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# Effect of Soft-Tissue Pathology on Detection of Pedal Osteomyelitis in Diabetics

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Three-phase bone scans were performed on 30 diabetic patients suspected of having acute pedal osteomyelitis; 23 also had a pedal ulcer, seven had coexisting cellulitis, and 14 had diminished pedal pulses. Fifteen patients were receiving antibiotics at the time of the scan. A tissue diagnosis was available in 18 patients and 12 had no clinical evidence of infection on follow-up. Focal *arterial* hyperemia combined with focally increased activity on blood-pool and delayed (2–3 hr) scans were interpreted as acute osteomyelitis. Scans showing *venous* hyperemia were interpreted as soft-tissue pathology without acute osteomyelitis. Companion radiographs were reviewed independently. The sensitivity and specificity of the scans for osteomyelitis were 0.94 and 0.79, respectively, while radiographic sensitivity was 0.93 and specificity was 0.50. The presence of soft-tissue ulcers or cellulitis, peripheral vascular disease, or recent antibiotic therapy had no significant adverse effect on the accuracy of the three-phase scan in diagnosing osteomyelitis.

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Patients with diabetes mellitus frequently have peripheral neuropathy, poor distal extremity circulation, and various types of foot pathology. It is clinically important to distinguish soft-tissue diseases such as cellulitis and ulceration from osteomyelitis, which requires more aggressive therapy (1). Serial radiographs may demonstrate progressive destructive changes when osteomyelitis is present, but are not sensitive early in the course of the infection (2). Interpretation of radiographs frequently is complicated by the presence of diabetic osteopathy (3). In addition, radiographic evidence of periosteal new bone formation and subchondral osteoporosis in diabetics are often due to noninfectious etiologies such as chronic edema, vascular stasis, mechanical stress, or previous subliminal trauma (4,5).

Three-phase bone scanning has been shown to be a useful technique for diagnosing acute osteomyelitis (6). Examination of flow and blood-pool images as well as conventional delayed views significantly improves the

specificity of the examination without diminishing its high sensitivity. The sensitivity and specificity of this technique for diagnosing pedal osteomyelitis in diabetic patients have been reported (7), but the effect of other diabetic foot disorders, especially soft-tissue ulcers, on the accuracy of three-phase bone imaging was not evaluated. The current retrospective study examines the accuracy of three-phase bone scanning of the feet in diabetics, and specifically addresses the effects of soft-tissue pathology on the scintigraphic detection of osteomyelitis.

## MATERIALS AND METHODS

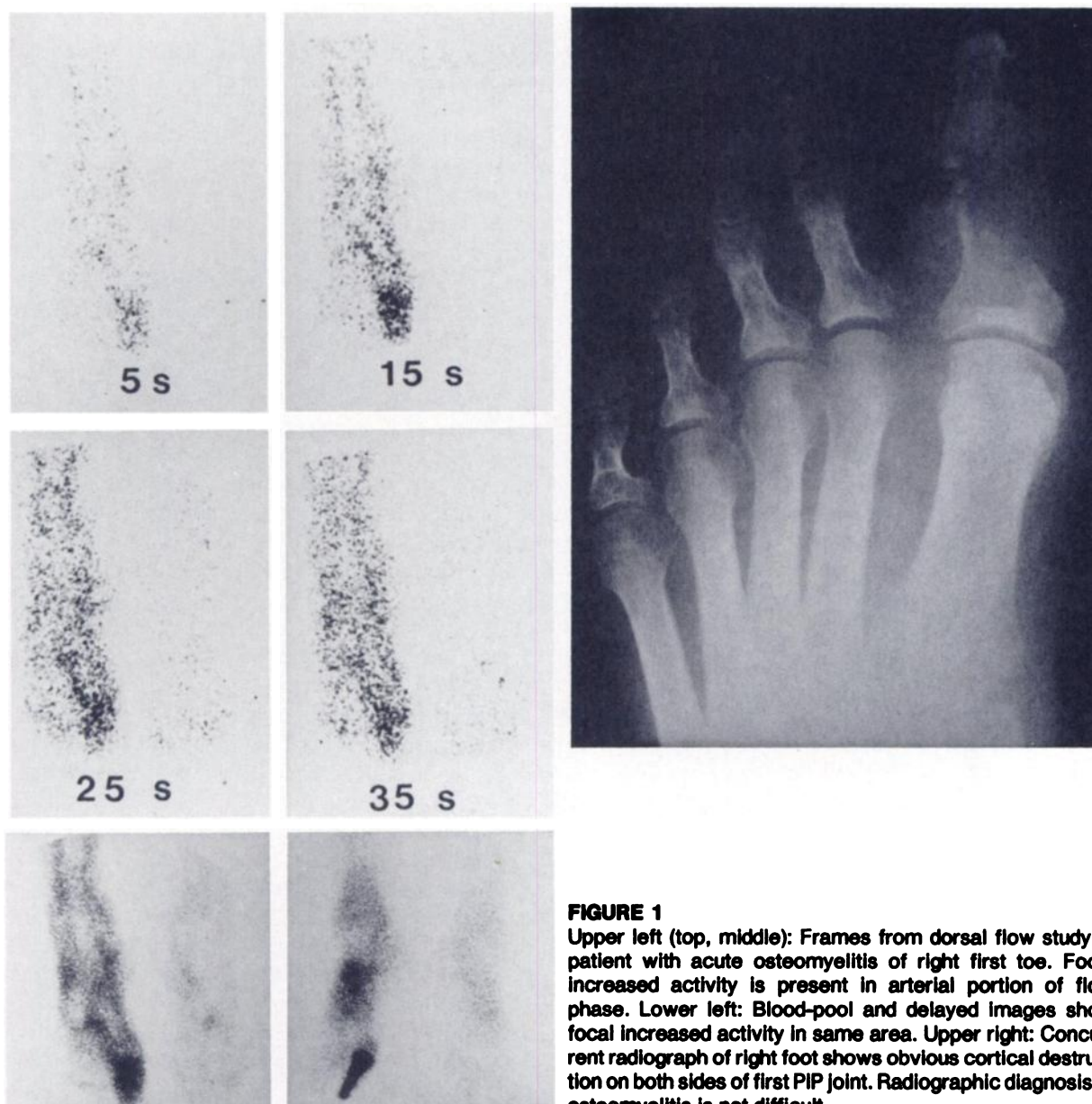
Three-phase bone scans of 30 diabetic patients with suspected pedal osteomyelitis for whom a proven diagnosis was available were identified from among a series of 114 consecutive three-phase scans performed at our institution. These patients (16 men, 14 women) ranged in age from 29 to 83 yr (mean age 61 yr). All but three patients were known to be diabetic for at least 5 yr prior to this study. Osteomyelitis was demonstrated in 16 of these patients by positive bone biopsy ( $n = 11$ ), bone culture ( $n = 4$ ), or both ( $n = 1$ ). Resolution of symptoms without prolonged antibiotic therapy (less than 10

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**FIGURE 1**  
Upper left (top, middle): Frames from dorsal flow study in patient with acute osteomyelitis of right first toe. Focal increased activity is present in arterial portion of flow phase. Lower left: Blood-pool and delayed images show focal increased activity in same area. Upper right: Concurrent radiograph of right foot shows obvious cortical destruction on both sides of first PIP joint. Radiographic diagnosis of osteomyelitis is not difficult

days) in 14 patients was considered proof of the absence of osteomyelitis as indicated in the discharge diagnosis. Two of these patients also had a negative biopsy or culture. Twenty-three of the 30 patients (77%) had a soft-tissue ulcer at the site clinically suspected for osteomyelitis. Significant peripheral vascular disease (clinically absent or faint distal pulses) was present in 14 patients. Fifteen patients were on antibiotics for a mean of 4 days (range 1–9 days) at the time of the scan; one patient was receiving long-term therapy (INH and Rifampin) for tuberculosis.

Three-phase bone imaging was performed following the bolus injection of 20 mCi of technetium-99m ( $^{99m}\text{Tc}$ ) diphosphonate. The initial flow study was performed in a dorsal or plantar projection to obtain optimal visualization of the area in question. Both feet

(when present) were included in the field of view. Five-second images were obtained for a total of 100 sec starting at the time of injection. This was done to insure full visualization of the arrival of the bolus. A 300,000 count blood-pool image was obtained immediately following the flow study without repositioning the patient or camera. Delayed images in multiple projections were obtained 3 hr later. Concurrent radiographs (AP, lateral, and oblique projections) were available in 25 patients; eleven of these had old radiographs for comparison. The mean interval between radiographs and scans was 2.5 days.

The three-phase bone scans were reviewed independently by two observers who had no knowledge of radiographic, clinical or pathologic data. Increased activity seen on any phase of the scintigraphic study was graded

**TABLE 1**  
Three-Phase Bone Scintigraphy in Diabetics  
with Suspected Acute Pedal Osteomyelitis  
(n = 30)

Item	Final diagnosis	
	+	-
Scan +	15	3
Results -	1	11
Sensitivity = 0.94		
Specificity = 0.79		

as focal or diffuse. Increased activity on the flow phase of the study (hyperemia) was classified in accordance with the time of its appearance relative to the surrounding soft tissues. Hyperemia which was recognizable before or at the same time as the appearance of activity in the surrounding tissues was considered to be "arterial"; hyperemia which became evident only after activity appeared in the surrounding tissues was considered to be "venous." Scans were interpreted as showing acute osteomyelitis only when an area showed focal arterial hyperemia and increased activity on the blood pool and delayed images in the same location (Fig. 1).

Radiographs were reviewed independently by two different observers. Comparisons with previous radiographs were made when old films were available. Osteomyelitis was diagnosed when focal cortical and/or medullary destruction, or destruction of opposing joint space surfaces, was present (Fig. 1).

## RESULTS

The three-phase bone scan interpretations of the two observers agreed in 26 of 30 (88%) cases. Three of the remaining four scans were initially interpreted as equivocal by one of the observers. Agreement on the scintigraphic diagnosis was reached by the observers prior to knowledge of the final diagnosis after a brief joint review of the scans. The results are summarized in Table 1 and show a 0.94 (15/16) sensitivity and a 0.79 (11/14) specificity. The single false-negative study occurred in a patient in whom the infected bone was necrotic (i.e., avascular) on gross examination at the time of the scan. No photon-deficient area was appreciated on the scan. The three false-positive scans included one patient with a clinically occult, acute phalangeal fracture. The fracture occurred 3 days prior to the scan and was radiographically visualized only in retrospect. Another false-positive scan occurred in a patient with acute inflammatory gout, while the third was in a patient with radiographic evidence of florid bone destruction who showed clinical and radiographic improvement without antibiotic therapy. More than half of the patients with osteomyelitis had absent dorsalis pedis or posterior tibial pulses, and in 40% (six of 15 patients

with perfused, infected bone) both these pulses were absent. It is noteworthy that despite the circulatory abnormalities, arterial hyperemia was clearly evident.

Twenty-three patients with pedal ulcers had scans. In these patients the scintigraphic sensitivity for osteomyelitis was 0.92 (12/13) and the specificity 0.80 (8/10) (Table 2). In 12 of 14 patients with arterial phase hyperemia at the ulcer site on the flow study, osteomyelitis was present. All 14 of these sites also showed focally increased activity on the blood-pool and static images. The two false-positive scans included the patient with the acute fracture. In the absence of arterial hyperemia in the ulcer bed, only one of nine patients had subjacent osteomyelitis. Venous hyperemia alone was present at six ulcer sites that had no subjacent osteomyelitis (Fig. 2). Three of these six patients had normal static images, and three showed increased activity on the delayed views. The remaining two patients with pedal ulcers had normal three-phase scans.

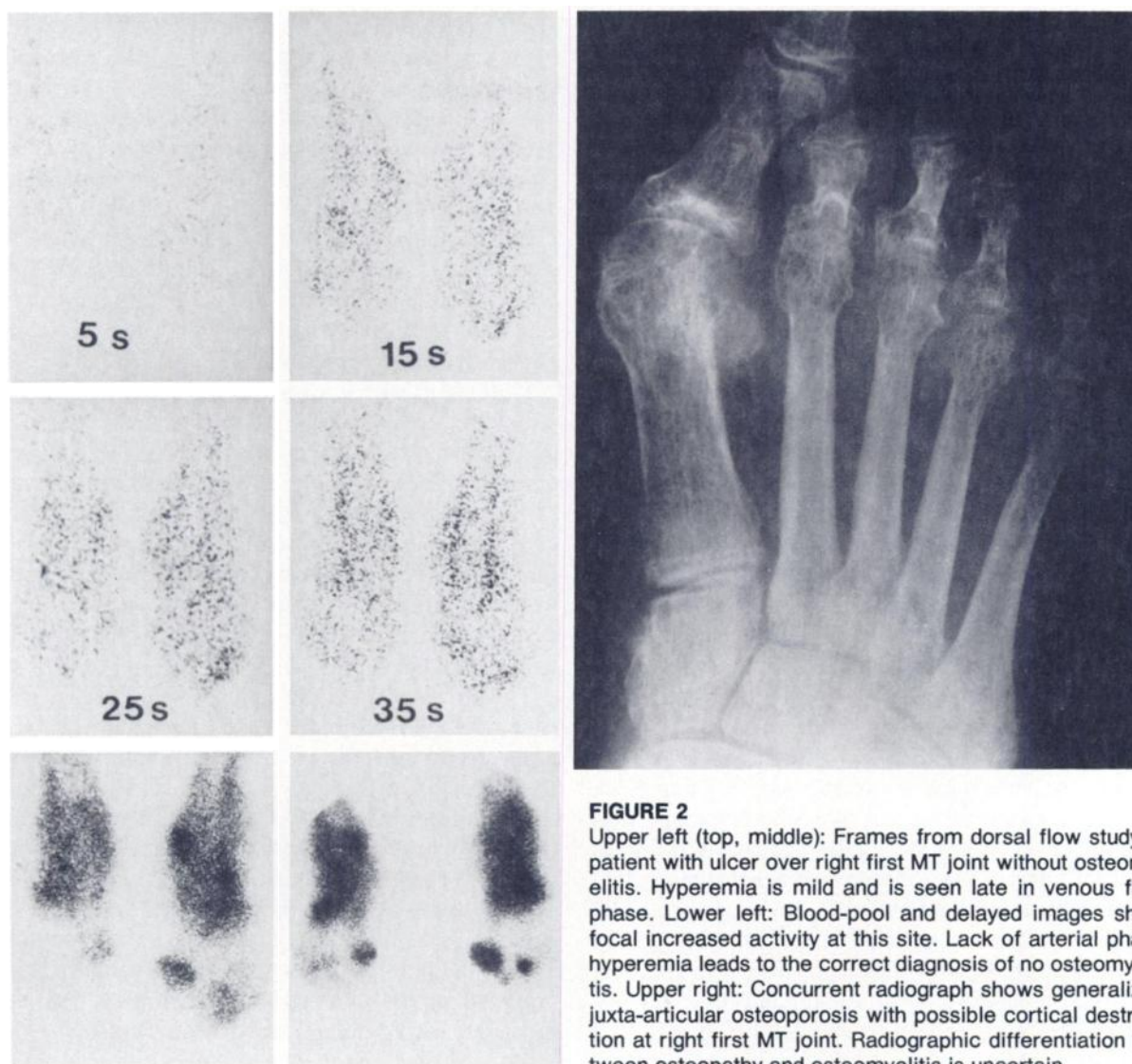
Seven patients were noted to have cellulitis on physical examination, and each had an ulcer within the area of cellulitis. Five of these patients showed diffuse hyperemia on the flow phase of the study. A superimposed area of focal arterial hyperemia was present in four of the patients, and each had osteomyelitis. Focal arterial hyperemia alone was present in the remaining two patients, both of whom had osteomyelitis. Diffusely increased unilateral activity was seen in only two of 18 flow studies obtained in patients without cellulitis. Both patients had severe bilateral peripheral vascular disease documented angiographically.

Two patients had scans demonstrating large areas of markedly increased activity in the ankles (bilateral in one case) on the arterial flow, blood-pool, and delayed images. These areas were subsequently shown radiographically to be neuropathic joints.

The utility of obtaining the flow study in addition to the blood-pool and static images was further demonstrated in two patients who had intense focal activity at ulcer sites on the blood-pool and static images. Flow studies showing only venous hyperemia led to the correct diagnosis, i.e., soft-tissue pathology without osteomyelitis (Fig. 2). In two additional patients with mildly increased focal blood pool activity, flow studies showing no hyperemia or venous hyperemia were only help-

**TABLE 2**  
Radionuclide Angiographic Findings in Patients  
with Soft-Tissue Ulcers  
(n = 23)

Item	Final diagnosis	
	Osteomyelitis	No osteomyelitis
Arterial	12	2
Hyperemia Venous	1	6
None	0	2



**FIGURE 2**

Upper left (top, middle): Frames from dorsal flow study in patient with ulcer over right first MT joint without osteomyelitis. Hyperemia is mild and is seen late in venous flow phase. Lower left: Blood-pool and delayed images show focal increased activity at this site. Lack of arterial phase hyperemia leads to the correct diagnosis of no osteomyelitis. Upper right: Concurrent radiograph shows generalized juxta-articular osteoporosis with possible cortical destruction at right first MT joint. Radiographic differentiation between osteopathy and osteomyelitis is uncertain

ful in correctly excluding the presence of osteomyelitis. There were no patients in whom a false-negative diagnosis was made because of the addition to the flow study.

Radiographs were interpreted as showing osteomyelitis in 14 of the 15 patients (93%) proven to have skeletal infection, and in five of the 10 (50%) without osteomyelitis (Table 3). Thus, the radiographs were as sensitive as the scans in detecting osteomyelitis, but were less specific. However, possibly due to the small number of patients, the differences between scintigraphic and radiographic performance were not statistically significant. The five patients with false-positive radiographs included the three with false-positive scans, as well as two in whom the scan was negative for osteomyelitis. All showed focal areas of cortical destruction radiographically. In four of these five patients the abnormality was in a periarticular region.

## DISCUSSION

Radiographs have traditionally played a major role in helping to determine the therapeutic regimen for diabetic patients with foot pathology. However, the radiographic diagnosis of pedal osteomyelitis in these

**TABLE 3**  
Radiography in Diabetics with Suspected Acute  
Pedal Osteomyelitis  
(n = 25)

Item	Final diagnosis	
	+	-
X-ray +	14	5
Results -	1	5
Sensitivity = 0.93		
Specificity = 0.50		

patients is often difficult (3-5). Even in normal patients, bony abnormalities were not usually appreciated on routine radiographs until almost two weeks after the onset of osteomyelitis (2,8,9). In diabetics, the radiographic findings in osteomyelitis may differ from normals; periosteal reaction may be minimal or absent and destructive changes may progress at unpredictable rates (5,11). In addition, diabetic osteopathy alone produces radiographic abnormalities that can simulate osteomyelitis, e.g., sclerosis and/or osteopenia, bony fragmentation and periosteal reaction are all common (3,10), especially in bone underlying a soft-tissue ulcer (4). Peri-articular zones of osteoporosis have been noted in the affected extremities of 15% of diabetic patients; in three-quarters of these cases, areas of complete destruction of the articular cortex are present (Fig. 2). The difficulties in radiographic interpretation posed by these abnormalities have led to the investigation of other imaging modalities to aid in establishing the diagnosis. The difference between the radiographic results in this series and the lower sensitivity and higher specificity usually reported in the literature may be due to differences in interpretation of some of these subtle changes, to differences in our patient population, as well as to the limited number of patients involved.

Skeletal scintigraphy is a sensitive method for detecting a wide variety of osseous diseases, including osteomyelitis (13-15), but the similar appearance of many different types of abnormalities on delayed images often makes the findings nonspecific. Several years ago it was shown that the specificity of bone scintigraphy for osteomyelitis could be improved by evaluating a blood-pool image obtained shortly after injection (14,16). More recently, it has been shown that three-phase bone scanning can further improve the diagnostic specificity for osteomyelitis, even in diabetic patients (6,7).

It has been known for some time that nonosseous pathology can alter skeletal uptake of radionuclide. Bone in areas of soft-tissue hyperemia will show relatively increased tracer activity (17,18). This factor is of particular concern in diabetic patients, in whom the question of osteomyelitis is often raised because of an inflammatory soft-tissue process, e.g., cellulitis or ulceration. The initial reports regarding the use of three-phase bone scanning to detect osteomyelitis suggested that skin ulcers might lead to false-positive diagnoses of osteomyelitis (6). The work of Park et al. (7) on the utility of three-phase bone scintigraphy in diabetics with foot disease did not directly address this question. The high frequency of ulceration at possible sites of osteomyelitis in diabetics' feet (77% in our series) underscores the importance of resolving this issue.

In our patient population, osteomyelitis was present subjacent to an ulcer in slightly more than half the cases (12 of 23). Hyperemia of some type usually was present in ulcerated regions, but ulceration with osteomyelitis

could be distinguished from uncomplicated ulceration by the scintigraphic appearance of the hyperemia (Figs. 1,2). The hyperemic area appeared early in the arterial phase of the flow study when osteomyelitis was present, and its intensity decreased in the venous flow phase. Conversely, the hyperemia of ulceration without osteomyelitis appeared in the venous phase of the radionuclide angiogram. Two false-positive studies that showed arterial hyperemia in the absence of osteomyelitis were due to the other acute inflammatory processes in the underlying bone (acute fracture, acute gout with radiographic bone changes).

Patients in our series had received up to 9 days of antibiotic therapy before the time of the scan. Nevertheless, arterial hyperemia was present in all cases of osteomyelitis in vascularized bone. This result seems to confirm earlier reports that more than two weeks of antibiotic therapy is necessary before hyperemia to infected bone is significantly diminished (19). In addition, the presence of either cellulitis or large vessel peripheral vascular disease did not hinder our ability to diagnose osteomyelitis.

The three neuropathic joints seen in our patients were distinguished from foci of osteomyelitis by their location and the large area of scintigraphic abnormality. The involved ankles showed intense increased activity on the arterial flow, blood pool and delayed phases of the study. However, the abnormality involved the entire joint rather than being confined to a distinct focus. The arterial hyperemia seen in these joints may be due to persistent acute trauma (i.e., repeated small fractures). These findings suggest that it will be difficult for scintigraphy to detect osteomyelitis superimposed on a neuropathic joint. Radiographs in such patients reveal disorganized neuropathic areas which present similar interpretive problems with regard to diagnosing osteomyelitis.

The results of the current study suggest that the scintigraphic features of pedal osteomyelitis include focal arterial hyperemia accompanied by increased blood pool and delayed activity. When osteomyelitis is absent, hyperemia secondary to soft-tissue pathology such as ulceration or cellulitis may be focal or diffuse, but occurs in the venous phase of the radionuclide angiogram. When clinical and radiographic correlation are used to exclude conditions that may mimic osteomyelitis and to define areas of bone necrosis that cannot accumulate tracer, three-phase scintigraphy appears to be reliable. It minimizes the uncertainties involved in radiographic diagnosis, and appears to provide an effective means for diagnosing pedal osteomyelitis in diabetic patients.

## REFERENCES

1. Murphy DP, Jan JS, File TM, Jr: Infectious complica-

- tions in diabetic patients. *Primary Care* 8:695-714, 1981
2. Sherman RD: The nature of radiologic diagnosis in disease of bone. *Radiol Clin North Am* 8:227-239, 1970
  3. Mendelson EB, Fisher MR, Deschler TW, et al: Osteomyelitis in the diabetic foot: A difficult diagnostic challenge. *Radiographics* 3:248-261, 1983
  4. Staple TW: Radiography of the diabetic foot. In *The Diabetic Foot*, Levin ME, O'Neal LW, eds. 3rd ed. St. Louis, C.V. Mosby, 1983, pp 201-231
  5. Steinberg G: Trophoneuropathic bone changes versus osteomyelitis in diabetes mellitus. *Geriatrics* 26:111-116, 1971
  6. Maurer AH, Chen DCP, Camargo EE, et al: Utility of three-phase skeletal scintigraphy in suspected osteomyelitis. *J Nucl Med* 22:941-949, 1981
  7. Park HM, Wheat LJ, Siddiqui AR, et al: Scintigraphic evaluation of diabetic osteomyelitis. *J Nucl Med* 23:569-573, 1982
  8. Waldvogel FA, Medoff G, Swartz MN: Osteomyelitis: A review of clinical features, therapeutic considerations, and unusual aspects. *N Engl J Med* 282:316-322, 1970
  9. Capitano MA, Kirkpatrick JA: Early roentgen observations in acute osteomyelitis. *Am J Roentgenol* 108:488-496, 1970
  10. Clouse ME, Gramm HF, Legg M, et al: Diabetic osteoarthropathy: Clinical and roentgenographic observations in 90 cases. *Am J Roentgenol* 121:22-34, 1974
  11. Butt WP: The radiology of infection. *Clin Orthop* 96:20-30, 1973
  12. Duszynski DO, Kuhn JP, Afshani E, et al: Early radionuclide diagnosis of acute osteomyelitis. *Radiology* 117:337-340, 1975
  13. Majd M, Frankel RS: Radionuclide imaging in skeletal inflammatory and ischemic disease in children. *Am J Roentgenol* 126:832-841, 1976
  14. Gilday DL, Paul DJ, Paterson J: Diagnosis of osteomyelitis in children by combined blood pool and bone imaging. *Radiology* 117:331-335, 1975
  15. Eymontt MJ, Alavi A, Dalmka MK, et al: Bone scintigraphy in diabetic osteoarthropathy. *Radiology* 140:475-477, 1981
  16. Handmaker H, Leonards R: The bone scan in inflammatory osseous disease. *Semin Nucl Med* 6:95-105, 1976
  17. Thrall JH, Geslien GE, Corcoran RJ, et al: Abnormal radionuclide deposition patterns adjacent to focal skeletal lesions. *Radiology* 115:659-663, 1975
  18. Charkes ND: Skeletal blood flow—implications for bone scan interpretation. *J Nucl Med* 21:91-98, 1980
  19. Deutsch SD, Grandsman EJ, Spraragen SC: Quantitative regional blood flow analysis and its clinical application during routine bone scanning. *J Bone Joint Surg* 63A, 295-305, 1981