in the rest of the body may help in making a more definitive diagnosis (Fig. 3).

GI tumors

In AIDS patients, Kaposi's sarcoma, lymphoma, and other tumors involve the GI tract, liver, and spleen. An enlarged spleen with reduced uptake on ^{99m}Tc sulfur colloid on liver-spleen imaging is usually the result of Kaposi's sarcoma in the AIDS patients (*4*). Liver enlargement and defects are frequently seen in AIDS patients due to liver infections and neoplasms. The ^{67}Ga scan is often negative in Kaposi's sarcoma while it is usually positive in infections and lymphoma. On the other hand ^{111}In WBC scans are usually positive for infections but are rarely positive for malignancy. Thallium in contrast is positive for tumor but not with infections and has been found useful to diagnose Kaposi's sarcoma (*29*).

Oral or rectal squamous cell carcinoma may be suggested by intense positive oral or rectal ^{67}Ga uptake and negative ^{111}In WBC studies in an HIV positive patient. Biopsy can easily confirm these abnormalities.

Dermatologic Lesions

a. Herpes infections

Primary varicella and herpes zoster may be an early indicator for AIDS because it frequently occurs in persons who later acquire AIDS (*36*). The potential for spread to both staff personnel as well as other HIV positive individuals must be kept in mind when scanning a patient with active varicella or herpes zoster infection; skin lesion examination and biopsy are usually diagnostic. If skin uptake of ^{111}In WBC or ^{67}Ga is seen herpes zoster may be suggested. Unlike Kaposi's sarcoma, RBC blood-pool imaging is usually negative in herpetic skin lesions. Inflammatory skin lesions as herpes and hepatitis are more likely to be spread from AIDS patient to health personel than the HIV infection. Mucocutaneous herpes simplex is common in homosexual male patients. This disease presents as oropharynx, perianal, and rectal ulcers which frequently recurs. Careful physical exam can usually detect these ulcers. Biopsy and viral cultures can confirm this disease.

b. Kaposi's sarcoma

Skin lesions are common presentation for Kaposi's sarcoma in AIDS patients. Red blood cells pooling on Tc-RBC imaging (Fig. 12) and ^{201}Tl scintigraphy (*29*) is useful to distinguish Kaposi's sarcoma from inflam-

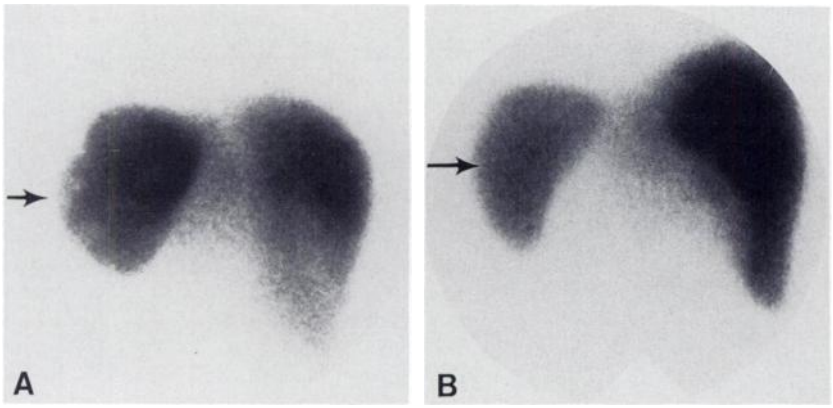

FIGURE 12
A posterior oblique view of the spleen on [^{99m}Tc]sulfur colloid images with discrete focal defects representing involvement with Kaposi's sarcoma in a patient with splenic enlargement (A). The more common diffuse decreased uptake pattern is present in the posterior view (B) in the same patient.

matory skin lesions. Since biopsy is usually diagnostic, diagnosis can be directed for Kaposi's skin lesions with nuclear imaging methods.

Musculoskeletal Disease

Bone scintigraphy and gallium scintigraphy have been used to exclude septic arthritis and osteomyelitis in HIV positive patients (*37*). AIDS-related myositis has been depicted on skeletal scintigraphy (*38*) and gallium scintiphotos. Joint pain is a common symptom in HIV positive individuals but when joint uptake is seen, it is more likely to be due to HIV related Reiter's syndrome, HIV related psoriatic arthritis or AIDS arthritis rather than septic arthritis (*37*). When septic arthritis or osteomyelitis is present it is often due to unusual organisms (*37*) as depicted in Figure 8.

Renal Pathology

Abnormal localization of ^{67}Ga in the kidneys has been correlated with impairment in renal function in the AIDS patient (*39*).

CONCLUSION

Nuclear medicine can be of significant help in the AIDS epidemic. When compared to routine radiologic studies, nuclear scintigraphy is useful due to earlier detection of tumor and infections. For most infections, diagnostic patterns are provided by gallium scintigraphy. CNS infections are optimally evaluated with ^{111}In WBC imaging, tumors are specifically detected with thallium scintigraphy, and AIDS dementia is possibly best assayed with PET or SPECT brain imaging. Total-body studies can provide diagnostic patterns of uptake which are highly suggestive of various pathological conditions. The travel history, together with the clinical data, lab data and correlative radiologic studies can also help to suggest the type of pathogen. Also, serial liver spleen scintigraphy, ^{67}Ga and ^{111}In WBC scintigraphy may be useful indicators of therapeutic response or prognosticators of outcome. As monoclonal antibody technology develops more specific diagnosis and treatment may be provided to HIV infected individuals.

Emphasis should be placed on the proper education of all individuals suspected of participating in activities that place them in a high risk category. In addition health personnel must become familiar with the proper handling of all patients with appropriate universal precautions being taken.

It is unlikely that health workers will develop AIDS if emphasis is placed on the proper handling of all patients suspected of having AIDS. There is a greater risk of contracting tuberculosis, hepatitis and herpes zoster than AIDS. Also, if health workers are ill (i.e., in an immune macrophage stimulate state), it is advisable that they avoid handling HIV containing fluids.

It is currently recognized that if an individual contracts an HIV infection conventional blood tests may remain negative for many years (*40*). A mean time of over 7 yr may be present between the time of HIV exposure and when AIDS is diagnosed. Sophisticated HIV DNA detection methods have recently been developed using HIV gene amplification techniques (*40*). Although the test is currently expensive, it can immediately detect if an individual has contracted HIV (*40*). This method to detect HIV DNA sequences will be used more frequently when the test becomes more automated, allowing earlier recognition and perhaps earlier successful therapeutic intervention in the future.

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