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Radiolabeled Immunoglobulin Scintigraphy for the Diagnosis of Spondylodiscitis

TO THE EDITOR: Datz et al.'s article on the efficacy of ^{111}In -polyclonal immunoglobulin G (IgG) to detect infection and inflammation (1) contains one case of spondylodiscitis in which scintigraphy with ^{111}In -IgG yielded a positive result. Another five true-positive results have been obtained with this tracer in cases of spondylodiscitis caused by various organisms (2).

Labeled leukocytes have difficulty establishing the diagnosis of spondylitis/spondylodiscitis (3-5). Uptake of ^{67}Ga is aspecific. Therefore, polyclonal IgG potentially could be useful for this diagnosis. However, since no other spinal diseases have been included in the above mentioned series, questions about the specificity of this method for the diagnosis of spondylodiscitis still need to be addressed.

Results obtained with $^{99\text{m}}\text{Tc}$ -IgG have been less encouraging. In one study using iminothiolane-derived IgG, three cases of spondylitis were found false-negative with $^{99\text{m}}\text{Tc}$ -IgG (6). Another study using DTPA conjugated IgG, reported one false-negative and two true-positive results (7). Our own experience with $^{99\text{m}}\text{Tc}$ -IgG for the diagnosis of spondylodiscitis is summarized in Table 1. Images were obtained at approximately 5 and 24 hr after injection of 555 MBq $^{99\text{m}}\text{Tc}$ -IgG labeled via its iminothiolane derivative.

From these cumulative data, it would appear that $^{99\text{m}}\text{Tc}$ -IgG lacks sensitivity for the diagnosis of spondylodiscitis, perhaps unlike its ^{111}In -labeled counterpart. Differences between the bio-distribution of ^{111}In - and $^{99\text{m}}\text{Tc}$ -IgG have also been observed in animal models of focal infection (8). Technetium-IgG radiolabeled via the hydrazino nicotinamide derivative is known from animal studies to behave more like ^{111}In -IgG (9).

In conclusion, although radiolabeled IgG may hold promise for

the diagnosis of infectious spondylitis, further studies in more extensive patient groups are required to define its specificity and sensitivity in this respect, as well as the radiolabel and radiolabeling method of choice.

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REPLY: There are a number of problems with using radionuclide infection imaging agents for diagnosing osteomyelitis/discitis of the spine, especially in postoperative patients.

Indium-111-leukocytes detect most musculoskeletal infections with reported sensitivities ranging from 83% to 100%. Several recent studies, however, have shown that ^{111}In -leukocytes are less sensitive for spine infections. In 22 patients with biopsy proven osteomyelitis/discitis, Whalen et al. found that the leukocyte scan had a sensitivity of only 13% (2). Palestro et al. studied 71 patients with suspected vertebral osteomyelitis and found only 39% had increased activity. A total of 7% had normal studies and 54% had photopenic defects (3). Unfortunately, photopenia on leukocyte scans is not specific for osteomyelitis. Cold defects have been described in tumor, radiation, fracture, Paget's disease, degenerative arthritis and following surgery (4).

It is unclear why labeled leukocytes do not detect vertebral infections as well as other musculoskeletal infections. A pathophysiologic explanation has been offered by Palestro (5). Vertebral osteomyelitis likely originates as a septic embolism that lodges in a metaphyseal artery. Retrograde propagation into the metaphyseal anastomosis circumferentially around the vertebral body may involve other metaphyseal arteries, with the development of sequential septic infarcts. Occlusion of such a large number of vessels may impede white cell migration to the site of infection. Lower sensitivity in spine infections may be partially explained by the difficulty in detecting cold defects compared to hot lesions. The timing of the scan may also be important. At the

TABLE 1

Technetium-99m-IgG Imaging in Six Patients with Suspected Spondylodiscitis

Sex	Age	Location	Verification procedure	Imaging
M	77	L4-L5	CT, MRI, culture (<i>Candida parapsilosis</i>)	TP*
F	47	L1L2	CT, MRI	FN
M	47	L4L5	Ziehl staining of surgical specimen	FN
F	32	L3L4, L4-L5	Follow-up	TN†
F	41	L5S1	MRI	TN
F	24	Lumbar spine	Follow-up	TN

*Abscess with extravertebral extension.

†Previous spondylodiscitis due to *Pseudomonas aeruginosa*.

TP = true-positive; FN = false-negative, TN = true-negative.

start of imaging, it may appear hot; with time, the activity may decrease and eventually become cold. Such changes have been described in bone infarcts when imaging with ^{99m}Tc -methylene diphosphonate.

Many patients with suspected infections undergo antibiotic therapy before imaging. Could antibiotic treatment be the cause of lower sensitivity? We have shown that antibiotics do not significantly affect the sensitivity of the leukocyte scan in soft-tissue infections (6). It seems unlikely that antibiotics would affect leukocyte entry into inflammatory sites in the spine differently than they would in other locations.

Finally, chronicity of infection could theoretically affect leukocyte kinetics. Studies with a small numbers of patients have shown decreased sensitivity in chronic infections. We, however, studied 155 patients with chronic infections who had undergone ^{111}In -leukocyte imaging and found only a slight decrease in sensitivity in chronic infections (7).

Antigranulocyte antibodies have also shown a low sensitivity for spinal infections. In 20 cases of chronic osteomyelitis, six peripheral infections showed increased antibody uptake, whereas all eight cases of spinal osteomyelitis showed cold defects (8). Others have noted decreased sensitivity in central bone infections with antigranulocyte antibodies (9).

The sensitivity of radiolabeled polyclonal IgG for vertebral infections is less clear. In a comparison of antigranulocyte antibodies and technetium-polyclonal IgG, five of eight cases which were negative with antigranulocyte antibodies were positive with polyclonal IgG (8). These investigators felt the high normal marrow uptake of antigranulocyte antibodies due to labeling of granulocytic precursors made identification of increased uptake in the spine difficult. Polyclonal IgG has lower marrow uptake, which improves the target-to-background ratio in this region. As noted by De Geeter, however, others have found poorer results with ^{99m}Tc -polyclonal IgG. As De Geeter states, there may be differences between ^{111}In - and ^{99m}Tc -IgG. Indeed, IgG retention in abscesses varies with the radioisotope used to label the protein (10). Further clinical studies of the effectiveness of polyclonal IgG in the spine will be necessary to determine its utility for vertebral osteomyelitis/discitis.

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of a new infection imaging agent, In-111-polyclonal IgG, in normal subjects. *J Nucl Med* 1995;in press.

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Clarification of the Final Fanny

TO THE EDITOR: In regard to the July 1994 First Impressions (1), I do not think the clinical and scintigraphic findings correlate with the stated mechanism of injury. The images clearly show the abnormality on the left buttocks. If the patient sustained this injury on the stairway depicted, she would have been forced to sit reversed with her legs dangling over the banister (a difficult task for someone with advanced rheumatoid disease). I can think of three possible explanations:

1. The L-R markers are reversed on the posterior image, a not uncommon problem in our laboratory.
2. The photo of the stairway is reversed.
3. The actual facts are not what were presented.

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REPLY: Congratulations to Dr. Rudd for such an astute observation. Dr. Rudd's confusion is understandable because the picture of the staircase was not from the patient's house but is an example from an architectural textbook to demonstrate final and banister. The facts given and markers on the posterior view are correct.

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Technetium-99m-RBC Scintigraphy in Liver Metastasis

TO THE EDITOR: Farlow et al. reported a case in which a liver metastasis from a neuroendocrine carcinoma displayed "the typical appearance of a hepatic hemangioma with perfusion to blood-pool mismatch and an increase in blood-pool activity from early to delayed images" on ^{99m}Tc -red blood cell (RBC) scintigraphy.

We studied a 62-yr-old male with carcinoma of the urinary bladder who was admitted for follow-up studies. Abdominal ultrasonography revealed a solitary hepatic lesion in the left lobe close to the porta hepatis. The lesion was solid with a hypochoic pattern measuring 2 cm in diameter. No focal defect was identi-