Detection of Subacute Infectious Foci with Indium-111-Labeled Autologous Leukocytes and Indium-111-Labeled Human Nonspecific Immunoglobulin G: A Prospective Comparative Study

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In 35 patients suspected of an infectious focus, the outcome of scintigraphy with ^{111}In-labeled autologous leukocytes (WBC) and ^{111}In-labeled human nonspecific immunoglobulin G (IgG) was evaluated in a prospective comparative study. Clinical, roentgenologic and microbiologic findings were considered to be proof of the presence of infection or inflammation. In this group of patients with mainly subacute infections, ^{111}In-IgG scintigraphy performed significantly better than ^{111}In-WBC scintigraphy, especially in infections of the locomotor system, but also in various soft-tissue infections. Both techniques showed disappointing results in patients with disseminated yersinia infection and in some patients with tuberculosis. Overall sensitivity and specificity was 74% and 100% for ^{111}In-IgG scintigraphy and 52% and 78% for ^{111}In-WBC scintigraphy, respectively.

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Indium-111-labeled autologous leukocyte (^{111}In-WBC) scintigraphy is widely accepted as the standard technique for the scintigraphic delineation of infectious and inflammatory foci. High accuracy of this imaging procedure has been reported, especially in acute infections (*1*). However, preparation of ^{111}In-WBC is time-consuming, complicated, and costly. Moreover, obtaining sufficient viable leukocytes is more difficult when the peripheral leukocyte count is less than 2×10^9 /liter and practically impossible when less than 0.5×10^9 /liter.

Several reports suggested the utility of ^{111}In-labeled human nonspecific polyclonal immunoglobulin G (IgG) scintigraphy for the detection of infectious foci (*2–5*). Indium-111-IgG is a convenient radiopharmaceutical that can be prepared as a kit and labeled in less than 30 min. If the performance of ^{111}In-IgG scintigraphy would be equal or better than that of ^{111}In-WBC scintigraphy, adequate imaging of focal infection and inflammation becomes available on a wider scale. The present study reports the results of a direct comparison of ^{111}In-IgG scintigraphy to ^{111}In-WBC scintigraphy in a prospective study of patients with subacute infection.

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PATIENTS AND METHODS

Radiopharmaceuticals

Indium-111-WBC. Total WBC count and differentiation were determined. Forty to 50 ml of blood was drawn by venipuncture in a syringe containing 10 ml acid citrate dextrose (ACD). Under strictly sterile conditions, 6 ml 6% hydroxyethyl starch were added to 50 ml of ACD-blood. The erythrocytes were allowed to sediment for 1 hr. The supernatant was removed and centrifuged for 10 min at 150 g. The cell pellet was washed with 5 ml of a 1% human serum albumin (HSA) solution in isotonic phosphate-buffered saline (PBS) buffer (pH = 7.4) and centrifuged once more for 10 min at 150 g. The cell pellet was resuspended in 1.5 ml of a 1% HSA solution in isotonic PBS buffer. Twenty-five to 30 MBq ^{111}In-oxine solution (^{111}In-oxine DRN 4908, Mallinckrodt Diagnostica Holland, Petten, The Netherlands) in 0.2 *M* Tris(hydroxymethyl)aminomethane (pH = 8.0) were added to the cell suspension and incubated for 30 min at room temperature. The cells were centrifuged a third time for 10 min at 150 g, the supernatant discarded and the cell pellet was resuspended in 5 ml of a 1% HSA solution in isotonic PBS buffer. Morphologic integrity of the leukocytes was checked by light microscopic examination. Labeling efficiency, determined by measuring cell-associated and supernatant activity in a sample of the labeled WBC suspension, was always higher than 95%. A dose of 25–30 MBq of ^{111}In-WBC was injected intravenously.

Indium-111-IgG. Diethylenetriaminepentaacetic bicyclic anhydride (bicyclic DTPA) was conjugated to HIV and HBsAg-negative, human, nonspecific, polyclonal IgG (Sandoglobulin, Sandoz AG, Nuernberg, FRG) according to the method described

by Hnatowich and colleagues (*6*). Two to three DTPA ligands were coupled to one IgG molecule. The purified DTPA-conjugated IgG was diluted to 2 mg/ml with 0.15 *M* acetate (pH = 6.5) and sterilized by membrane filtration. Aliquots of 0.5 ml of the conjugate were radiolabeled with ^{111}In (Indium chloride, Amersham International Ltd., Buckinghamshire, UK) via citrate transchelation. Radiochemical purity was determined by ITLC-SG chromatography (Gelman Laboratories, Ann Arbor, MI) with 0.1 *M* citrate (pH = 5) as the solvent. Labeling efficiency was always higher than 95%. A dose of approximately 1 mg of IgG-labeled with 75 MBq ^{111}In was injected intravenously.

Study Design

Since both radiopharmaceuticals were labeled with ^{111}In, the investigations had to be separated in time to allow clearance of the radiopharmaceutical that was administered first. The maximal ^{111}In dose that can be safely injected with leukocytes is limited to 30 MBq (*7,8*). This strict limitation of ^{111}In does not apply to the administration of ^{111}In-IgG (*9*). Therefore, in this study ^{111}In-WBC scintigraphy was performed first and ^{111}In-IgG scintigraphy 1 wk later; in that way adequate images of both radiopharmaceuticals could be obtained, while imaging times remained reasonable. Immediately before the administration of ^{111}In-IgG, the remaining activity of ^{111}In-WBC in the liver and the spleen region was determined and compared to the activity in the ^{111}In-IgG image that was obtained 4 hr postinjection.

Patients

Patients with normal or elevated peripheral leukocyte counts in whom ^{111}In-WBC scintigraphy was indicated because of a suspected focal infection or inflammation were eligible for the study. Patients who did not have a stable medical condition for the interval between the two imaging techniques were excluded.

No patient had a history suggestive of IgA- or IgG-deficiency or adverse reaction to previous IgG administration. Pregnant and lactating females were excluded. Informed consent was obtained from all patients. The study was approved by the Institutional Review Board of the University Hospital Nijmegen.

Thirty-five patients were studied (17 males, 18 females; mean age 51.8 yr, range 18 – 87 yr). The mean WBC count was 8.9×10^9 /liter (range $3.6 - 19.0 \times 10^9$ /liter). The relative number of granulocytes was always higher than 60% of the total WBC count. None of the patients was immunocompromised.

Three other patients were excluded from the study: one patient due to progressive disease, one patient due to regression of an infectious focus, and in the third patient the scintigraphic results could not be verified.

Imaging Procedures

Scintigraphic images were obtained with a Siemens Orbiter gamma-camera connected to a Scintiview image processor (Siemens Inc., Hoffman Estates, IL). All images were collected in digital format in a 256 × 256 matrix. A medium-energy, parallel-hole collimator (173 keV peak, 15% symmetric window; 247 keV peak, 15% symmetric window) was used.

Both ^{111}In-WBC and ^{111}In-IgG images were acquired at 4, 24 and 48 hr postinjection for a preset time of 5, 7.5, and 10 min respectively. At least once, 24 hr postinjection, spot views of the total body were obtained.

The remaining ^{111}In-WBC activity in the liver and spleen region, determined immediately before ^{111}In-IgG injection, was always lower than 10% of the ^{111}In-IgG activity in the same region on the image obtained 4 hr after ^{111}In-IgG administration.

All images were interpreted by three observers blinded to the results of the verification procedures. An ^{111}In-WBC scintigraphy was interpreted as positive if consistent, focally increased uptake was seen during the study, excluding known causes for artifacts. An ^{111}In-IgG scan was interpreted as positive if focally increasing accumulation could be noted over time, since hyperemic noninflamed lesions initially show some uptake but no further accumulation of ^{111}In-IgG over time (*5*).

The results of the scintigraphic findings were verified by clinical, roentgenological and ultrasonographic methods and, if possible, by bacterial cultures. The outcome of the two imaging techniques was analyzed, using the χ^2 - test.

RESULTS

The clinical characteristics, scintigraphic results and verification procedures are summarized in the Tables 1 and 2. Table 1 represents those patients with infections predominantly of the locomotor system; Table 2 those patients with other types of infection. All possible infections were either subacute—duration of illness for several weeks—or chronic—duration of illness for months or even years.

All lesions in the locomotor system (Table 1) were correctly identified with ^{111}In-IgG scintigraphy. Two cases of arthritis and two cases of osteomyelitis were missed with ^{111}In-WBC scintigraphy. One rib lesion on ^{111}In-WBC scintigraphy could not be proven by other diagnostic techniques. Figure 1 shows concordant ^{111}In-IgG and ^{111}In-WBC images of a soft-tissue infection caused by hemolytic Streptococci in Patient 9.

In Patient 15 (Table 2) abscesses in the liver, caused by *Bacteroides fragilis*, were seen on the ^{111}In-WBC scintigraphy, while ^{111}In-IgG was distributed homogeneously in the liver. This was the only patient with verified infectious foci, which were correctly identified with ^{111}In-WBC, but missed with ^{111}In-IgG scintigraphy.

Figure 2 represents the images of Patient 16 who has diverticulitis. With ^{111}In-IgG scintigraphy, inflammatory activity was adequately detected, while ^{111}In-WBC scintigraphy showed no abnormalities. In a splenectomized patient (no. 17) ^{111}In-WBC scintigraphy indicated left-sided, subphrenic activity, while no elevated ^{111}In-IgG uptake was seen. At surgery, neither abdominal infection nor accessory splenic tissue were found.

Figure 3 shows the images of Patient 32 who had renal failure due to polycystic kidneys and *Escherichia coli* infection of a renal cyst. There is increased ^{111}In-IgG uptake, but no abnormal ^{111}In-WBC accumulation.

Two patients had malignant tumors. In Patient 8, a mediastinal malignant non-Hodgkin's lymphoma was diagnosed. Patient 23 had an alveolar cell carcinoma of the lung and a malignant non-Hodgkin's lymphoma. The tumors did not show pathologic ^{111}In-WBC or ^{111}In-IgG accumulation.

When using lesions rather than patients, sensitivity and specificity in this group of patients was 74% and 100% for ^{111}In-IgG scintigraphy and 52% and 78% for ^{111}In-WBC

TABLE 1
Clinical Characteristics, Scintigraphy and Verification Results for Patients with Infections of the Locomotor System

Patient no.	Sex/ Age (WBCC)	Duration	Suspected focus	Scintigraphy		Verification	
				WBC	IgG	Proc.	Result
1	F/79 (8.7)	2 mo	Shoulder	+	+	P	\
			Knee	+	+	P	— MT infection
			Lumbar spine	+	+	P	/
			Total-hip prosthesis	−	−	F, R	no evidence of infection
2	F/59 (8.4)	2 mo	Proximal femur	+	+	S	nonspecific osteomyelitis
			Lumbar spine	−	−	P	no infection
			Femoral blood vessels	+	−	F	no evidence of infection or thrombosis
3	F/51 (6.4)	3 mo	Sternum	−	−	F, R, C	no evidence of persisting infection
4	M/54 (13.1)	10 yr	Tibia	+	+	F, R	osteomyelitis of tibia (productive fistula)
5	M/32 (11.1)	1 yr	Delayed healing of tibial fracture	−	−	S	noninfected osteosynthesis after tibial fracture
6	F/43 (7.5)	2 mo	Toe	−	+	C, R	SA osteomyelitis of toe
7	F/87 (4.9)	2 wk	Knee	−	+	P	synovitis
			Total-hip prosthesis	−	−	F, R	no evidence of infection
8	M/34 (6.6)	4 wk	Sternum	−	+	C, R, F	SM osteomyelitis
9	F/61 (15.6)	3 wk	Upper leg/pelvic soft tissues	+	+	P	HS infection
10	F/76 (11.7)	4 mo	Total-hip prosthesis	−	−	F, R	no evidence of infection
11	F/66 (4.7)	6 wk	Thoracic spine	+	+	P	HS infection
			Hip	−	+	P	HS infection
12	F/27 (3.6)	3 wk	Shoulder	+	+	S	SA arthritis
13	M/60 (17.2)	3 wk	Upper leg	+	+	S	\
			Shoulder	+	+	S	— SA infection
			Foot	+	+	P	/
14	F/67 (4.9)	9 mo	Total-hip prosthesis	−	−	F, R	no evidence of infection

WBCC = white blood cell count ($\times 10^9$/liter). C = bacterial cultures; E = endoscopy; F = clinical follow-up of at least 3 mo; P = puncture/biopsy; R = roentgenologic procedures, including CT scanning and ultrasonography; S = surgery; BF = *Bacteroides fragilis*, CA = *Candida albicans*; EA = *Enterobacter aerogenes*; EC = *Escherichia coli*; HS = β-hemolytic streptococcus; MT = Mycobacterium tuberculosis; SA = *Staphylococcus aureus*; SM = Streptococcus mitis; and SP = Streptococcus pneumoniae.

scintigraphy, respectively. The differences between the two techniques are significant ($\chi^2 = 6.50$, $p < 0.01$).

DISCUSSION

The results of the present prospective comparative study indicate that ^{111}In-IgG scintigraphy performed significantly better than ^{111}In-WBC scintigraphy in this group of patients with subacute infections. The majority of the detected infections was localized in the locomotor system. The usefulness of ^{111}In-IgG scintigraphy for the detection of infections of the locomotor system corroborates the results in a previous study from our group in which no comparison was made with ^{111}In-WBC scintigraphy (*5*). The relatively poor performance of ^{111}In-WBC scintigraphy in subacute infectious bone and joint disease is in agreement with the findings of other authors (*1*,*10*,*11*).

The scintigraphic result in the patient with liver abscesses cannot be explained satisfactorily. A possible explanation for the normal ^{111}In-IgG images could be that the degree of inflammation decreased with treatment (a daily dose of 2 g of metronidazole intravenously).

The performance of ^{111}In-IgG scintigraphy in abdominal infections is in agreement with data in the literature (*2*). Although accessory splenic tissue was not found at surgery in the splenectomized patient, it could have been the cause for the false-positive ^{111}In-WBC scintigraphy. Unfortunately, ^{99m}Tc-sulphur colloid scintigraphy could not be performed.

Both ^{111}In-WBC and ^{111}In-IgG scintigraphy missed a case of endocarditis. This was not surprising since ^{111}In-IgG shows a physiologic high blood-pool activity in all patients, thereby obscuring possible cardiac lesions. Moreover, these small lesions show only mild inflammation.

In four patients with vascular lesions, ^{111}In-WBC scin-

TABLE 2
Clinical Characteristics of Scintigraphy and Verification Results for Patients with Other Types of Infection

Patient no.	Sex/ Age (WBCC)	Duration	Suspected focus	Scintigraphy		Verification	
				WBC	IgG	Procedure	Result
15	M/23 (8.8)	1 mo	Liver	+	–	R, C	multiple BF liver abscesses
16	F/80 (5.7)	3 wk	Lower abdomen	–	+	E	diverticulitis of the sigmoid
17	F/32 (8.9)	1 mo	Abdomen, persisting infection after splenectomy	+	–	S	no infection, no accessory splenic tissue
18	F/42 (10.9)	1 mo	Abdomen	–	–	S	polycystic ovaries, no infection
19	M/49 (5.1)	1 mo	Treated EC sepsis, no focus	–	–	F, C, R	no evidence of persisting infection
20	F/65 (5.0)	6 mo	Fever of unknown origin	–	–	F, C, R	no cause identified
21	M/27 (5.6)	1 yr	Fever of unknown origin	–	–	F, C, R	no infectious focus identified, fever of hypothalamic origin
22	M/60 (10.2)	4 wk	Fever of unknown origin	–	–	F, R, C	no cause identified
23	M/76 (5.3)	4 wk	Fever of unknown origin	–	–	F, C, R	no evidence of infection, fever caused by malignant lymphoma or lungcarcinoma
24	M/81 (10.8)	4 wk	Endocarditis	–	–	C, R	EA infection
			Femoral blood vessels	+	–	F	no evidence of infection or thrombosis
			Rib	+	–	F, R	no evidence of infection
25	F/42 (8.8)	6 mo	Aorto-bifemoral Vascular graft	–	–	S	infected graft (intestinal bacteria)
26	F/22 (9.2)	6 wk	Pulmonary tuberculosis	–	–	C, R	primary MT infection upper lobe of left lung
			Hilar lymph node involvement	+	–	R, F	no evidence of lymph node involvement
27	M/38 (11.1)	4 wk	Pulmonary tuberculosis	+	+	C, R	primary MT infection upper lobe of both lungs
28	M/30 (19.0)	6 wk	Pulmonary tuberculosis	+	+	C, R	primary MT infection both lungs
29	M/59 (6.6)	6 wk	Pulmonary tuberculosis	–	–	C, R	miliary MT infection of lungs
30	F/55 (8.9)	1 mo	Eye (prior to scintigraphy: surgical and medical treatment for CA endophthalmitis)	–	–	F	no evidence of persisting infection
31	M/75 (11.4)	3 wk	Eye	–	+	S	SP endophthalmitis
			Shoulder	–	–	P	no evidence of infection
32	M/58 (10.4)	2 wk	Polycystic kidneys	–	+	C, F	EC infection of renal cyst
33	F/59 (6.1)	2 mo	Polycystic kidneys	–	–	F, C	no evidence of infection
			Treated pyelonephritis of renal transplant	–	–	F, C, P	no evidence of persisting infection
34	M/25 (7.2)	3 wk	Positive yersinia serology, no focus	–	–	F, R	no focus identified
35	M/18 (10.7)	1 yr	Positive yersinia serology, no focus	–	–	F, R	no focus identified

See Table 1 for definitions.

tigraphy showed two sites of accumulation in the femoral vein or artery. Since clinical examination and follow-up ruled out infection or thrombosis, the two lesions had to be considered false-positives. Both techniques apparently missed a low-grade infection of a vascular graft. However, data in the literature suggest that ^{111}In-IgG scintigraphy is a good technique for evaluation of vascular graft infection (*4*).

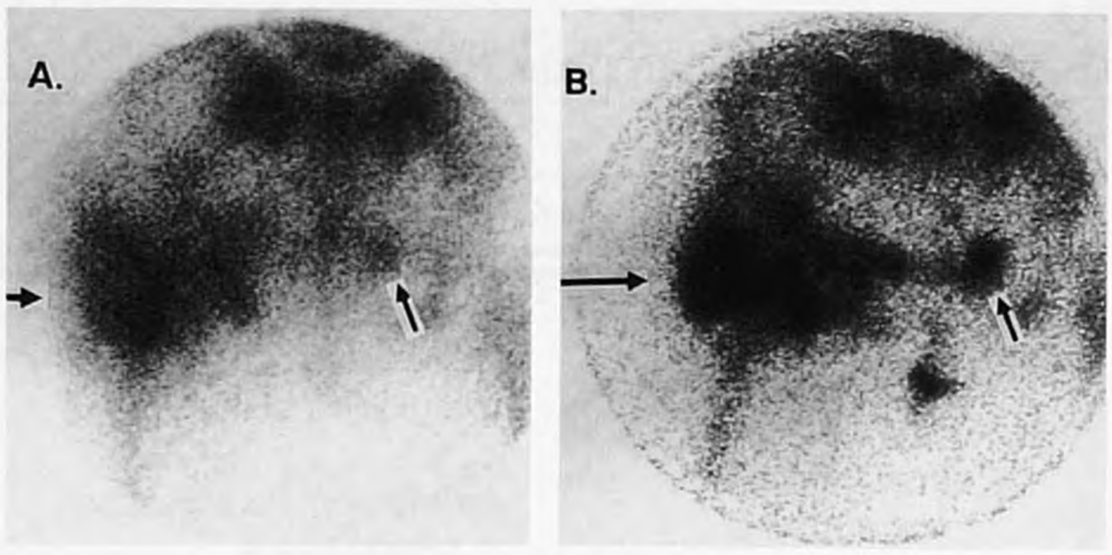

FIGURE 1. Concordant ^{111}In-IgG and ^{111}In-WBC scintigraphies: soft tissue infection of the upper left leg (large arrows), extending to the bladder region (small arrows), in Patient 9, due to hemolytic streptococci. (A) ^{111}In-IgG scintigraphy, posterior view of the pelvis, 48 hr postinjection. (B) ^{111}In-WBC scintigraphy, posterior view of the pelvis, 48 hr postinjection.

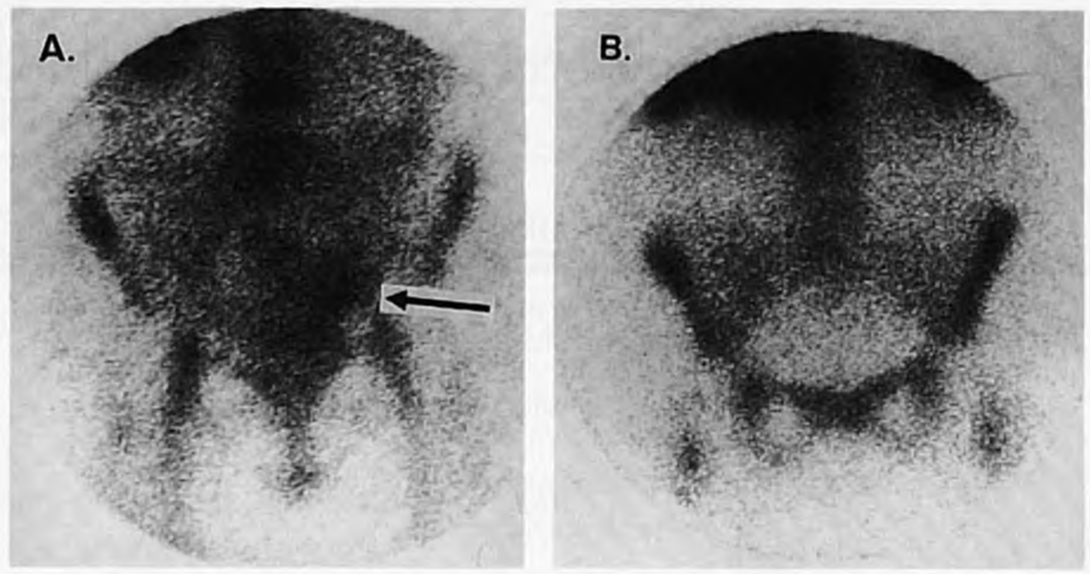

FIGURE 2. True-positive ^{111}In-IgG scintigraphy and false-negative ^{111}In-WBC scintigraphy: diverticulitis of the sigmoid, proven at endoscopy, in Patient 16. (A) ^{111}In-IgG scintigraphy, anterior view of the pelvis, 48 hr post-postinjection: increased ^{111}In-IgG uptake in the lower left abdomen (arrow). (B) ^{111}In-WBC scintigraphy, anterior view of the pelvis, 48 hr postinjection: no abnormal accumulation of activity in the abdomen.

Both techniques showed variable results in the delineation of tuberculous infection. Large lesions were adequately detected, whereas small infectious foci were missed. One probable explanation for the negative WBC scintigraphies is that lymphocytes and macrophages, rather than granulocytes, are involved in a tuberculosis infection.

The detection of an infected renal cyst with ^{111}In-IgG was only possible because this patient had renal failure and was on hemodialysis. In patients with normal renal function, it will be nearly impossible to delineate infection in the kidneys, since the physiologic ^{111}In-IgG uptake in kidneys will most probably obscure pathologic accumulation. The utility of ^{111}In-IgG scintigraphy for detection of infectious foci in uremic patients is not well established. Tolkoff and Rubin suggest that under these circumstances ^{111}In-IgG accumulation in infectious foci is poor (*12*).

The normal scintigraphy of the two patients with active disseminated yersiniosis can probably be explained according to the literature by the small size of the infectious foci and the localization in mesenteric lymphnodes and parenchymatous organs (*13*). Detection of such small lesions with moderately increased activity is not possible due to a relatively poor target/non-target ratio and to the limited resolution of the gamma camera, especially when localized in organs with relatively high physiologic activity uptake such as liver and kidneys.

The subacute nature of the infections we studied, in many patients not accompanied by leukocytosis, could partially explain the relatively large number of false-negative ^{111}In-WBC results. The number of WBC appears not to be a major factor in ^{111}In-IgG accumulation, since ^{111}In-IgG accumulated in infectious foci in granulocytopenic patients (*14*).

Indium-111-WBC have a half-life in the circulation of approximately 6 hr (*15*). This fast blood clearance results in low background activity. With ^{111}In-IgG scintigraphy, target-to-background ratios were lower due to the relatively slower blood clearance of ^{111}In-IgG ($t_{1/2}$ approximately 24 hr) (*5*). However, this did not significantly interfere with image interpretation at 24 and 48 hr.

When designing the comparative study, several options were considered. A random sequence of the two techniques would have been the best choice. This was reluctantly rejected for a number of reasons. The ^{111}In dose that can be safely injected with leukocytes is limited to 30 MBq

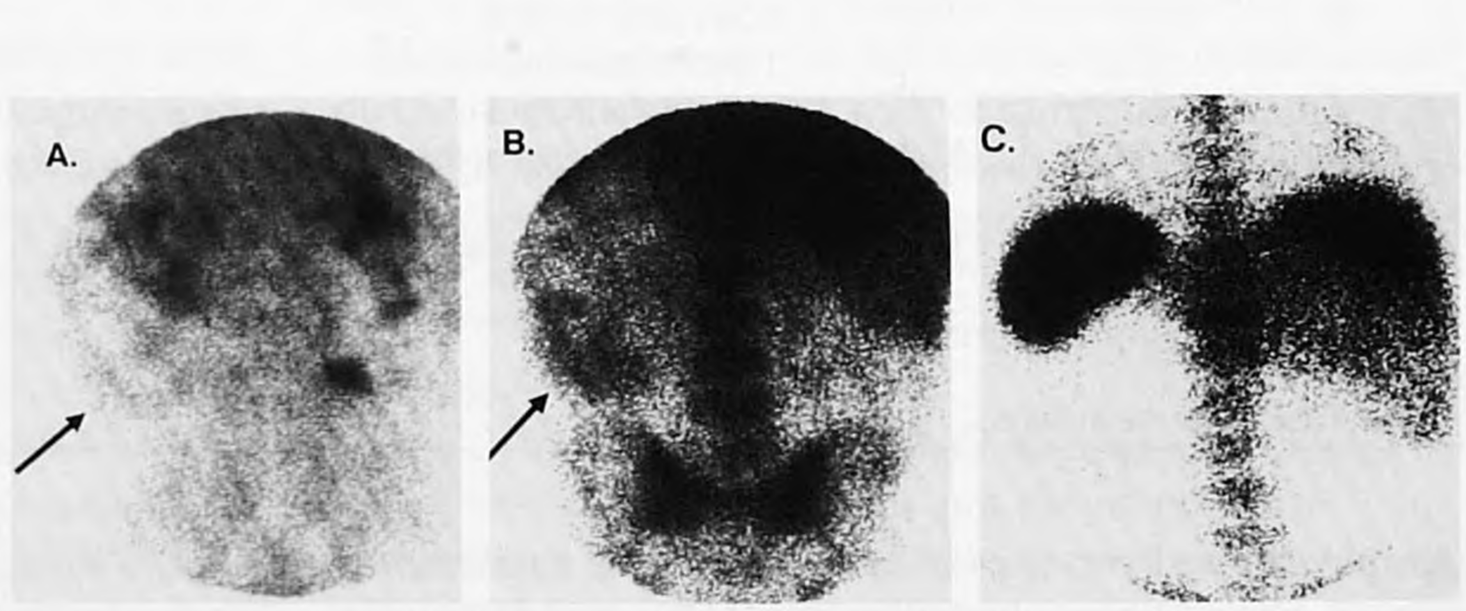

FIGURE 3. True-positive ^{111}In-IgG scintigraphy and false-negative ^{111}In-WBC scintigraphy: *Escherichia coli* infection of a cyst in the left kidney of Patient 32 with renal failure due to polycystic kidneys. The patient was on hemodialysis. (A) ^{99m}Tc-mercaptoacetyltriglycine scintigraphy, posterior view of the kidneys, 15 min postinjection: identification of residual kidney function. Note: no functional kidney tissue in the lower pole of the left kidney (arrow). (B) ^{111}In-IgG scintigraphy, posterior view, 48 hr postinjection: increased uptake in the lower pole of the left kidney (arrow). (C) ^{111}In-WBC scintigraphy, posterior view, 48 hr postinjection: absence of accumulation of activity in the renal regions.

because of possible chromosomal damage to long-lived T-lymphocytes and the radiation burden to the spleen (*7,8*). Biodistribution and kinetic studies showed that this strict limitation does not apply to the administration of ^{111}In-IgG (*9*). If one would choose to perform the investigations in a random sequence, it would be necessary to lower the injected ^{111}In-IgG dose to approximately 15 MBq for the first investigation. This would lead to unacceptably long imaging times or to statistically inadequate images. Injection of the full dose of 75 MBq ^{111}In-IgG before the ^{111}In-WBC scintigraphy would increase the time span between the two studies to at least 2 wk in order to avoid significant ^{111}In-IgG contribution to the ^{111}In-WBC images. Moreover, ^{111}In-WBC scintigraphy, being the standard procedure, was considered to be of clinical importance and therefore was accepted in the final study design as the first procedure. In the current study, there was no significant contribution of ^{111}In-WBC activity in the ^{111}In-IgG images.

When comparing ^{111}In-WBC and ^{111}In-IgG scintigraphy in a fixed sequence, the two investigations had to be separated in time. This introduces some inevitable bias. Indium-111-Ig scintigraphy was systematically placed in a disadvantageous position, since many patients were treated for a longer period of time. Only patients with disease in a relatively stable and subacute condition were eligible for the study. Patients with acute infections, who required immediate invasive therapy after completion of ^{111}In-WBC scintigraphy, were not studied in this protocol. Nevertheless, we feel that our patients are representative candidates for such imaging procedures, since a major indication for these scintigraphic techniques is localization of chronic infection. While data in the literature as well as our own experience suggest that acute infections can be adequately detected with both ^{111}In-WBC and ^{111}In-IgG scintigraphy (*2,16*), clinical examination and other imaging techniques are usually sufficient.

Alternatives for comparative studies between WBC and IgG scintigraphy would be to label one of the two pharmaceuticals with ^{99m}Tc. Buscombe et al. found that ^{99m}Tc-IgG and ^{111}In-WBC scintigraphy showed excellent concordance (*17*). In this study, the authors co-injected both radiopharmaceuticals. They did not provide information as to whether ^{111}In scatter in the ^{99m}Tc window at 24 hr postinjection could have possibly contributed to some extent to the concordance between the two techniques at 24 hr postinjection. In their study protocol, ^{111}In-WBC scintigraphy was the gold standard. In our study, we found 13 false-negative with ^{111}In-WBC scintigraphy, mainly in patients with low-grade bone and joint infections. An important question is whether ^{99m}Tc-labeled IgG performs equally to ^{111}In-IgG. In artificially induced calf muscle abscesses in rats, we found that ^{99m}Tc-labeled IgG shows relatively poor uptake when compared to ^{111}In-IgG uptake, although target/non-target ratios were similar (*18*). Another alternative for comparing ^{111}In-IgG scintigraphy with labeled WBC could be ^{99m}Tc-labeling of WBCs. Technetium-99m-hexamethylpropyleneamine-oxime (HMPAO) labeled WBCs seems to be a useful technique for labeling leukocytes with ^{99m}Tc and appears promising in chronic infectious disease in humans (*19–21*). However, a disadvantage of this technique is that rapid biliary excretion of ^{99m}Tc-HMPAO interferes with interpretation of abdominal images obtained later than 2–3 hr postinjection. The ^{99m}Tc-colloid labeling of leukocytes in whole blood is poorly established (*22–24*). A major limitation of every radiopharmaceutical labeled with ^{99m}Tc is that imaging beyond 24 hr after injection is impossible.

Although ^{67}Ga has been used successfully in the evaluation of patients with subacute and chronic illness, the multi-peak high energy gamma rays, the physiologic bowel excretion and the nonspecific uptake in tumors and in areas of increased bone turnover make ^{67}Ga-citrate a less optimal radiopharmaceutical for delineating infection (*17, 21*).

The mechanism of ^{111}In-IgG accumulation is not fully elucidated as yet. Increased vascular permeability and nonspecific macromolecular entrapment in inflammatory foci is the most probable hypothesis (*14,25*). Notwithstanding the uncertainty of the mechanism of accumulation of IgG, the present study shows that ^{111}In-IgG scintigraphy performs significantly better in patients with subacute infections than ^{111}In-WBC scintigraphy. In addition, ^{111}In-IgG is a more convenient radiopharmaceutical in that it is readily available as a sterile, pyrogen-free kit for fast labeling, obviating the need for handling the patient's blood or a 3-hr labeling procedure. Moreover, since IgG is a human protein, there is no risk for the development of human anti-mouse antibodies that may cause side effects (*26,27*).

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