

## AIDS DIAGNOSIS AND MONITORING IMPROVED BY RADIONUCLIDE PROCEDURES

**P**anic among the general public in the United States over the spread of acquired immunodeficiency syndrome (AIDS) has reached such epidemic proportions that afflicted children may be barred from attending school and the military plans to implement a screening program and reject exposed applicants. One factor leading to the rampant fear is the difficulty in diagnosing AIDS.

Two nuclear medicine procedures show promise as a diagnostic test for *Pneumocystis carinii* pneumonia (PCP), the most common AIDS-related opportunistic infection.

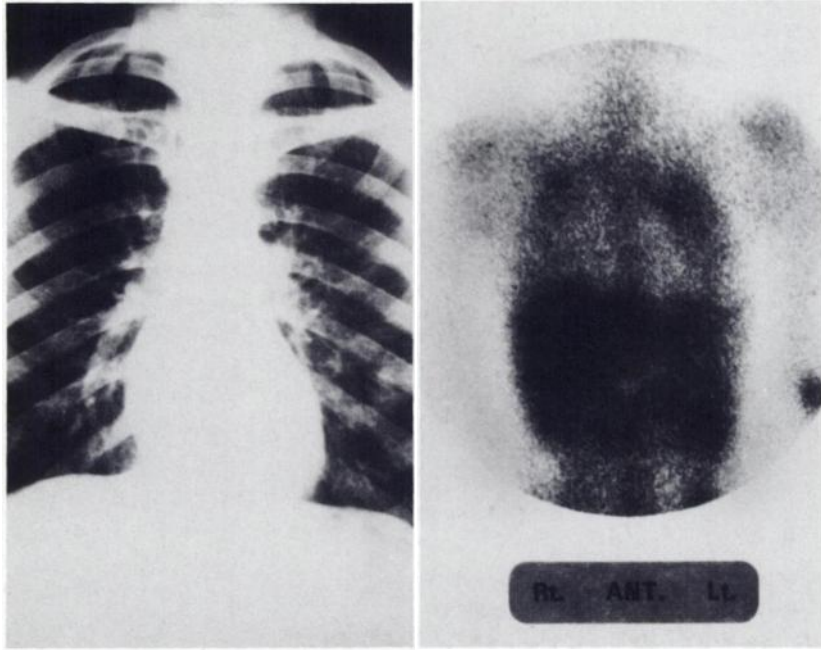
Since the late 1970s, investigators have studied the use of gallium-67 scintigraphy to detect PCP (1-5). In a more recent development, other investigators are pursuing early noninvasive PCP diagnosis with technetium-99m DTPA aerosols (6).

Another radionuclide procedure, bone marrow scintigraphy, is under study as a potential diagnostic tool for patients at various stages of immunodepression caused by AIDS.

### More sensitive than chest x-ray

The radionuclide lung studies provide higher sensitivity than chest x-rays, and detect PCP in patients at high risk for AIDS at an earlier stage of development. The nuclear imaging studies can indicate the presence of PCP in these patients when chest radiographs are normal or equivocal. About 30-40 percent of chest x-rays remain normal, even during a fulminant course of PCP.

In addition, the scans provide an important tool for monitoring PCP treatment, which is done empirically since there is no established optimal



*This patient's chest x-ray (left) shows only a nodular infiltrative density in the left lower lung. A gallium-67 scan (right) taken the same day shows extensive lung involvement with *P. carinii* infection.*

(Courtesy of The Mount Sinai Medical Center, New York)

course of therapy for PCP.

An investigative group at the Mount Sinai Medical Center in New York recently reported an assessment of gallium-67 scanning for diagnosis and follow-up of 34 patients with PCP (7).

The results showed an overall sensitivity of 94 percent and a specificity of 74 percent. Among patients with normal or equivocal chest radiographs at the time of admission, the results showed a sensitivity of 86 percent and a specificity of 85 percent—not a significant difference from the overall figures.

“One major advantage of the gallium-67 scan is that for patients in high-risk groups who present with PCP symptoms, a biopsy may be

deferred if the scan is negative,” explained Lois B. Shane, MD, a physician in the nuclear medicine department at Mount Sinai.

A lung biopsy is still required, however, to confirm diagnosis if the gallium-67 scan is positive. “Furthermore, a scan with patchy or localized uptake (as in early disease) may be helpful in directing the optimal site for bronchoalveolar lavage or transbronchial biopsy,” said Dr. Shane.

“At Mount Sinai, we recommend that PCP patients be continued on treatment as long as the follow-up gallium-67 scans are positive—even if the patient appears clinically recovered,” said Dr. Shane. She explained that there is a high rate of relapse in

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PCP patients, some of which is due to incomplete treatment.

When the follow-up scan is finally negative, said Dr. Shane, studies have shown that the lung biopsy also is negative. "In patients with a negative gallium scan following treatment, a second biopsy is probably not necessary," she added.

Eliminating an unnecessary invasive test for a number of patients also lowers the risk of exposing medical personnel to the AIDS virus, noted Dr. Shane. "The pulmonary and infectious disease people here are convinced of the gallium scan's usefulness, and I hope that institutions that are not now using this procedure will eventually include it routinely to help in PCP detection and follow-up," said Dr. Shane.

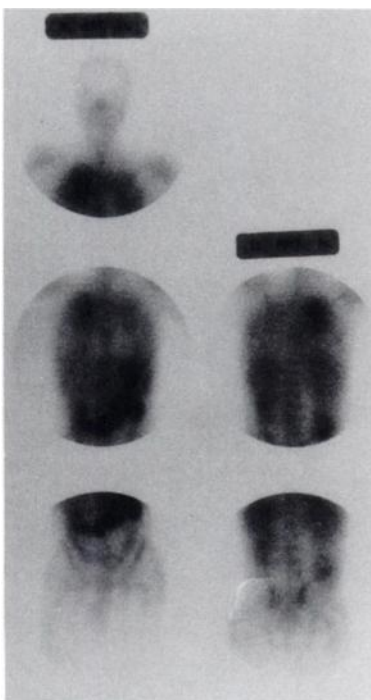
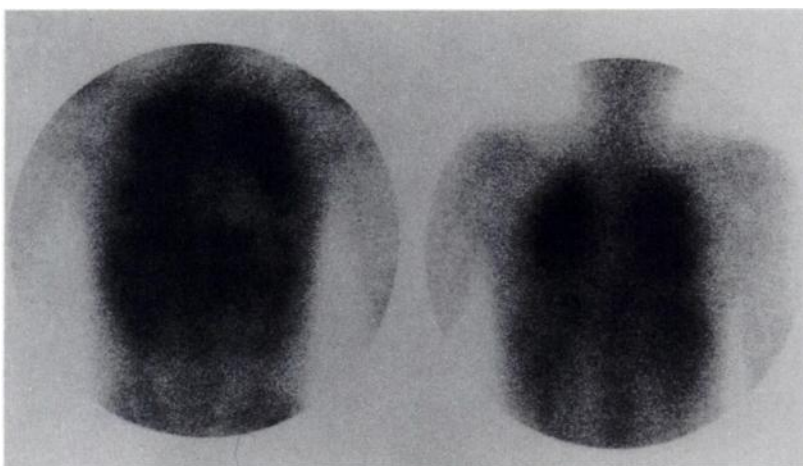
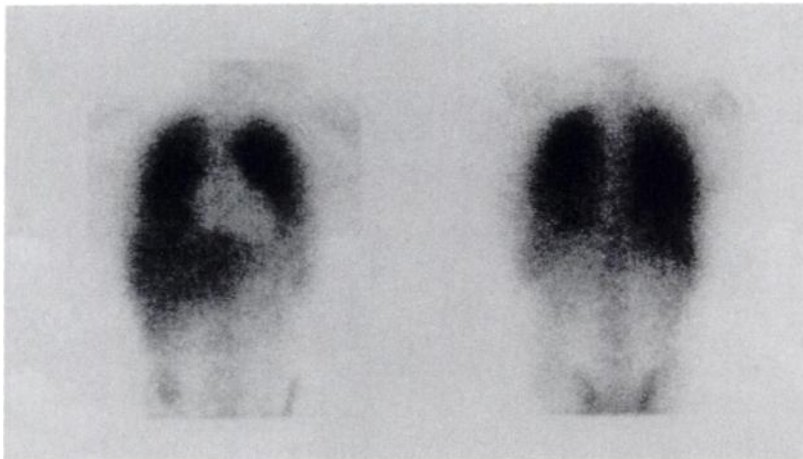
### Rapid clearance

Whereas the gallium-67 scan images areas of active inflammation and infection, technetium-99m DTPA aerosol lung clearances detect injury to pulmonary epithelia.

"Because infection with PCP causes alteration of the type I epithelial cells as the primary event, we studied patients with PCP to determine if it causes rapid clearance of technetium-99m DTPA," explained Gregory R. Mason, MD, assistant professor of medicine at the Harbor-University of California, Los Angeles (UCLA) Medical Center in Torrance, CA.

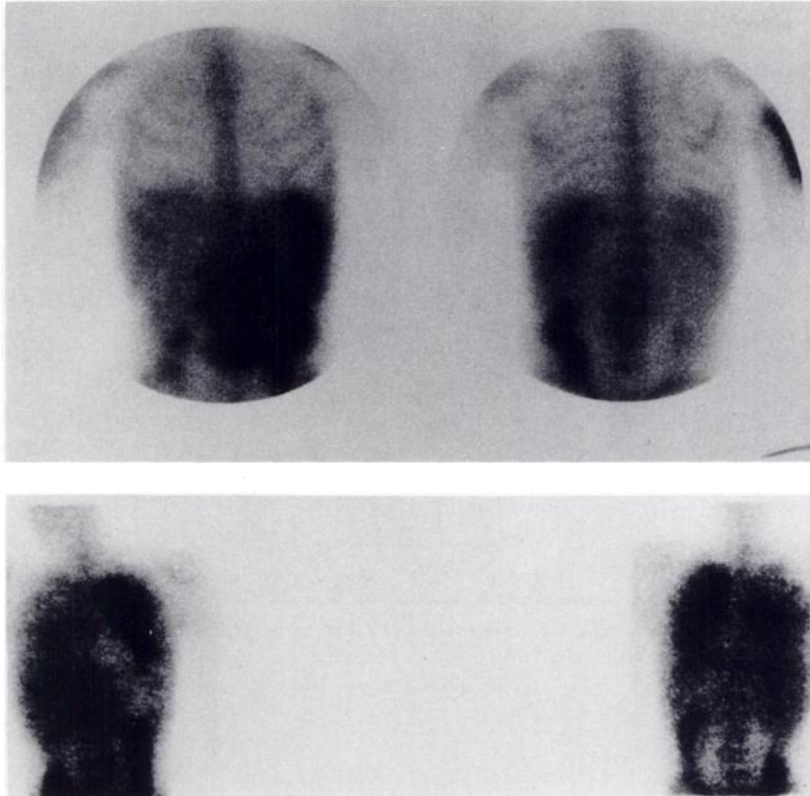
Results of a recent Harbor-UCLA study, presented at The Society of Nuclear Medicine's Annual Meeting this year in Houston, showed a dramatic difference between the rapid clearance rate in PCP patients versus control subjects.

The average clearance rate in seven PCP patients was  $7.5 \pm 3.6$  percent/minute, compared to  $1.3 \pm 0.6$  percent/minute in 20 normal subjects. All of the participants were nonsmokers.



*Lois B. Shane, MD, explained this sequence of lung studies from one patient with AIDS: (top left) Patient is admitted with respiratory symptoms and has a floridly positive gallium-67 scan. (middle left) After two weeks of therapy, the scan shows only slight improvement; there is still significant residual infection. (bottom left) After continued therapy the lungs appear much improved, but still show the presence of active infection. (top right) Therapy is extended until the gallium-67 scan is normal. (bottom right) Six months later the patient returned with a reinfection, which proved to be fatal. It is of note that the patient's chest roentgenograms remained normal throughout the course of both infections.*

(Courtesy of The Mount Sinai Medical Center, New York)



When asked about the high percentage of smokers among intravenous drug abusers and homosexual men (the two major groups at high risk for AIDS) compared to the general public, Dr. Mason pointed out that there is still a significant difference between the clearance rates of smokers and PCP patients. "Smoking doubles the clearance rate, whereas the presence of PCP increases the clearance rate by a factor of four or five," he explained.

Three patients studied from five to 38 days following therapy had improvement in clearance rate, demonstrated to be persistent after clinical recovery, reported the Harbor-UCLA group.

Ismael G. Mena, MD, director of nuclear medicine at Harbor-UCLA, said that the inhaled aerosol clearance procedure is used extensively at several institutions.

The early work in this research was initiated by George V. Taplin, MD,

before his death in 1979. Dr. Taplin was a pioneer in developing the lung perfusion and the lung aerosol scans (8). "He viewed the aerosol clearance studies as truly functional studies of the lung," said Dr. Mena.

"The ability to quantitate injury to the pulmonary epithelium may directly reflect the ability of *Pneumocystis carinii* to invade the lung. We conclude that technetium-99m DTPA clearance may be a useful test to help diagnose and monitor the activity of PCP infection," said Dr. Mason.

#### Bone marrow imaging

Investigators at the University Hospital in Frankfurt, Germany, have recently begun to study the scintigraphic bone marrow status in AIDS patients.

Dr. Ingo Brandhorst, a physician in the Division of General Nuclear Medicine (Head, Prof. Dr. Hör), reported preliminary results of a work in progress during the European

Nuclear Medicine Congress in London last month.

Previous studies have indicated that macrophage defect, one aspect of immunodepression, is present in AIDS patients (9,10). The Frankfurt group is evaluating the reticuloendothelial portion of bone marrow and the distribution pattern of the sessile macrophages.

#### "Pre-AIDS" patients also studied

Using technetium-99m human albumin nanocolloid, Dr. Brandhorst et al. studied bone marrow distribution patterns and the presence or absence of focal cold lesions (11) in a group of 21 patients with a positive human T-cell leukemia virus (HTLV-III) antibody titre, and at various stages of lymphadenopathy syndrome (LAS, or "pre-AIDS"), or with advanced immunodepression accompanied by Kaposi's sarcoma and/or PCP (AIDS). (Like PCP, Kaposi's sarcoma is associated with AIDS.)

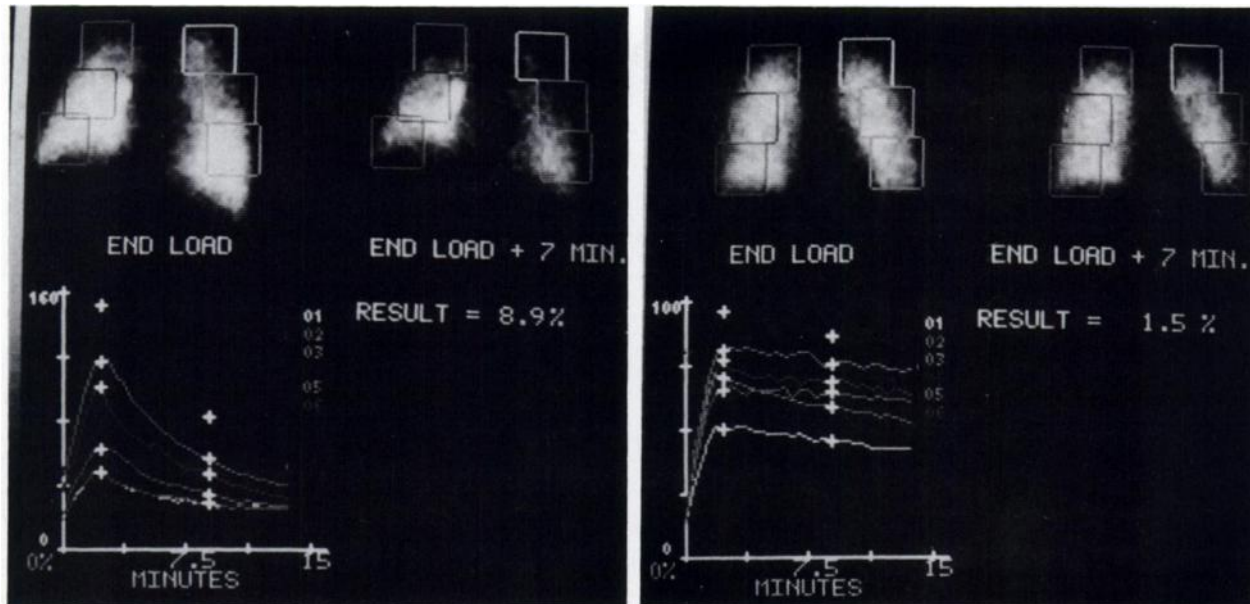
First results showed that 80 percent of the study population had abnormal bone marrow scans. Twelve patients showed bone marrow extension to the knees and/or elbows. Three out of the 11 LAS patients and seven out of the 10 AIDS patients presented focal lesions. Two LAS patients and two AIDS patients had normal scans.

The study population consisted of 17 homosexual males, one heterosexual male with a prostitute contact in East Africa, two female intravenous drug abusers, and one heterosexual female from East Africa.

"There is an above-average incidence of Kaposi's sarcoma in East Africa, suggesting a population at risk for AIDS," noted Dr. Brandhorst.

Although Dr. Brandhorst stressed that it is too early to draw conclusions from these preliminary results, he said that "we assume that our procedure might receive widespread acceptance as a part of initial

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**The appearance of a lung scintiscan (left) immediately after inhalation (End-load) and 7 minutes later (E/L + 7 min) in a patient with PCP. The rate of disappearance over six regions of interest is shown below and is expressed as the percent decline per minute. At right is an example of a normal lung scintiscan. (Courtesy of Harbor-UCLA Medical Center)**

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diagnosis, and possibly for staging and follow-up of the treatment course to assess the occurrence of complications, and finally to derive functional parameters of prognostication."

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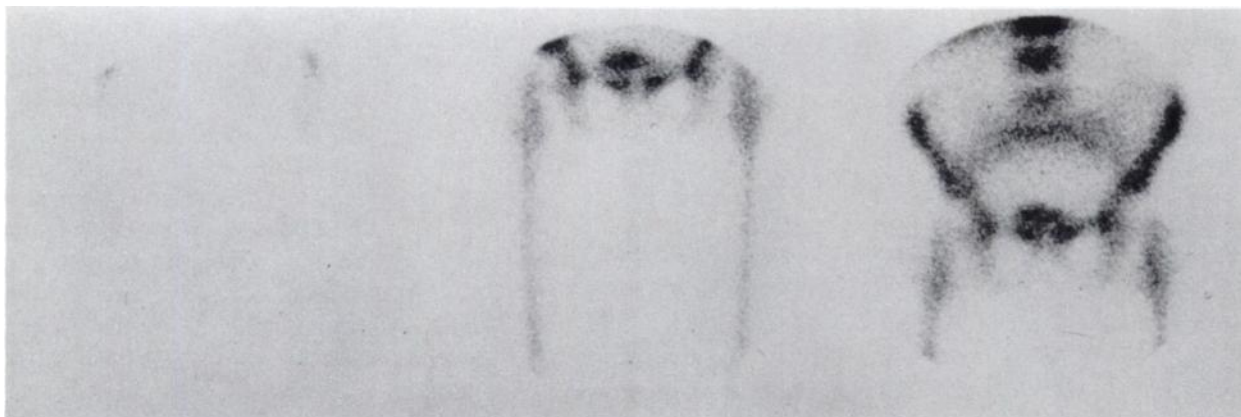
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**Bone marrow scan (left to right: lower legs, upper legs, pelvis) in a 51-year-old male homosexual suffering from AIDS accompanied by PCP. Note the bone marrow extension type II (extension up to the knees in anterior view).**

(Courtesy of University Hospital Frankfurt)