

Scintigraphic Detection of Osteomyelitis with Tc-99m MDP and Ga-67 Citrate: Concise Communication

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Using both Tc-99m methylene diphosphonate and gallium-67 citrate, images of the lower extremities in New Zealand white rabbits were obtained on sequential days after inoculation of tibias with *Staphylococcus aureus*. Gallium-67 scintigraphy was positive earlier in the course of infection than Tc-99m MDP scintigraphy. In addition to 4-hr Ga-67 scintigrams, 24-hr and 48-hr scintigrams were obtained, contributing substantially to interpretation. However, 72-hr Ga-67 scintigrams contributed little additional information.

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Because the early signs and symptoms of osteomyelitis are nonspecific, it is common clinical practice to use Tc-99m MDP and/or Ga-67 citrate scintigraphy to supplement the clinical and laboratory diagnosis (1,2). When scintigrams were compared with radiographs, scintigraphy was consistently found to be more sensitive at an earlier time (1-8). Therefore, the diagnosis and early treatment of osteomyelitis depends on the accurate interpretation of gamma imaging. Although the sensitivity and accuracy in diagnosing osteomyelitis has been studied with Tc-99m MDP by itself (3,5,6,9), and in combination with Ga-67 citrate (4,10,11), the latent period from introduction of an infection to positivity of the Tc-99m MDP and Ga-67 citrate scintigrams in acute osteomyelitis has not been well studied (12-14). The purpose of the present work was to examine this question in an animal model and briefly summarize the current literature.

METHODS

Six groups of four New Zealand white rabbits were inoculated using the model of Norden to establish os-

teomyelitis (15). After the right hindleg was shaved, the rabbit was anesthetized with 2.0 cc of ketamine and 0.4 cc acepromazine. An 18-gauge needle was inserted into the tibial shaft and a suspension of *Staphylococcus aureus* and sodium morrhuate was injected. As controls, six additional rabbits were inoculated with sodium morrhuate alone.

After inoculation, the groups were sequentially labeled one through seven, the numbers corresponding to the postinoculation day that each was selected for study. For Group 1, Ga-67 and Tc-99m MDP were injected at 24 hr after the *S. aureus* inoculation; for Group 2, the same procedure at 48 hr, and so on. Each group contained one control member who received no *S. aureus*.

Gallium-67 citrate images of the lower extremities, in an anterior view, were made at 6, 24, 48, and 72 hr after injection of the tracer, using a large-field gamma camera with a parallel-hole, medium-energy collimator, with 20% windows set at 185 keV and 300 keV. Each image had 100,000 counts. Images from each rabbit were interpreted independently by three staff physicians beginning with the Tc-99m MDP image and followed by the 6, 24, 48, and 72-hr Ga-67 citrate images.

At the end of the 72-hr Ga-67 image, the rabbits were killed. The right tibia was isolated, flushed with sterile phosphate buffer at pH 7.4, and cultured on trypticase soy agar (15). The plates were incubated for 48 hr at 37°C and the colonies counted.

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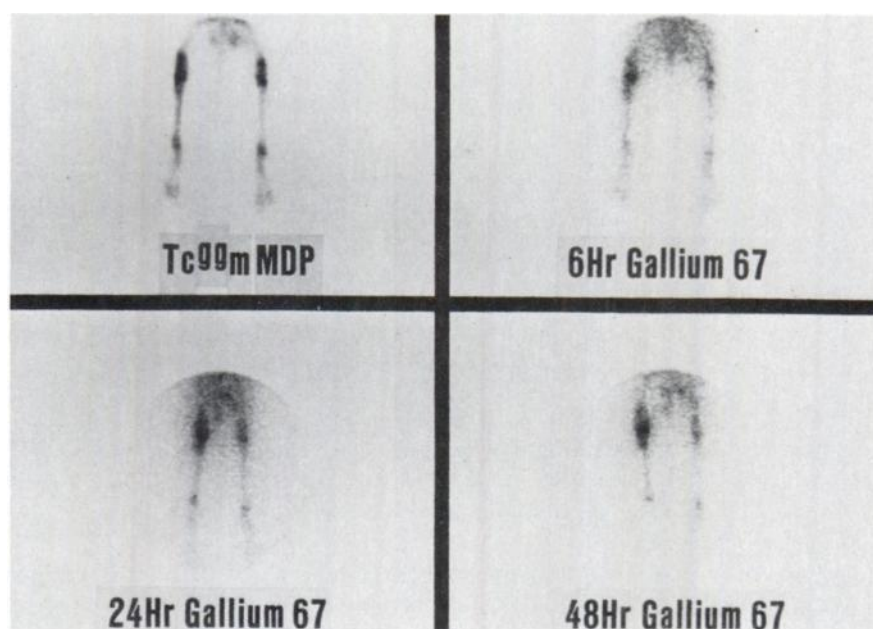


FIG. 1. Images of lower extremities 5 days after inoculation demonstrate abnormal Tc-99m MDP and Ga-67 accumulation in right distal femur and proximal tibia.

RESULTS

Five animals were eliminated from the study because of failure to establish osteomyelitis. In the control rabbits, no abnormal Tc-99m MDP activity was found, but in Groups 4 and 5 mild Ga-67 activity was seen very focally in the tibia on the 24- and 48-hr images. The activity was substantially less intense than the accumulations seen with active osteomyelitis.

No Tc-99m MDP images showed abnormal activity until Day 3 and, as seen in Table 1, the number of positive images in each group increased progressively until Day 6, when all were positive. The false-negative Tc-99m MDP image at Day 5 should be noted.

Gallium-67 began to accumulate at Day 2 after inoculation and became uniformly positive at Day 3. The false-negative Tc-99m MDP on Day 5 also had an accompanying false-negative Ga-67 image. Culture of that bone, however, demonstrated substantial growth of organisms. By Day 3, close correlation was seen between the Ga-67 scintigrams and Tc-99m MDP, as shown in Fig. 1. Before Day 3, the Ga-67 scintigram was more sensitive (see Fig. 2).

DISCUSSION

Organisms can invade and seed the bone by extension from an adjacent soft-tissue infection, directly from an open fracture, or hematogenously (2). A medium for infection that is immunologically isolated appears necessary for the successful growth of organisms once planted in the bone marrow. In animal models, direct injection of an inoculum into the blood or bone is unsuccessful unless a sequestrum has been preformed by

mechanical damage or by injecting a sclerosing agent into the marrow cavity (15,16). Since most models provide a rather large inoculum and a preformed sequestrum, the clinical course in these models probably progresses more rapidly in the early stages of osteomyelitis than in humans. Human studies, on the other hand, suffer from the difficulty of establishing the diagnosis of osteomyelitis with certainty.

Acute hematogenous osteomyelitis begins as an intramedullary process, extending to the bone cortex secondarily (2). It may be logical to assume, therefore, that an agent responsive to inflammation within the bone marrow would be more sensitive for detecting osteomyelitis (17). The Tc-99m MDP, in addition to exhibiting increased uptake secondary to metabolic change in the bone cortex, may also exhibit increased uptake secondary to increased blood flow (18,19). Since the initial enthusiasm for the scintigraphic detection of osteomyelitis by Tc-99m MDP bone image (3,6,10,20,21), however, reports have appeared that question its sensitivity (9,22-24). Sullivan et al. (9) reviewed the scintigraphic findings in 21 children with culture-proven osteomyelitis. Only 14 of 21 scintigrams were correctly interpreted as osteomyelitis. Ash et al. (24), reviewed the bone-image findings in ten infants and found a sensitivity of only 42%. To increase the sensitivity of Tc-99m MDP in detecting osteomyelitis, blood-pool imaging was added to the usual delayed scintigrams, but the results have been disappointing. Gilday et al. and Maurer et al., (21,25) report an increase in the specificity of scintigraphy for osteomyelitis when blood-pool imaging is added. This is designed to allow soft-tissue involvement to be differentiated from osseous changes alone. We have

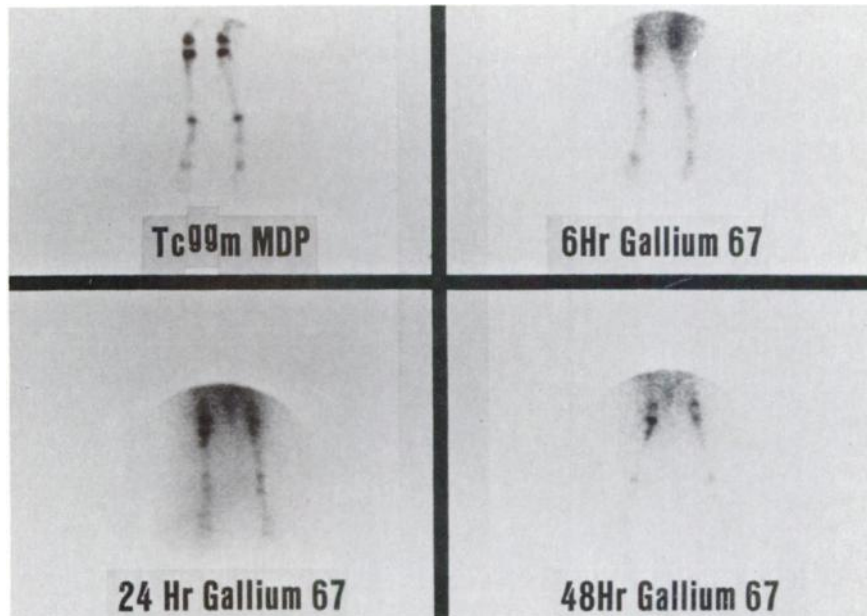


FIG. 2 Two days after inoculation there is normal Tc-99m distribution in this rabbit's lower extremity. Ga-67, however, concentrates abnormally in right proximal tibia.

found such blood-pool images to be of little help, since we still cannot determine whether, in addition to the cellulitis, the bone is also involved.

Gallium-67 citrate has been used for the detection of osteomyelitis. Originally suggested by Handmaker as a possible adjunct to the Tc-99m MDP image to increase its specificity (11,26), the gallium scintigram has proven to be useful for the imaging diagnosis of osteomyelitis (4,10,27,28). We also have shown that in an animal model, Ga-67 citrate was specific, if not very sensitive, for predicting the cure of osteomyelitis (29). Recently Dye et al. (14) suggested that Ga-67 may be more sensitive than Tc-99m MDP for detecting osteomyelitis. In a comparison study, Ga-67 citrate was found to be more specific than Tc-99m MDP for following the clinical course of osteomyelitis under treatment (30). We have

compared Ga-67 citrate and Tc-99m MDP for the diagnosis of osteomyelitis. Gallium-67 citrate scintigraphy shows abnormal accumulation of the tracer earlier than does Tc-99m MDP. Both have false-negative images early in the course, becoming more sensitive as the course progresses. Since symptoms appear at a variable time after osteomyelitis is established, this may explain the range of sensitivities reported in the literature from less than 50% to over 90%.

We agree with prior recommendations by Handmaker and Hoffer (17,31), and recommend a Tc-99m MDP image at first presentation of a patient with osteomyelitis. If the bone image is negative at 4 hr, a Ga-67 citrate image should be obtained, with delay up to 48 hr before the image is read as negative. If clinical suspicions are high, repeat images in 2 to 3 days should be done.

TABLE 1. SUMMARY OF RESULTS

Day after inoculation	Tc-99m MDP	6 hr Ga-67	24 hr Ga-67	48 hr Ga-67	72 hr Ga-67
1(1)*	1/1(-)	1/1(-)	1/1(-)	1/1(+/-)†	1/1(+)
2(3)	3/3(-)	3/3(-)	1/3(-)1/3(+/-)1/3(+)	1/3(-)2/3(+)	1/3(-)2/3(+)
3(3)	2/3(-)1/3(+)	1/3(-)1/3(+/-)1/3(+)	3/3(+)	3/3(+)	3/3(+)
4(4)	2/4(-)2/4(+)	2/4(+/-)2/4(+)	4/4(+)	4/4(+)	4/4(+)
5(4)	3/4(+)-1/4(-)	1/4(-)1/4(+/-)2/4(+)	1/4(-)3/4(+)	1/4(-)3/4(+)	1/4(-)3/4(+)
7(3)	3/3(+)	3/3(+)	3/3(+)	3/3(+)	3/3(+)

* Total number of rabbits in each group.

† +/- Indicates either questionable activity or activity that could be either soft tissue or bone.

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