The British Journal of Radiology, 73 (2000), 443–450

Pictorial review

The diabetic foot

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Abstract. Foot complications in diabetics often lead to amputation. Ulceration is the most common complication in the diabetic forefoot and underlies more than 90% of cases of pedal osteomyelitis. The diagnosis of osteomyelitis is, nevertheless, difficult, and imaging is an important part of the work-up. Plain radiographs, although useful for anatomical information, are neither sensitive nor specific. Three-phase bone scintigraphy is sensitive but not specific. Labelled leucocyte scintigraphy and MRI are both useful and are complementary to one another. Labelled leucocyte scintigraphy is valuable for diagnosis as well as follow-up of pedal osteomyelitis. MRI offers exquisite anatomical detail, which is invaluable for guiding surgical management. The principal complication in the mid and hind foot is the neuropathic or Charcot joint. Although infection of the neuropathic joint is infrequent, its diagnosis is difficult. The extensive bony changes that accompany this disorder severely diminish the value of radiography and bone scintigraphy. It is not always possible to distinguish the marrow oedema of neuropathy from that of osteomyelitis and the role of MRI in the evaluation of this entity is still uncertain. Uptake of labelled leucocytes in the absence of infection may occur and is owing, at least in part, to haematopoietically active marrow. Combined leucocyte/marrow scintigraphy holds considerable promise for identifying the infected Charcot joint.

Foot complications, the foremost cause of morbidity, mortality and disability in diabetics, often lead to lower extremity amputations. Although prompt and accurate diagnosis reduces the need for amputation, detection is often difficult. Disorders of the forefoot are distinct from those of the mid and hindfoot, and require different diagnostic approaches (Figure 1).

The forefoot

Pedal ulcers, the most common complication of the diabetic forefoot, are portals of entry for infection and directly overlie more than 90% of cases of pedal osteomyelitis. Most patients lack clinical signs and symptoms (other than the ulcer) and the diagnosis is frequently overlooked. Imaging is therefore essential in their evaluation (Figure 2) [1].

Demineralization, periosteal reaction and bony destruction, the classic radiographic triad of osteomyelitis, appear only after 30–50% of the bone is destroyed, a process that takes up to 2 weeks. This triad may also be seen in other diabetic foot conditions such as joint deformity and fracture. Although the accuracy of plain radiography for early diagnosis of pedal osteomyelitis is only about 50–60%, this is still the initial screening investigation performed on the diabetic foot. Radiographs are readily obtained, relatively inexpensive and, even when not diagnostic, provide important anatomical information that is useful for the interpretation of many of the other studies performed (Figure 3) [2].

Abnormal bone marrow signal, soft tissue mass and cortical destruction on MRI are strongly suggestive of osteomyelitis. The demonstration of sequestrum formation, sinus tracts and associated soft tissue ulceration increases the diagnostic certainty. Although it is not always possible to distinguish between marrow oedema and infection, the accuracy of MRI is about 80–90%. Furthermore, MRI provides superb anatomical detail, useful for guiding surgical management (Figure 4) [3].

Focal hyperperfusion, focal hyperaemia and focal bony uptake on delayed images are often considered diagnostic of osteomyelitis on three-phase bone scintigraphy. Unfortunately, this same pattern may also be seen in fracture, the neuropathic joint and longstanding cellulitis, conditions that regularly coexist in the diabetic foot (Figure 5). The addition of 24-h images, the

Received 3 March 1999 and in revised form 15 July 1999, accepted 12 August 1999.

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four-phase bone scan, reportedly enhances specificity [2]. Diphosphonate accumulation in normal (lamellar) bone ceases about 4 h after injection while it presumably continues to accumulate for several hours more in abnormal or woven bone. Diphosphonate uptake in osteomyelitis should, therefore, be greater at 24 h than at 4 h. Both visual and semi-quantitative analyses have been used, with a reported accuracy of about 85%. Woven bone is not unique to osteomyelitis; false positive results occur in fractures, tumours and severe degenerative changes (Figure 6). Complementary gallium imaging improves the specificity of bone scintigraphy. The large number of equivocal results obtained, however, is a significant drawback to this combined technique [2].

Labelled leucocytes do not usually accumulate at sites of new bone formation without infection and are very useful for both diagnosis and follow-up of pedal osteomyelitis, with an accuracy of about 80–90%. Relatively low count rates and a paucity of landmarks with the ^{111}In label do not pose a significant problem since in more than 90% of cases osteomyelitis directly underlies an ulcer (Figure 7). $^{99}Tc^{m}$-exametazime (HMPAO) labelled leucocyte imaging gives higher resolution images, and offers same-day imaging with comparable results [2, 4] (Figure 8).

Among newer agents used to diagnose infection, one of the most extensively studied is a $^{99}Tc^{m}$-labelled murine monoclonal antibody fragment (MN_3), which binds with the normal cross reactive antigen-95 (NCA-95) present on leucocytes. Results are comparable with those obtained with *in vitro* labelled leucocytes [5, 6]. Advantages are the short preparation time (<30 min *vs* 2–3 h for *in vitro* labelled leucocytes), no blood product handling, immediate imaging (1–2 h) and high resolution images (Figure 9) [7].

The mid/hind foot

Approximately 5% of diabetics with neuropathy develop a neuropathic or Charcot joint, usually involving the tarsal or tarsometatarsal joints. Continued ambulation on an insensitive joint causes joint instability and eventually degeneration, subluxation and destruction. Clinically, the neuropathic joint is swollen (often massively) and unstable (collapsed longitudinal arch), with crepitus (due to extensive bone and cartilage destruction), palpable loose bodies and large osteophytes. Pain, when present, is generally less than would be expected from the appearance of the joint. Synovial effusions, usually non-inflammatory or haemorrhagic, may contain mononuclear cells [8].

The most common radiographic finding is a longstanding Lisfranc fracture–dislocation with eburnation and fragmentation of the tarsometatarsal joints. Unusual calcaneal fractures and talocalcaneal joint dissolution as well as talar collapse into the calcaneus, distal fibular fractures and talar angulation within the ankle mortise are also part of this entity. Ultimately, massive bony sclerosis, osteophytosis and osseous debris make it extremely difficult to establish the presence or absence of infection (Figure 10).

CT may show sequestra, cortical defects, periosteal new bone and intraosseous gas. This technique cannot, however, distinguish between suppuration, reactive granulomatous tissue, oedema and fibrosis [5].

On MRI, disorganized destruction, dislocation, marrow oedema, effusion, and loss of bone and joint definition characterize the neuropathic joint. Difficulties in distinguishing the oedema of neuropathy from that of osteomyelitis make the precise role of MRI, with reported specificities ranging from 0–100%, uncertain (Figure 11) [6, 9].

The dramatic bony changes of the Charcot joint invariably result in a positive three-phase bone scan even in the absence of infection (Figure 12) [6, 10].

Labelled leucocyte accumulation without infection has been attributed to the inflammation and fractures that are part of this entity. However, the effusions are rarely inflammatory and the predominant cell type is mononuclear. The inflammatory response accompanying fractures is polymorphonuclear only in its earliest phase. Labelled leucocyte imaging is not sensitive for detecting non-neutrophilic inflammatory or infectious conditions, and it is therefore unlikely that uptake in the uninfected Charcot joint can be ascribed solely to inflammation. Data from our institution indicate that such uptake is due, at least in part, to haematopoietically active marrow. Conversion of fatty into haematopoietically active marrow in induced arthritis has been observed in animals and perhaps a similar process occurs in the Charcot joint. Furthermore, bone marrow is an integral part of fracture repair, and fractures are constituents of the neuropathic joint. The presence of marrow decreases the specificity of the labelled leucocyte study, a well recognized phenomenon in other parts of the skeleton. Interpreting the labelled leucocyte image in conjunction with a marrow scan, which reduces false positive results, holds considerable promise for determining whether or not infection is present in the Charcot joint (Figures 13 and 14) [10].

Despite the myriad of available procedures, diagnosing complications of the diabetic foot remains a challenge. For pedal osteomyelitis the most useful studies are labelled leucocyte

scintigraphy and MRI. Besides availability and experience, the information desired will govern the choice of imaging study to be performed. Labelled leucocyte imaging, excellent for diagnosing osteomyelitis and monitoring response to therapy, is best suited for patients in whom medical therapy is planned. MRI provides excellent anatomical detail and is invaluable for surgical planning.

Diagnosis of a Charcot joint, with or without infection, is problematic. Although more extensive investigations are warranted, available data suggest that leucocyte/marrow scintigraphy can accurately answer this question.

The role of radiolabelled antibodies in diabetic foot infection has yet to be defined. These compounds target white cells and will probably eliminate the need for *in vitro* labelling of leucocytes, which is a significant improvement. It is equally likely, however, that the limitations of traditional white cell imaging will also apply to these agents.

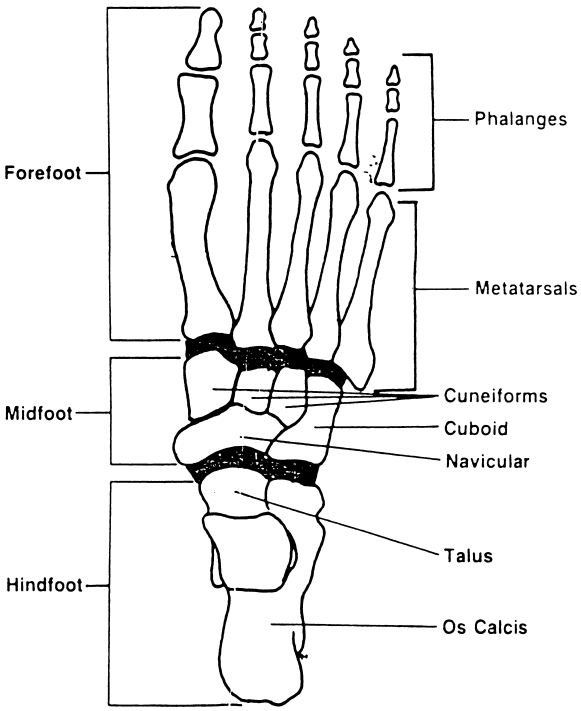


Figure 1. Diagrammatic representation of the divisions of the foot.

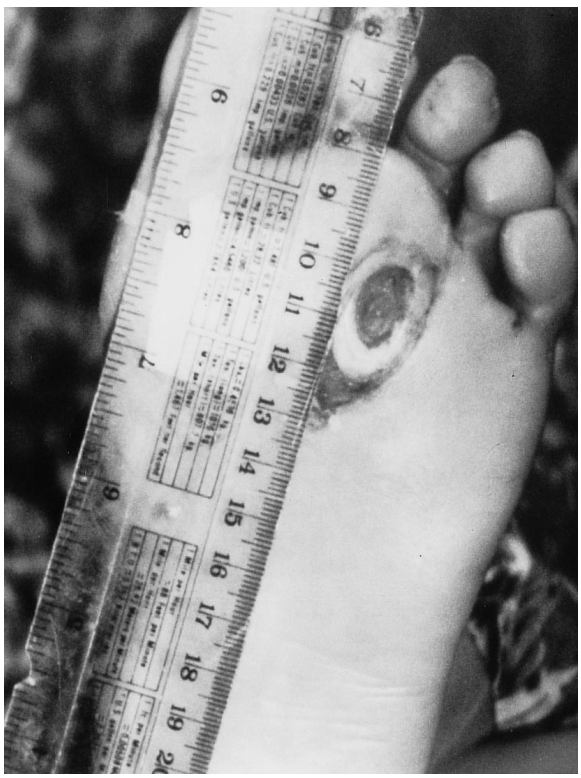


Figure 2. Typical pedal ulcer in a diabetic patient, overlying the left fourth metatarsal bone.

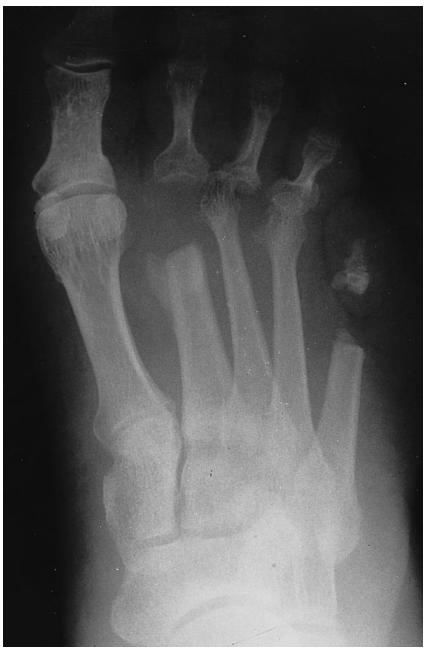
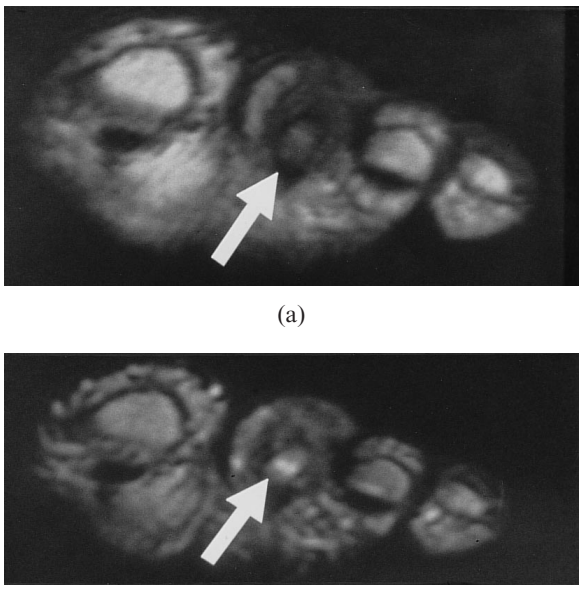


Figure 3. Osteomyelitis of the distal metatarsal and proximal phalanx of the third digit. Erosive changes, osteopenia and widening of the joint space. Note previous surgical resection of the distal second and fifth metatarsals.



(a)

(b)

Figure 4. Coronal (a) T_1 and (b) T_2 weighted images from a patient with osteomyelitis of the left second toe. There is marrow oedema, characterized by decreased signal intensity on the T_1 weighted image (a) and increased signal intensity on the T_2 weighted image (b), as well as soft tissue swelling and induration.

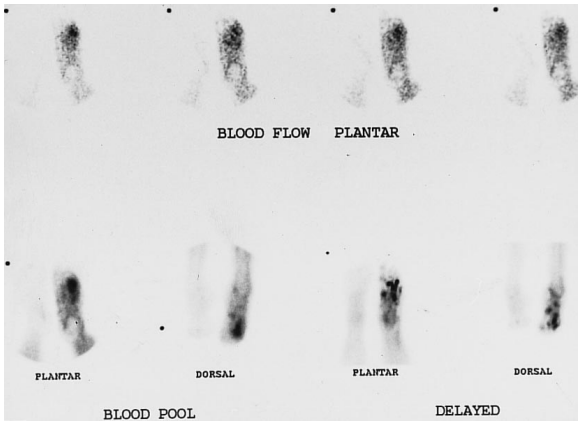


Figure 5. A three-phase bone scan demonstrates focal hyperperfusion, hyperaemia and bony uptake in a diabetic patient with osteomyelitis of the left fourth metatarsal.

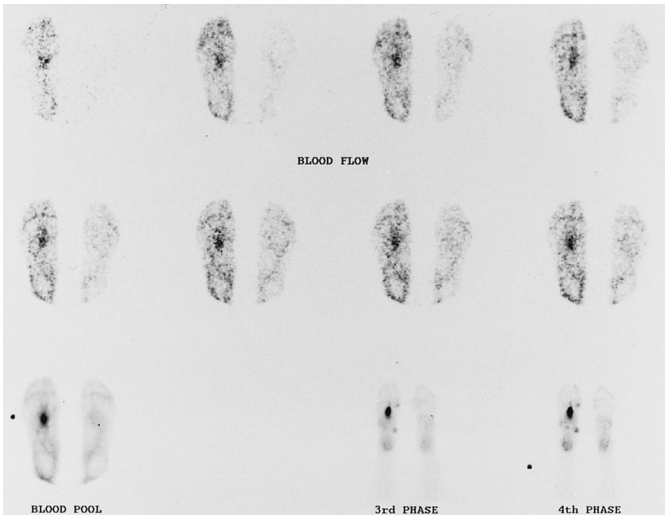


Figure 6. Four-phase bone scan. The three-phase bone scan is consistent with osteomyelitis of the right second metatarsal. Both visually and semi-quantitatively uptake in this bone increases from the third to the fourth phase, as expected in osteomyelitis. The actual diagnosis, however, was a stress fracture.

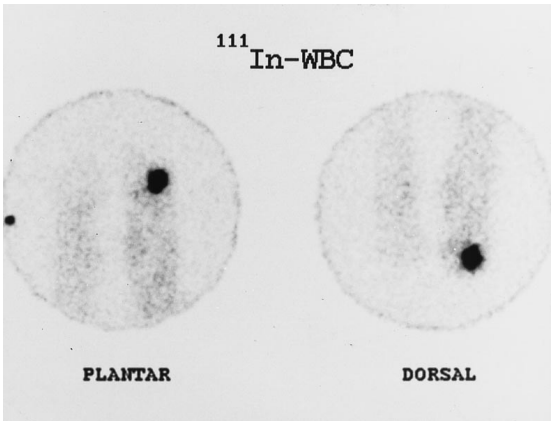
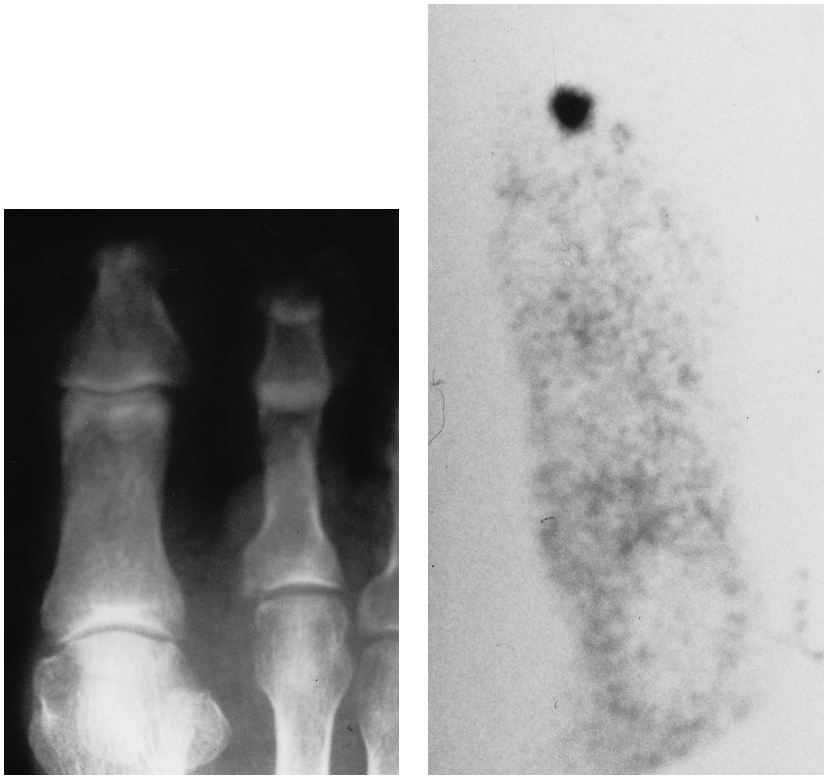


Figure 7. ^{111}In labelled leucocyte scan demonstrating intense uptake in the left fourth metatarsal. (Same patient as in Figure 5.)



(a) (b)

Figure 8. (a) Radiograph, which is normal, and (b) $^{99}Tc^{m}$-HMPAO labelled leucocyte image of a patient with osteomyelitis of the right second toe. Note the improved resolution of the $^{99}Tc^{m}$ image compared with the ^{111}In labelled leucocyte image in Figure 7 (courtesy of Dr Holly Dey, MD).

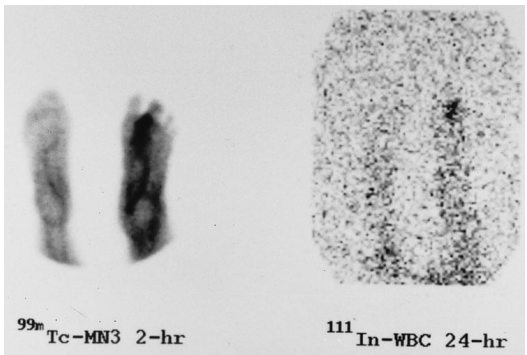


Figure 9. Osteomyelitis of the left second metatarsal. Note the superior image quality of the $^{99}Tc^{m}$-MN_3 image compared with that of the ^{111}In labelled leucocyte image.

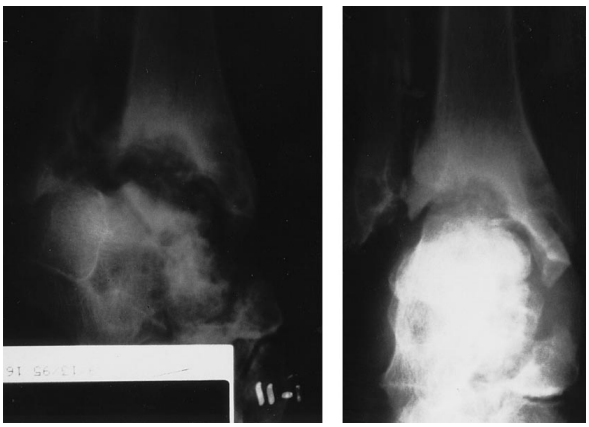
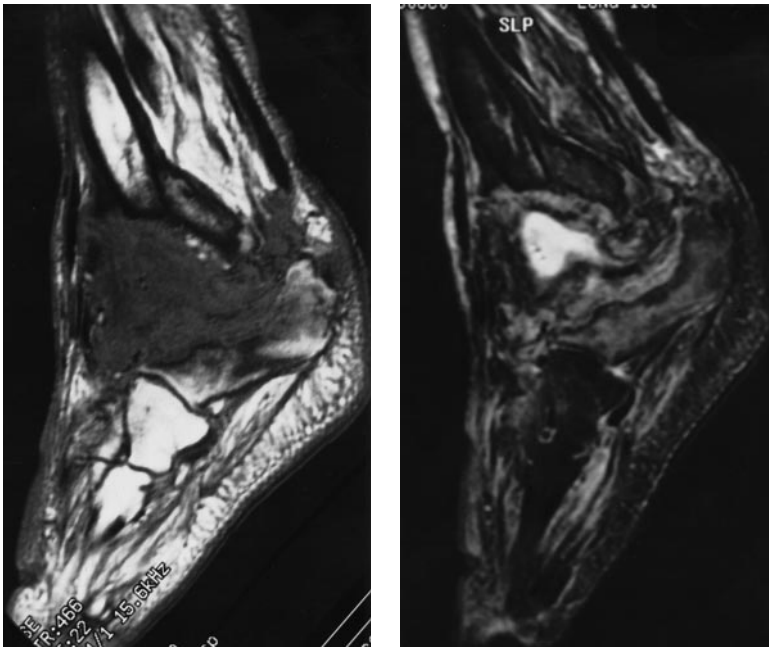


Figure 10. Radiographs reveal bony destruction, new bone formation, tarsal dislocation and a distal fibular fracture consistent with a Charcot joint.



(a) (b)

Figure 11. (a) T_1 weighted and (b) fat suppressed T_2 weighted sagittal images show marked deformity and resorption of the distal tibia, talus and calcaneus with soft tissue thickening and localized fluid collection in the talar dome and along the subcutaneous tissues over the medial malleolus. Although there is marrow oedema and effusion, focal sparing of segments and fragments of the involved bones and preservation of fat planes indicate absence of infection.

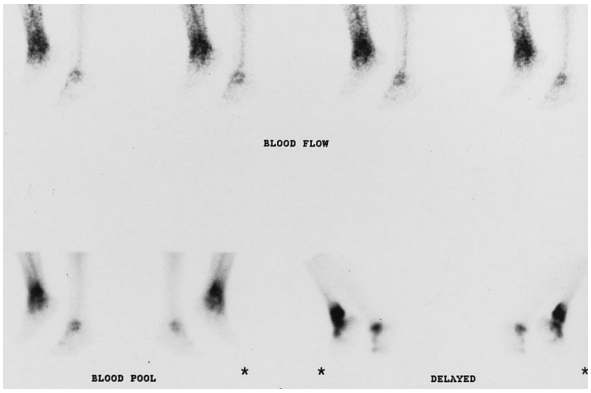


Figure 12. A positive three-phase bone in an uninfected Charcot joint.

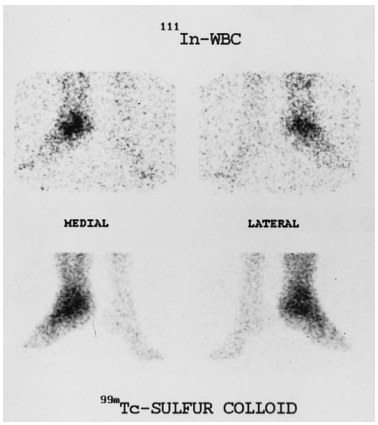
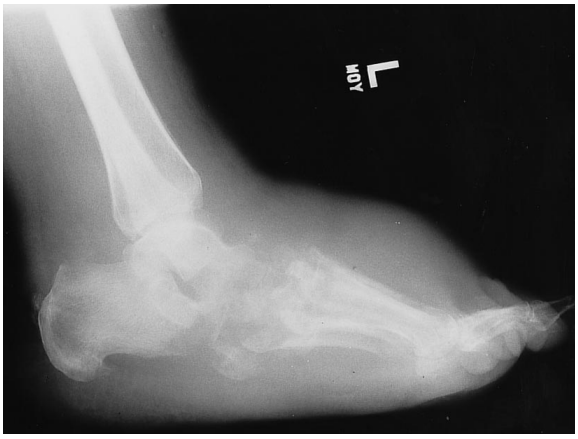
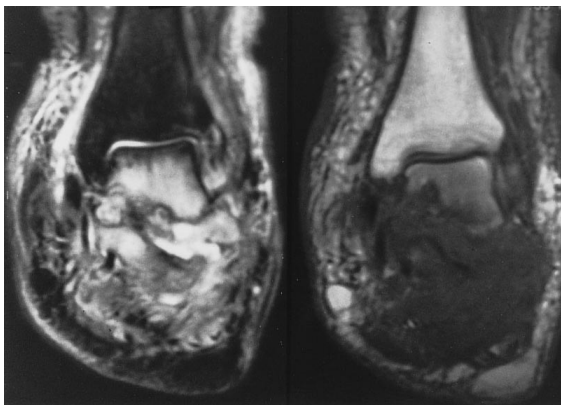


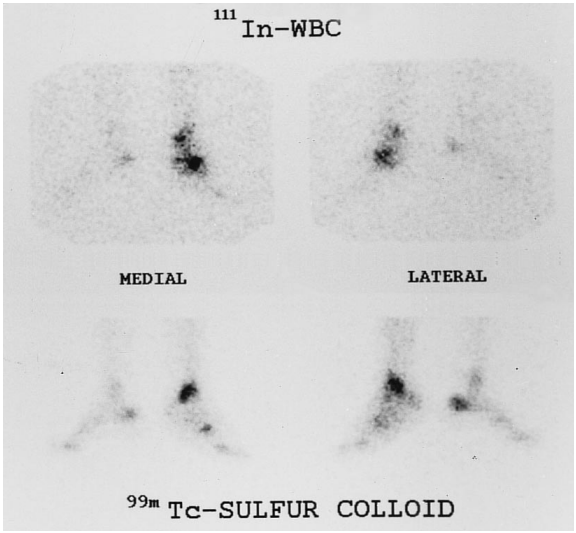
Figure 13. Increased labelled leucocyte uptake in an uninfected Charcot joint. The marrow scan has a similar appearance, confirming that the activity on the white cell image is due to marrow, not infection.



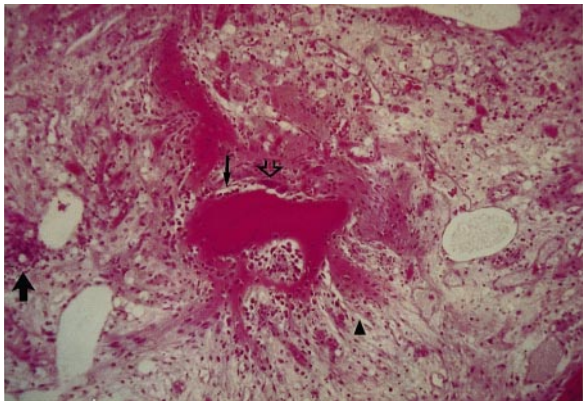
(a)



(b)



(c)



(d)

Figure 14. (a) Radiograph shows soft tissue swelling, extensive osteolysis and disorganization of the tarsal and metatarsal bones. (b) MRI (T_1 weighted on left; T_2 weighted on right) shows marrow oedema as well as widening, erosive changes and effusion of the subtalar joint, interpreted as suggestive of septic arthritis. (c) The combined leucocyte/marrow scan demonstrates congruent uptake of both tracers in the distal tibia and talus, indicative of marrow. There is leucocyte uptake in the distal tarsal and proximal metatarsal bones without corresponding activity on the marrow scan (incongruent uptake), consistent with osteomyelitis. (d) Specimen photomicrograph demonstrates osteomyelitis with new bone formation (arrowhead), osteoblasts (thin arrow), osteoclasts (open arrow) and haematopoietically active marrow (thick arrow), confirming the findings on the leucocyte/marrow study (reproduced with permission, [10]).

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