^{67}GALLIUM IN 68 CONSECUTIVE INFECTION SEARCHES

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When employed in the study of peripheral infections, ^{67}Ga scanning is sensitive and accurate. When used as a diagnostic tool for suspected abdominal abscesses, it locates and delineates abscesses in somewhat over half the cases. Moreover, the true-negative rate is high and the false-positive rate is acceptably low. Gallium scans should be interpreted with all available clinical information. The coexistence of neoplasm is a problem which at present is not completely resolved.

Since the report of Hayes and Edwards in 1969 (*1*), ^{67}Ga-citrate has frequently been used as a tumor-scanning agent. After incidental note was made of its uptake in infectious processes (*2,3*), Blair, et al (*4*) and Harvey, et al (*5*) successfully detected and delineated experimental abscesses in animals. In 1973, Littenberg, et al (*6*) noted significant gallium uptake in 11 of 12 septic patients. In 1974, Silva, et al showed a 70% correct detection rate in 25 patients with a wide variety of infectious processes (*7*). The present study describes the findings in the first 68 consecutive patients studied prospectively in this laboratory to elaborate and to evaluate further the potential value of ^{67}Ga in detecting and delineating infectious disease. A number of the patients studied initially were included in an earlier report (*7*).

METHODS AND MATERIALS

Patients over the age of 18 in whom an infectious process was suspected were referred from the clinical services of Wilford Hall Medical Center. After informed consent was obtained, the patients were given an intravenous injection of 1–3 mCi ^{67}Ga as the citrate (Diagnostic Isotopes, Upper Saddle River, N.J.). Images were obtained at 48 hr and on occasion again at 72 hr.

Initially a number of studies were made with an Anger camera but as the study progressed, virtually all images were made with a rectilinear device. With the Anger camera (Pho/Gamma III and Pho/Gamma HP, Searle Radiographics, Des Plaines, Ill.) the isotope peak was set at 290 keV with a 25% window. With rectilinear scanners a 230-keV window with an 80-keV base setting was used (encompassing all the major gallium peaks) (Picker Magnascanner, Dual Probe Ohio-Nuclear). Most patients were given a mild purgative the evening before the first scan; a number of patients were given additional purgatives for a 72-hr study.

Upon completion of the first 68 studies, the inpatient records of all the patients were reviewed. Interpretation of the infection screens was correlated with the clinical results contained within each patient's record. Each record was reviewed to ascertain whether or not an infectious process had been present; this judgment was usually made by surgical, pathological, or autopsy evidence but on several occasions by unequivocal response to antibiotic therapy

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in clinically suspicious circumstances, (e.g., a palpable tender abdominal mass resolving with antibiotic therapy or a clinical orbital cellulitis with spinal fluid pleocytosis resolving with antibiotics).

RESULTS

Sixty-eight patients underwent prospective gallium infection surveys in the period March 1972 through December 1973. Twenty-two patients were correctly classified as having an infectious process (Table 1); 37 patients were correctly thought to have no scintigraphically detectable infection. Seven studies were finally believed to be false negatives (clinical infection with a normal scan) and two studies were interpreted as positive in which no infection was demonstrated clinically (Tables 2 and 3).

TABLE 1. TRUE-POSITIVE GALLIUM IMAGES IN 22 PATIENTS

Infection sites	Infectious process
Pulmonary	Coccidioidal lung abscess
	Pseudomonas pneumonia
	Infected lung bulla
Extremities	Infected decubitus
	Parameningeal abscess (2)
	Osteomyelitis (M. abscessus) (2)
	Septic arthritis (S. aureus)
	Septic arthritis (N. meningococcus)
Abdominal	Wound abscess (4)
	Deep abscesses (8)

TABLE 2. FALSE-NEGATIVE SCANS

Infectious process	Number of cases
Bronchiectasis	1
H. influenza pneumonia	1
Subphrenic abscess	2
Ascending cholangitis	2
LUQ abscess	1
	7

TABLE 3. DEEP ABDOMINAL INFECTION SUSPECTS IN 37 PATIENTS

	Scan diagnosis			
Clinical diagnosis	TN	FP	TP	FN
Neg 25	24 (96%)	1 (4.0%)	—	—
Pos 12	—	—	7 (58.3)	5 (41.6)

DISCUSSION

The diagnosis of occult infection remains a difficult clinical problem. Too often the clinician is faced with a difficult diagnostic problem in which currently available tests are unrevealing or equivocal. Clearly, better methods of diagnosing occult infection would be of benefit.

In this study, 39 of 68 patients originally suspected of having infection were clinically found to have no evidence of infection; 37 were correctly identified as not having an infection by prospective scan interpretation. This true-negative rate (94.9%) is reassuring.

Of the twenty-nine patients clinically shown to have infection, scan interpretation correctly identified sites of infection in 22 (75.9%). However, seven (24.1%) had clinically identified infections that were not detected by scan.

False-negative scans. The false-negative scan patients are enumerated in Table 2. In two cases of right subphrenic abscess demonstrated surgically, the diagnosis could not be made on the scan even retrospectively. We feel this negativity may relate to the normally high accumulation of gallium in the liver; this well-recognized limitation of the gallium scan is distressing. Two cases of ascending cholangitis were scintigraphically normal. In both these cases, the infectious process was quite diffuse and quite possibly did not allow sufficient contrast between affected and unaffected areas. A large left upper-quadrant abscess in a postcarcinoma pancreatectomy patient was interpreted as normal gut activity. In retrospect, this area is clearly positive and was misdiagnosed apparently because the very enormity of this process was not imagined. The reasons for a normal thoracic scan in a case of active purulent bronchiectasis and H. influenza pneumonia are not known.

False-positive scans. Two scintigraphs were incorrectly interpreted as positive. One patient had active regional ileitis and showed what was interpreted as abdominal collections of gallium persistent after adequate purging. Possibly the purge was not effective or alternatively the inflammatory process of ileitis may lead to a positive gallium scan.

One false-positive patient was finally adjudged to have aseptic rather than septic necrosis of the hip. Capsular, extrafemoral gallium accumulation in neovascularized tissue, as discussed below, may account for this finding.

Five cases were judged equivocal and have been treated herein as negative studies. All involved suspected intra-abdominal disease. In one, a subphrenic abscess was demonstrated surgically and this case has been listed as a false-negative result. In the other four no infectious process was ever demonstrated.

From these and previously reported data there seems little doubt that gallium becomes concentrated in infected tissues throughout the body. However, there are usually simpler and more reliable ways of determining infection in areas other than the abdomen—the physical examination, radiographs, and other radionuclidic techniques.

Having seen that gallium accumulates in a wide variety of infectious processes throughout the body, it remains to be shown whether this technique has value in intra-abdominal infectious processes where conventional diagnostic procedures are of limited value. In 41 cases abdominal infection was suspected. Gallium scanning correctly diagnosed four of four wound infections. Table 3 shows results of scanning in 37 patients with suspected deep abdominal infections. In 37 cases of suspected deep abdominal infections, 24 negative scans were truly negative as evidenced by subsequent clinical course and 7 positive scans were judged correctly as positive (Table 3). There was one false positive (active Crohn's disease); this case constitutes a "false positive" only insofar as inflammation was present without actual infection.

There were five false negatives (two subphrenic abscesses, two cases of ascending cholangitis, and one left upper-quadrant abscess) for a total abdominal false-negative rate of 41.7%. The true-positive deep abdominal infection detection success rate was therefore 7 of 12 or 58.3%. The four negative cases involving disease of the liver and biliary system underscore the severe limitations of ^{67}Ga in detecting infections in this area. Although Wagner's group (*8*) successfully visualized gallbladder empyema in a small number of cases, they did not report on experience with ascending cholangitis.

In ^{67}Ga-citrate evaluation of infections the active interface of physician (reader) and patient is imperative. Incision sites, colostomy bags, ileal conduits, and masses must be clinically evaluated by the nuclear physician at the time the scan is interpreted.

The mechanism of gallium localization in infectious processes has been discussed in an earlier publication (*7*). At present, we believe that gallium localization in infected tissues results from transport into the area as gallium-protein complexes, specifically as haptoglobin and transferrin complexes. Gunasekera, et al (*9*) have presented evidence that, quantitatively, albumin is the major carrier. Several investigators have suggested that gallium enters infected tissues bound to phagocytes (*10,11*). From current information there is nothing specific about the entry of gallium into infected tissues. This capacity may be shared by other metals, some of which may have more desirable radiopharmaceutical characteristics than ^{67}Ga.

As in other nuclear medicine procedures, exquisite sensitivity destroys specificity. It is not possible to differentiate tumor from infection when both coexist. Moreover, normally high liver activity and unpredictable bowel activity place the clinician at a disadvantage.

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