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*Review article*

# Imaging the diabetic foot

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**Abstract.** Early and accurate diagnosis of infection or neuropathy of the diabetic foot is the key to successful management. Angiopathy leads to ischemia which, in combination with peripheral neuropathy, predisposes to pedal skin ulceration, the precursor of osteomyelitis. Chronic hyperglycemia promotes production of glycosylated end products which accumulate on endothelial proteins, causing ischemia of the vasa nervorum. When combined with axonal degeneration of the sensory nerves, the result is hypertrophic neuroarthropathy. Should the sympathetic nerve fibers also be damaged, the resultant loss of vasoconstrictive impulses leads to hyperemia and atrophic neuroarthropathy. Plain radiography, although less sensitive than radionuclide, magnetic resonance (MR), and computed tomographic examinations, should be the initial procedure for imaging suspected osteomyelitis in the diabetic patient. If the radiographs are normal but the clinical suspicion of osteomyelitis is strong, a three-phase $^{99m}$Tc-MDP scan or MR imaging is recommended. An equivocal $^{99m}$Tc-MDP scan should be followed by MR imaging. To exclude osteomyelitis at a site of neuroarthropathy, a $^{111}$In white blood cell scan is preferable. To obtain a specimen of bone for bacteriological studies, percutaneous core biopsy is the procedure of choice, with the entrance of the needle well beyond the edge of the subjacent ulcer.

**Key words:** Diabetes mellitus – Foot complications – Angiopathy – Neuroarthropathy – Osteomyelitis

Diabetic patients spend more time in the hospital for foot problems than for any other complications of their disease. In the United States, 14% of all diabetic patients are hospitalized each year for an average duration of 6 weeks [1]. Indeed, foot complications of diabetes are the most common cause of nontraumatic lower extremity amputation in the United States, leading to as many as 50 000 such amputations per year [2], 51% of which represent a lost toe or forefoot [3]. Early and accurate diagnosis of infection or neuropathy and the prompt initiation of conservative therapy are the keys to management. Antibiotics and debridement may successfully cure localized infection before extension to the plantar compartments necessitates amputation. Similarly, early diagnosis of peripheral neuropathy allows timely preventive and protective interventions to avoid devastating neuroarthropathy.

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## Diabetic angiopathy

Angiopathy leads to ischemia which, in combination with peripheral neuropathy, predisposes the pedal skin to ulceration, the precursor of osteomyelitis. Calcification of the media of the digital arteries increases their rigidity, preventing them from adjusting to circulatory demands [4]. Thickening of the basement membrane of the capillaries inhibits perfusion of adjacent tissues [5, 6]. Diabetic macroangiopathy of the larger arteries of the lower extremities is characterized by uniform narrowing and irregularity of the lumen [7]. Necrobiosis lipoidica diabeticorum, a disorder of the soft tissues, particularly of the dorsum of the foot and pretibial region, results from a microangiopathy characterized by painless red skin papules that coalesce to form granulomatous masses that may invade bone or spontaneously regress [8].

## Diabetic neuroarthropathy

Diabetic neuroarthropathy results from damage to the spinal and peripheral nerves. The first published description of a typical painless neuropathic joint in a patient with diabetes mellitus was that of Jordan in 1936 [9]. With the decreasing incidence of tertiary syphilis and the progressively increasing lifespan of diabetic patients, di-

abetes mellitus has surpassed tabes dorsalis as the primary cause of neuroarthropathy ("diabetic pseudotabes"). Neuroarthropathy tends to develop between the fifth and seventh decades, following a period of diabetes of at least 15 years duration. The foot is involved in most cases, with the tarsal and tarsometatarsal joints being affected in 60%, the metatarsophalangeal joints in 30%, and the tibiotalar joint in less than 10% of cases. Loss of proprioception results in an ataxic gait, and loss of pain sensation allows repeated trauma to the feet, resulting in skin ulcers and neuroarthropathy [10] (Fig. 1).

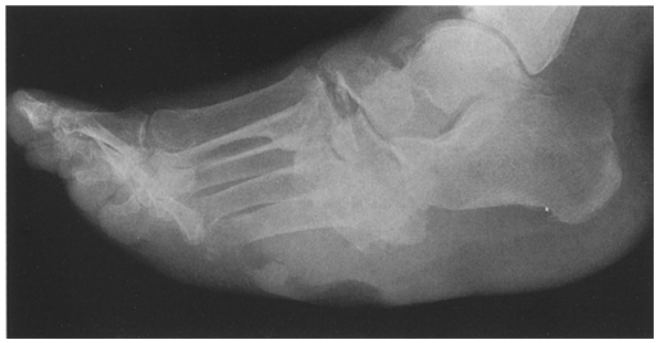
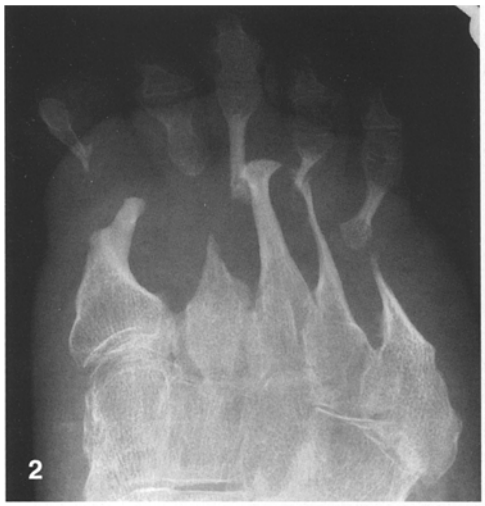


**Fig. 1.** Severe plantar ulceration and midfoot neuroarthropathy in this 57-year-old male diabetic have resulted from loss of proprioceptive and pain sensation, with consequent ataxic gait and repeated unrecognized trauma to the skin and joints. The findings are characteristic and include extensive subluxation, subchondral fragmentation, and sclerosis

There are two forms of neuroarthropathy: atrophic and hypertrophic. The former is characterized by osteoporosis, bone resorption, and dislocation, and the latter by osteophyte formation, sclerosis, eburnation, fragmentation, and dislocation. In the absence of diabetes, the hypertrophic form (Charcot joint) typically results from a syphilitic lesion in the posterior columns of the spinal cord (tabes dorsalis), and usually affects the lower extremities or spine, while the atrophic form typically results from a lesion in the central gray matter, characteristically a syrinx in the cervical region of the spinal cord, and most frequently involves the glenohumeral joint. In contrast, the neuropathy of diabetes affects the spinal and peripheral nerves, which contain sympathetic, sensory, and motor fibers, all or some of which may become involved. Involvement of sympathetic and sensory fibers leads to mechanical overuse of a joint secondary to loss



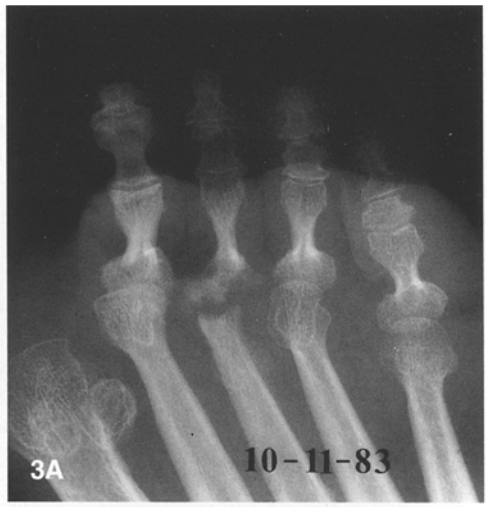
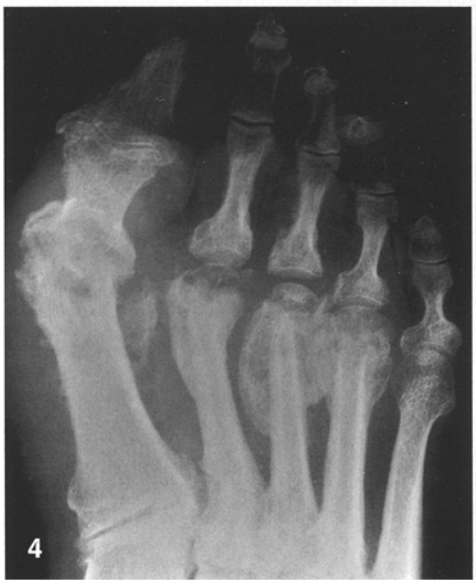




**Fig. 2.** Osteolytic neuroarthropathy in a 53-year-old diabetic man. The ends of the bones at the metatarsophalangeal joints have a "sucked candy-stick" appearance, reflecting neuroarthropathy in the presence of active hyperemia



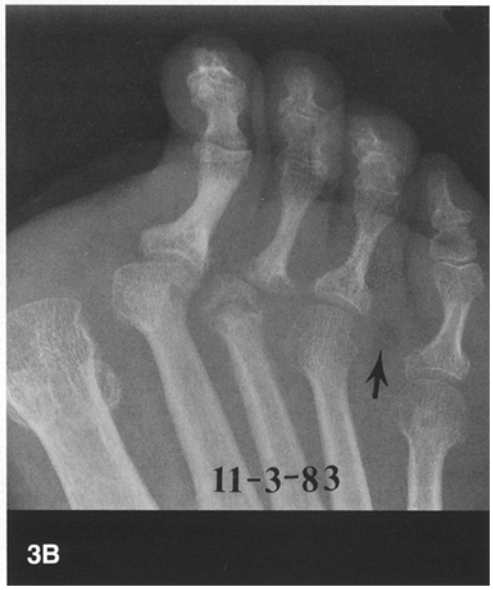
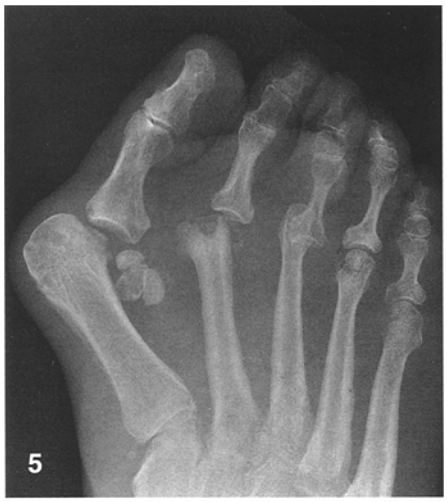
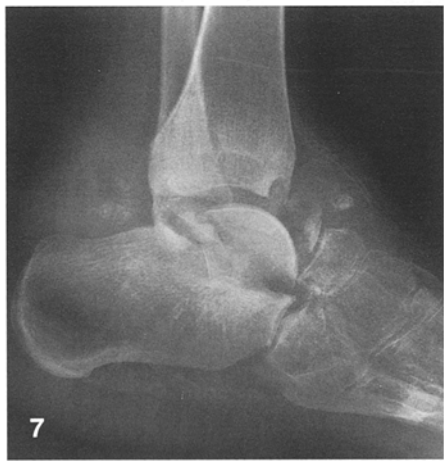
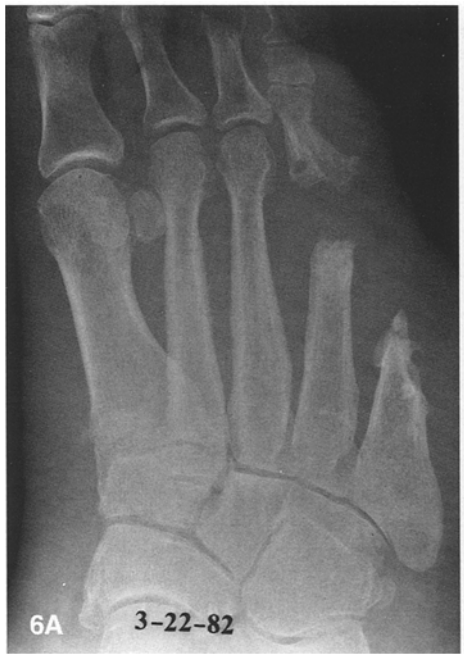




**Fig. 3A, B.** Combined infection and neuroarthropathy have led to subchondral bone destruction of the third metatarsophalangeal joint and fracture of the metatarsal head. The patient, a 63-year-old diabetic woman, has had an amputation of the great toe because of progressing chronic osteomyelitis that failed to respond to conservative therapy. **A** The foot at the start of antibiotic therapy. **B** Five weeks later, the abnormal architecture of the infected bone has become partially reconstituted. The *arrow* indicates a neurotrophic plantar ulcer

**Fig. 4.** Diabetic neuropathy in this 69-year-old man has resulted in unperceived chronic trauma, secondary fractures with striking callus formation, extensive traumatic periostitis, and sclerosis of the shaft of the second metatarsal



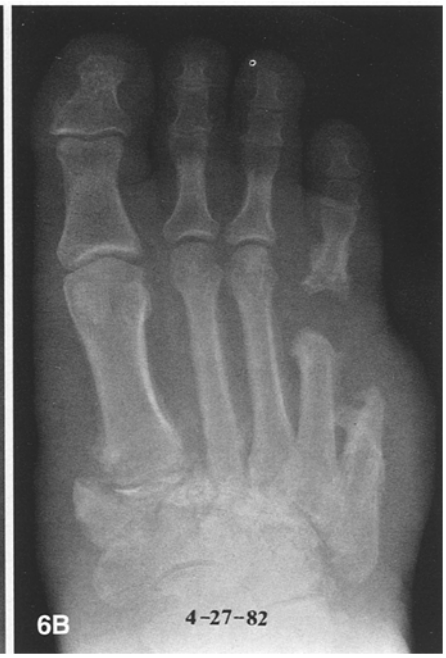




**Fig. 5.** Diabetic neuroarthropathy in a 54-year-old woman is marked by dislocation and disorganization of the first and second metatarsophalangeal joints and dislocation of the third

**Fig. 6A, B.** Rapidly progressive destruction of the midfoot and traumatic periostitis of the metatarsals in this 34-year-old diabetic man are characteristic of neuroarthropathy. **A** The patient has had partial resection of the fourth and fifth rays to treat chronic progressive osteomyelitis. The only abnormality in the other bones is the mild periosteal reaction along the shafts of the second and third metatarsals and some medial fragmentation of the first tarsometatarsal joint. **B** Approximately 1 month later, there has been striking destruction and subluxation at the tarsometatarsal joints (Lisfranc joint) and traumatic periostitis along the shafts of all metatarsals

**Fig. 7.** Diabetic neuroarthropathy of the hindfoot in a 26-year-old woman. The tibiotalar and subtalar joints show the characteristic five Ds: joint *d*istention, *d*islocation, bony *d*ebris, *d*isorganization, and increased bone *d*ensity

of protective pain and proprioceptive sensation, as well as active hyperemia secondary to loss of vasoconstrictive neural impulses, a combination of factors which tends to result in atrophic neuroarthropathy, most frequently occurring in the forefoot [11]. In contradistinction, absence of involvement of sympathetic fibers in the presence of lesions of sensory fibers tends to result in hypertrophic neuroarthropathy, most frequently occurring in the midfoot or hindfoot.

Diabetic peripheral neuropathy is defined as peripheral somatic or autonomic nerve damage attributable solely to diabetes mellitus. Peripheral neuropathy afflicts 10–15% of the 14 million American diabetics [2]. In fact, diabetes is the most common cause of peripheral neuropathy in the developed world, with alcohol ingestion a distant second [10]. Diabetic peripheral neuropathy may be classified into a symmetrical form, which predominantly involves sensory and autonomic nerves, and a focal asymmetrical form, which involves individual cranial or peripheral sensory and/or motor nerves [12]. The two forms may coexist. Symmetrical polyneuropathy, the more common of the two forms, is manifested by bilateral multifocal axonal degeneration associated with vascular disease, particularly of the distal portions of the lower extremities. The resultant sensory deficit has a characteristic ascending "glove and stocking" distribution. Chronic hyperglycemia leads to the production of advanced glycosylated end products which accumulate on endothelial proteins, causing ischemia of the endoneurial microvasculature (vasa nervorum) which also contributes to neuronal damage [13].

*The forefoot*

Abnormalities in the forefoot may reflect infection alone, neuropathy alone, or a combination of neuropathy, infection, and small-vessel disease. Although abnormalities in the midfoot and hindfoot are most likely to represent neuropathy, osteomyelitis of the calcaneus may arise secondary to an underlying infected plantar ulcer. Hypertrophic or atrophic neuroarthropathy may occur in the forefoot. In the atrophic type, osteolysis of the distal ends of the metatarsals combined with broadening of the bases of the proximal phalanges produce "pencil and cup" deformities that simulate those of leprosy;

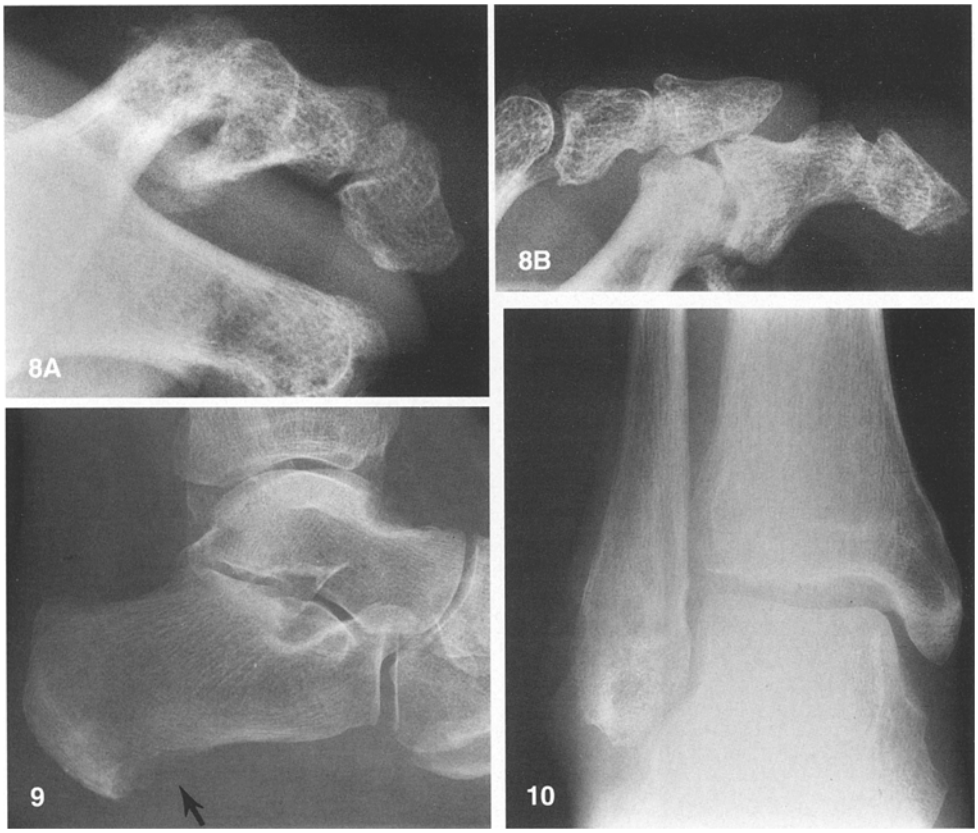



**Fig. 8A, B.** Neurotrophic ulcer at the tip of the second toe and resultant underlying osteomyelitis in a 50-year-old diabetic man. Compare the normal radiograph (**A**), obtained 3 months before, to **B**, where osteomyelitis is characterized by subtle destruction of the terminal tuft

**Fig. 9.** Osteomyelitis of the calcaneus *(arrow)* secondary to an underlying plantar neurotrophic ulcer in a 64-year-old diabetic woman

**Fig. 10.** Neurotrophic ulcer over the lateral malleolus has progressed to osteomyelitis of the subjacent fibula, characterized by cortical destruction in this 61-year-old diabetic man

"sucked candy-stick" or "sharpened pencil" deformities of the metatarsal heads may occur (Fig. 2). Alternatively, the metatarsal heads may become flattened or fragmented (Fig. 3). Dorsiflexion and shortening of the toes combined with plantar subluxation of the metatarsal heads predispose to neurotrophic ulceration of the soft tissues beneath the metatarsal heads and over the proximal interphalangeal joints. Unperceived chronic trauma may lead to periosteal reaction along the shaft of a bone in the absence of infection, and may evolve into sclerosis of the entire shaft (Fig. 4). Infection may accompany the neuropathic changes and accelerate joint destruction.

*The midfoot and hindfoot*

In the intertarsal and metatarsophalangeal joints, the earliest radiographic changes of neuroarthropathy are joint swelling and laxity, followed by subluxation, and subchondral fragmentation, new bone proliferation, and sclerosis (Fig. 5). Because the patient continues to walk and traumatize the foot, disuse osteoporosis is absent. Unrelenting trauma also results in another striking characteristic: rapidly progressive destruction, sometimes with disintegration of one or more tarsal bones within a period of only a few weeks (Fig. 6). The radiographic features of hypertrophic neuroarthropathy are easily remembered by the five Ds: joint *d*istention, *d*islocation, bony *d*ebris, *d*isorganization, and increased bone *d*ensity (Figs. 1, 4, 6, 7).

## Osteomyelitis of the diabetic foot

Over 90% of cases of osteomyelitis of the foot of diabetic patients result from the spread of infection from contiguous neurotrophic pedal ulcers [14]. When loss of pain sensation combines with poor blood flow to produce breakdown of the soft tissues, the resultant ulcers are more likely to become infected than are skin lesions of nondiabetic patients, and the infections more severe and refractory to treatment. The ulcers tend to occur at sites of pressure over bony or joint prominences. In order of decreasing occurrence, the ulcers are found: (1) below the metatarsal heads (especially the first and fifth), (2) at the tips of the toes (Fig. 8), (3) over deformed interphalangeal joints (claw toes, hammer toes), (4) under the calcaneus (Fig. 9), and (5) over the malleoli (Fig. 10). These sites of ulceration correspond to the most frequent sites of osteomyelitis: in order of decreasing occurrence, they are the metatarsal heads, the phalanges, and the calcaneus [15].

Because ischemia inhibits bone resorption, periosteal new bone formation, and healing, the changes of osteomyelitis may be atypical in the diabetic patient. The resultant chronicity of the infectious process, combined with absence of pain and proprioceptive sensation, leads to bone sclerosis, pathological fractures, and subluxations, findings that mimic pure neuroarthropathy. Acute infection may give rise to a vicious cycle: infection predisposes to bone resorption which may lead to fracture, which in turn may lead to diminished vascularity because of traumatized intraosseous blood vessels, which in turn

may lead to osteonecrosis and, ultimately, chronic infection [16]. However, if an adequate blood supply is maintained, the abnormal architecture of the infected bone may become reconstituted during treatment (Fig. 3).

Pedal osteomyelitis may be difficult to diagnosis clinically because associated fever and bacteremia are uncommon and the erythrocyte sedimentation rate may be normal. Osteomyelitis, diagnosed by culture of a biopsy specimen, was found to underlie 68% of 41 diabetic foot ulcers in one study; 68% of 28 ulcers with underlying osteomyelitis occurred without systemic illness, and 64% of cases of osteomyelitis occurred without findings of inflammation on physical examination [17]. The most common causative organisms were *Staphylococcus aureus* and *Staphylococcus epidermidis.*

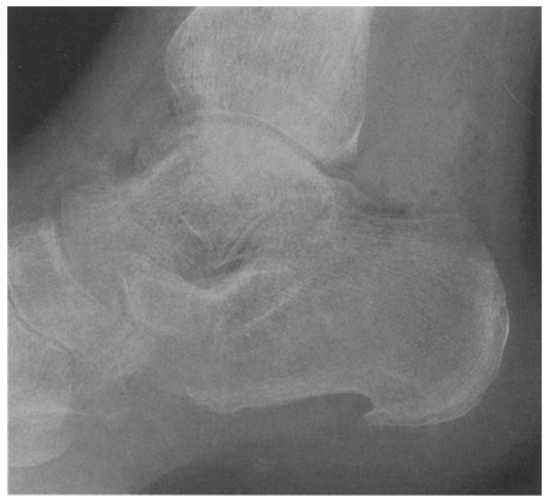


**Fig. 11.** Gas gangrene in a 53-year-old diabetic man

## Imaging procedures to evaluate the diabetic foot

Investigation of suspected osteomyelitis is the most frequent indication for imaging the feet of diabetic patients. Studies reporting the accuracy of various imaging techniques in evaluating diabetic pedal osteomyelitis are listed in Table 1.

**Table 1.** Estimated sensitivity and specificity of imaging techniques in evaluating diabetic pedal osteomyelitis (studies are in chronologic order in each category). (From Crim and Seeger [22])

| Study | No. of patients | % Sensitivity | % Specificity |
|---|---|---|---|
| *Plain radiographs* | | | |
| Park et al. [16] | 36 | 62 | 69 |
| Seldin et al. [18] | 30 | 93 | 50 |
| Larcos et al. [19] | 49 | 43 | 83 |
| Newman et al. [17] | 35 | 28 | 92 |
| Yuh et al. [20] | 24 | 72 | 60 |
| Kennan et al. [21] | 77 | 69 | 82 |
| Wang et al. [30] | 50 | 52 | 69 |
| *Three-phase $^{99m}$Tc-MDP bone scan* | | | |
| Park et al. [16] | 36 | 83 | 75[a] |
| Seldin et al. [18] | 30 | 94 | 79 |
| Larcos et al. [19] | 49 | 93 | 43 |
| Maurer et al. [24] | 13 | 75 | 56 |
| Yuh et al. [20] | 24 | 94 | 18 |
| Kennan et al. [21] | 77 | 100 | 38 |
| Newman et al. [17] | 35 | 69 | 39 |
| Weinstein et al. [25] | 32 | 69 | 83 |
| *$^{111}$In white blood cell scan* | | | |
| Larcos et al. [19] | 51 | 79 | 78 |
| Schauwecker et al. [26] | 35 | 100 | 83[b] |
| Maurer et al. [24] | 13 | 75 | 89 |
| Keenan et al. [21] | 46 | 100 | 78 |
| Seabold et al. [27] | 14 | 80 | 54[b] |
| Newman et al. [17] | 35 | 89 | 69 |
| *MR imaging* | | | |
| Yuh et al. [20] | 24 | 100 | 89 |
| Wang et al. [30] | 50 | 98 | 81 |
| Weinstein et al. [25] | 32 | 100 | 81 |

[a] Three patients with absent flow excluded from study; two of these had osteomyelitis

[b] All patients had neuropathic foot disease with clinical question of superimposed osteomyelitis

### *Plain radiography*

Although, when compared to radionuclide, magnetic resonance, and computed tomographic examinations, plain radiography is by far the least sensitive imaging modality for diagnosing pedal osteomyelitis in the diabetic patient, its specificity is comparable to that of the $^{99m}$Tc-MDP (methylene diphosphonate) scan [16–22]. False-positive diagnoses of osteomyelitis may reflect osteolysis and joint destruction due to neuroarthropathy in the absence of infection. Radiolucent foci in the soft tissues may represent air in cutaneous fissures or ulcers (Fig. 1), or dissecting into the underlying soft tissues, or they may reflect gas produced by *Escherichia coli, Aerobacter aerogenes, Klebsiella pneumoniae,* nonhemolytic streptococci, *Bacteroides* species, anaerobic streptococci and, rarely, *Clostridrium perfringens* (Fig. 11). The typical lack of sensitivity of the plain radiograph for diagnosing osteomyelitis in diabetics was shown in one series of cases in which only 28% of 25 patients with 41 pedal ulcers had a radiographic diagnosis of underlying osteomyelitis, whereas bone biopsy and culture revealed that 68% of the ulcers were actually associated with osteomyelitis [17]. The presence of osteoporosis and ill-defined erosions favors the diagnosis of osteomyelitis, whereas bone density is usually preserved in neuroarthropathy. However, neuroarthropathy in the forefoot may be atrophic, leading to difficulty in distinguishing it from osteomyelitis. In the midfoot and hindfoot, neuroarthropathy is usually hypertrophic with reactive bone proliferation and debris, features that are atypical of osteomyelitis.

### *Radionuclide imaging*

The various radionuclide examinations differ in their sensitivity and specificity for diagnosing osteomyelitis.

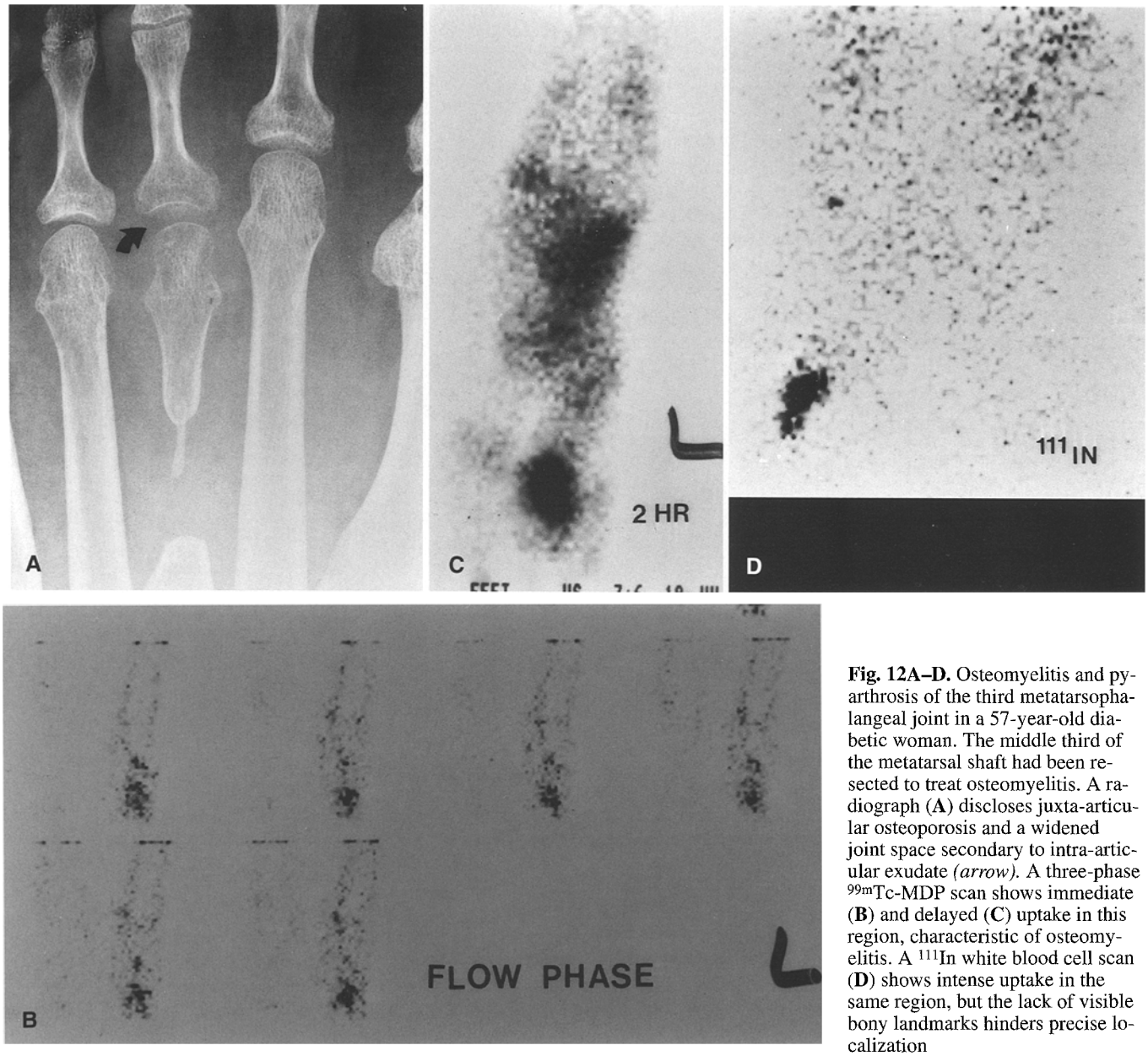



**Fig. 12A–D.** Osteomyelitis and pyarthrosis of the third metatarsophalangeal joint in a 57-year-old diabetic woman. The middle third of the metatarsal shaft had been resected to treat osteomyelitis. A radiograph (**A**) discloses juxta-articular osteoporosis and a widened joint space secondary to intra-articular exudate *(arrow)*. A three-phase $^{99m}$Tc-MDP scan shows immediate (**B**) and delayed (**C**) uptake in this region, characteristic of osteomyelitis. A $^{111}$In white blood cell scan (**D**) shows intense uptake in the same region, but the lack of visible bony landmarks hinders precise localization

The three-phase $^{99m}$Tc-MDP scan is more sensitive than plain radiography and has the second highest sensitivity of any radionuclide procedure for detecting osteomyelitis [16–25] (Fig. 12B, C). However, because the dynamics of the study reflect not only the rate of bone turnover, but also regional blood flow, capillary permeability, tissue perfusion, and other factors, the high sensitivity is gained at the expense of a high rate of false-positive diagnoses reflecting neuroarthropathy, especially in the midfoot and hindfoot, cellulitis, or periostitis secondary to soft tissue inflammation. Diffuse radionuclide activity may reflect peripheral vasodilation and hyperemia that result from impairment of the autonomic nervous system. On the other hand, ischemia may lead to a false-negative test [16]. A broad review of the literature has shown the mean sensitivity to be 85% and specificity 54%, with accuracy largely dependent on the prevalence of neuroarthropathy and the site of the suspected lesion [22]. Accuracy is poorest in the midfoot and hindfoot. In one study, a specificity of only 7% was found in the tarsometatarsal joints, where osteomyelitis is uncommon and neuroarthropathy is common [25].

$^{67}$Ga scintigraphy usually is not helpful to evaluate possible osteomyelitis in the diabetic patient because of a high rate of false-positive scans, primarily the result of neuroarthropathy. In contradistinction, the $^{111}$In WBC (white blood cell) scan has the highest sensitivity (mean=87%) of all radionuclide studies for osteomyelitis in the diabetic foot [17, 19, 21, 22, 24, 26, 27]. An absence of activity is usually sufficient to exclude an active infectious process. However, $^{111}$In WBC scans have been shown to be positive in as many as 31% of cases of non-infected neuropathic joints, especially those in which destruction is rapidly progressive [27]. One major draw-

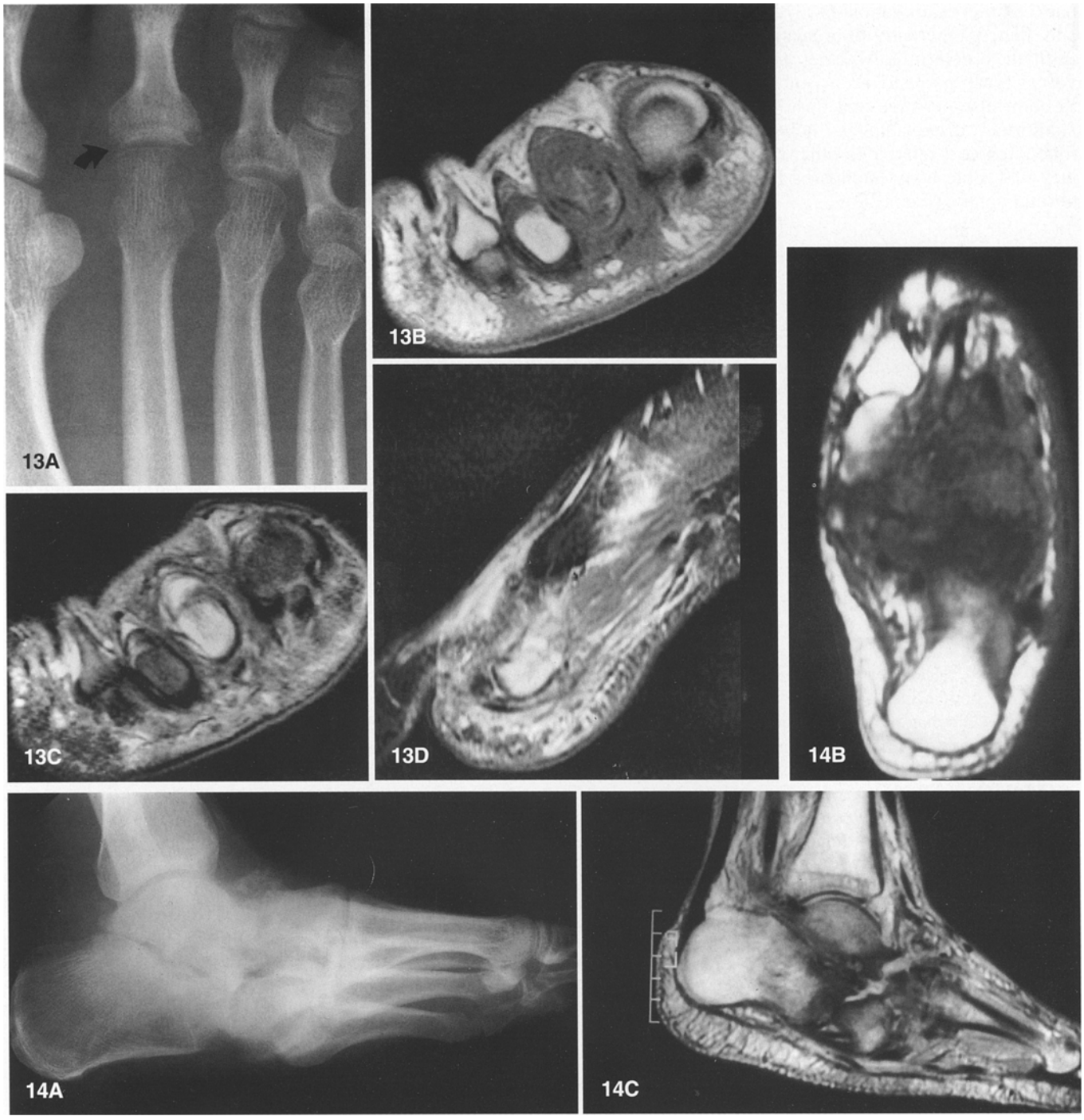



**Fig. 13A–D.** Osteomyelitis in a 35-year-old diabetic man. A radiograph (**A**) reveals marginal erosion, narrowing of the joint space *(arrow)*, and juxta-articular osteoporosis. Exudate and edema in and around the bone are characterized on a T1-weighted spin echo axial MR image (**B;** TR 500/TE 20) by intermediate signal intensity, and on a T2-weighted image (**C;** TR 40000/TE 104) by bright signal intensity. A STIR sagittal image features fat suppression (**D;** TR 2366/TE 40/TI 155), and shows a bright signal emanating from the edematous soft tissue and the exudate-filled head of the second metatarsal

**Fig. 14A–C.** Mid-foot neuroarthropathy in a diabetic man. The radiograph (**A**) shows typical changes of increased density, bony debris, disorganization, dislocation, and joint distention. The proton density (**B**) and gradiant echo (**C**) MR images show characteristic low signal intensity except for a small amount of intra-articular fluid causing increased signal intensity in the midfoot on the gradiant echo image

back to the examination is a relatively low count rate and, hence, inherently poor spatial resolution, making it difficult to determine whether an infection primarily involves bone, periosteum, or soft tissue, and contributing to both false-negative and false-positive diagnoses [24]. Additional disadvantages include a long preparation time, high cost relative to other radionuclide studies, and lack of visible bony landmarks for locating a site of abnormal uptake (Fig. 12D).

*Computed tomography*

Before the routine use of magnetic resonance (MR) imaging, computed tomography (CT) was utilized to assess the extent of bone and soft tissue infection, particularly in the plantar part of the foot, and to determine the site most appropriate for debridement or amputation [28]. The plantar soft tissues may be divided into intermediate, medial, and lateral muscular compartments, in order of decreasing volume. Within a given compartment the spread of infection usually occurs in a proximal direction. Cross-compartmental dissemination may occur through normal openings in the medial and lateral intermuscular septa. Although there has been no large-scale investigation comparing the usefulness of CT to MR imaging in the evaluation of osteomyelitis, MR images are generally believed to show the extent of infection more clearly [29]. However, sequestra, cortical destruction, periosteal new bone, and intraosseous gas may be observed in CT images and remain undetected in MR images. Although soft tissue abscesses and sinus tracts are shown better in MR images, they may be further defined in CT images by intravenous contrast enhancement. CT cannot accurately distinguish between suppuration, reactive granulation tissue, edema, and fibrosis.

*MR imaging*

MR imaging of the foot of the patient with diabetes may reveal evidence of ulceration, edema, and localized fluid collections in the soft tissues, joints, and tendon sheaths, and may show findings of osteomyelitis and neuroarthropathy (Fig. 13). MR imaging is the most sensitive (almost 100% in most series) of all imaging modalities for diagnosing osteomyelitis, and has a relatively high specificity (no lower than 81% in most series), allowing differentiation from cellulitis and soft tissue ulceration [20, 22, 25, 30]. False-positive scans may reflect occult fracture, osteonecrosis, surgical changes, and neuroarthropathy. Although the usual MR imaging findings of neuroarthropathy (low signal intensity on both T1- and T2-weighted images) differ from those of osteomyelitis (high signal intensity on T2-weighted images), this is not always the case (Fig. 14).

MR imaging can be extremely useful in the setting of nondiagnostic radiographs or an equivocal $^{99m}$Tc-MDP bone scan. Specific advantages of MR imaging over CT include superior soft tissue contrast resolution, lack of beam hardening artifacts, and multiplanar capability that allows direct imaging of the affected bone in any plane. MR imaging may be used to guide needle aspiration or biopsy of a suspected site of infection that may not be shown by other imaging modalities. The STIR (short-tau inversion recovery) pulse sequence suppresses the signal intensity of fat, thus increasing the conspicuity of marrow and soft tissue abnormalities (Fig. 13D). The signal intensity of exudate in the medullary cavity is identical to that of marrow edema on T1-weighted and T2-weighted images and on STIR images. In T2-weighted images, malignant tumor, hemorrhage, osteonecrosis and osteomyelitis may all manifest increased signal. Thus the MR imaging findings of osteomyelitis are nonspecific and must be correlated with the findings on clinical examination and other imaging studies.

## Recommendations for imaging suspected osteomyelitis in the diabetic patient

1. The initial screening examination should be plain radiography. Radiographic signs of osteomyelitis in the proximity of an ulcer should prompt a recommendation for treatment of osteomyelitis.
2. If the radiographs show osteolytic changes but no ulcer is present, osteomyelitis should be considered unlikely and the changes more likely a reflection of neuroarthropathy.
3. If the radiographs are normal but the clinical suspicion of osteomyelitis is strong, a three-phase $^{99m}$Tc-MDP scan or MR imaging is recommended. Although MR imaging is more sensitive for osteomyelitis, the radionuclide scan is usually less expensive. However, if the scan is negative or equivocal, osteomyelitis in an early stage still cannot be excluded, and MR imaging should proceed. In that situation, the actual cost of imaging is greater than it would have been had MR imaging been performed at the outset following the normal radiographic examination. MR imaging is better than a $^{111}$In WBC scan to localize the site of infection.
4. In the presence of radiographic signs of neuroarthropathy, a $^{111}$In-WBC scan is preferable to MR imaging to exclude osteomyelitis. Neuroarthropathy usually yields a negative $^{111}$In-WBC scan, although false-positive results may occur. If the $^{111}$In-WBC scan is positive, biopsy confirmation is recommended.
5. Biopsy allows isolation of a pathogen for specific antibiotic therapy. Percutaneous core biopsy is considered the procedure of choice by most authors. To avoid contaminating uninfected bone, the entry site of the needle should be beyond the edge of the subjacent ulcer. It should be noted that some authors favor open biopsy, arguing that percutaneous core biopsy is more likely to induce bone necrosis or spread the infection [13].

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