Diabetic Foot

A Comprehensive Guide for Clinicians

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CHRISTIAN MEDICAL COLLEGE
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Foreword
Andrew JM Boulton

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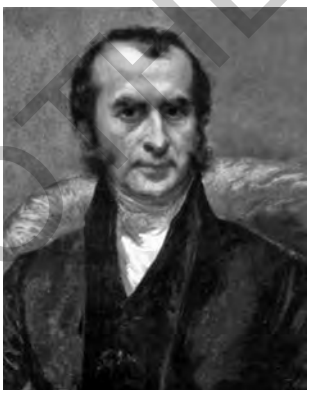
CONTENTS

MARCHAL de CALVI AND THOMAS HODGKIN

Marchal de Calvi in 1852 and Thomas Hodgkin in 1854, respectively, realized that there was an association between diabetes and gangrene of the foot. At that time, it was common to treat ulcers by prolonged bed rest, although it was noticed that the wounds would return once the patient was mobile again. A potential infection of foot ulcers could be a significant cause of morbidity and mortality in the 1850s, and hence the contribution of both Hodgkin and de Calvi was a significant advancement in the field. Hodgkin is also known for having described Hodgkin's Disease, a type of lymphoma, in 1832.



Thomas Hodgkin

Diabetic Foot Ulcers: Clinical Approach

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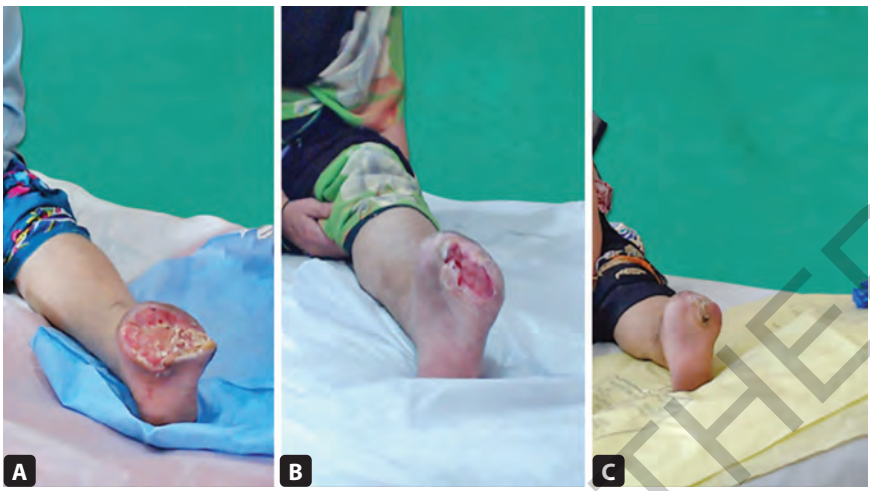
CASE SCENARIOS

A 54-year-old lady with a history of diabetes mellitus (DM) for 15 years presented with high-grade fever, redness, and swelling of the left foot with an ulcer on the lateral aspect for 7 days. There was active discharge from the wound which was foul-smelling. She had undergone amputation of the left great toe 4 years before. On examination, her vital signs were stable, she was febrile, the left foot examination revealed erythema up to the ankle with induration, and mottling seen on the fourth and fifth toes. There was a deep ulcer of 2 × 2 cm over the webspace between the fourth and fifth toes. Bilateral peripheral pulses were well felt. The left inguinal lymph nodes were enlarged and tender. On further evaluation, she had bilateral distal symmetrical peripheral neuropathy, bilateral moderate nonproliferative diabetic retinopathy, and microalbuminuria. Her investigations revealed a random blood glucose level of 303 mg/dL, normocytic anemia, and neutrophilic leukocytosis. An X-ray of the left foot was normal. The patient was given empirical intravenous antibiotics. The patient underwent a transmetatarsal amputation of the left foot. She was discharged after 4 days and was regularly followed up with daily dressings at home (**Figs. 1A** to **C**).

INTRODUCTION

Diabetic foot ulcers (DFUs) are frequently encountered in patients with DM. Nearly 25% of patients with DM are affected by foot ulcers during their lifetime, with a population-based annual incidence (in the United States of America) between 1 and 4.1%.[1] Diabetes remains the most common cause of nontraumatic amputation worldwide with a 15 times higher incidence than those without diabetes. Over 85% of lower limb amputations are preceded by foot ulcers.[2] A multicentric study done in four different centers in India found that the prevalence of diabetic foot infection was 6–11% and the prevalence of amputation was 3%.[3] Diabetic foot complications remain major medical, social, and economic problems across the world. According



FIGS. 1A TO C: Serial pictures of the foot ulcer (post-trans-metatarsal amputation) with time frame. (A) During the first visit; (B) After 6 months; (C) After 15 months.

to the 2007 data from the United States of America, $18.9 billion (1,800 crore in INR) was spent on the care of DFUs and $11.7 billion (800 crore in INR) on lower extremity amputations. Diabetes-related foot ulcer causes debilitating effects in the social, economic, and psychological aspects both among the patients and the caretakers. Most often the diabetes foot ulcer is preventable. Unfortunately, many patients due to lack of availability of adequate care tend to get delayed treatment and thereby end up with minor to major lower limb amputations.

One should keep involvement of mind the importance of salvaging the affected limb as well as the prevention of the involvement of the contralateral limb which is also at risk for acquiring a foot ulcer. Studies have proven that a patient with an amputation in one limb, has 10–20 times greater risk of amputation of any kind on the contralateral limb over a follow-up period of 3 years. In other words, half of patients will have another amputation within the first 5 years of an amputation. It is only possible by recognizing the factors that negatively influence the prognosis that the number of amputations can be reduced. It imposes a major economic burden to the individual and the society.[4]

The tragic rule of 15:

- 15–25% of people with diabetes will develop a foot ulcer in their lifetime.
- 15% of foot ulcers will develop osteomyelitis.
- 15% of foot ulcers will lead to an amputation.

Tragic rule of 50:

- 50% of amputations are at a trans-femoral/trans-tibial level.[5,6]
- 50% of patients need second amputation in 5 years.
- 50% of patients die at 5 years.[7,8]

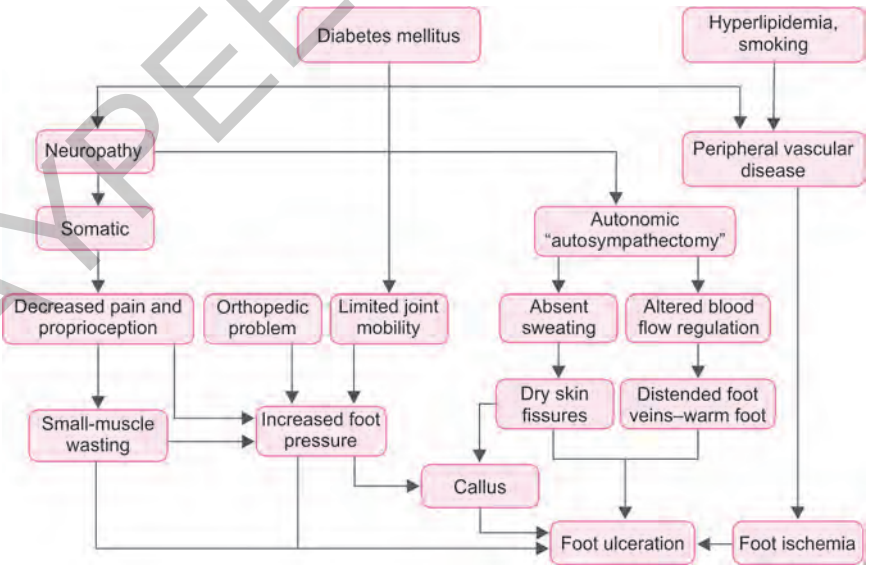
ETIOLOGY AND CLASSIFICATION OF DIABETIC FOOT ULCERS

Diabetic foot ulcers can be of three types—neuropathic, ischemic, and neuroischemic. Neuropathy, peripheral vascular disease, and increased foot pressure are the major pathogenic factors for development of the DFU. Pathogenesis of DFU is shown in **Flowchart 1**.

Neuropathic Ulcers

Neuropathy is associated with an 8- to 10-fold higher risk of ulceration and 2- to 5-fold higher risk of amputation. The mechanism behind the neuropathic ulcer is complex. First, it is because of a loss of protective sensation leading to reduced perception of pain. Second, the motor component of neuropathy causes intrinsic weakness of the muscular compartment, leading to deformation of toe flexion (mainly by interosseous and lumbricals), which results in formation of overloaded plantar areas. The intrinsic muscles of the foot are shown in **Figure 2**. Moreover, the autonomic dysfunction causes anhidrosis and thereby dry skin and arteriovenous (AV) shunting, leading on to alteration of blood supply to the skin and underlying bones.

Neuropathic ulcers usually occur on the plantar aspect of the foot most commonly under the first metatarsal head and tip of the toes (**Figs. 3A** to **C**). The most common cause of ulceration is due to the abnormal pressure distribution and consequent repetitive mechanical forces of gait and the resultant callus formation. Untreated callosity is a preulcerative lesion in the diabetic neuropathic foot (**Flowchart 2**).



FLOWCHART 1: Pathogenesis of diabetic foot ulcer.

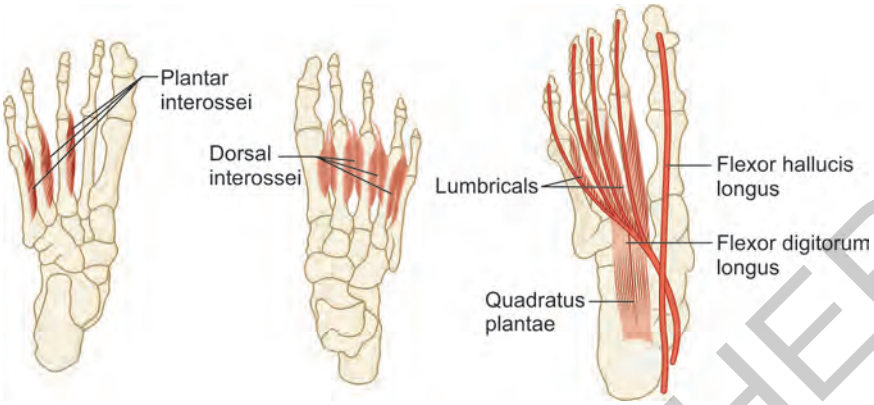
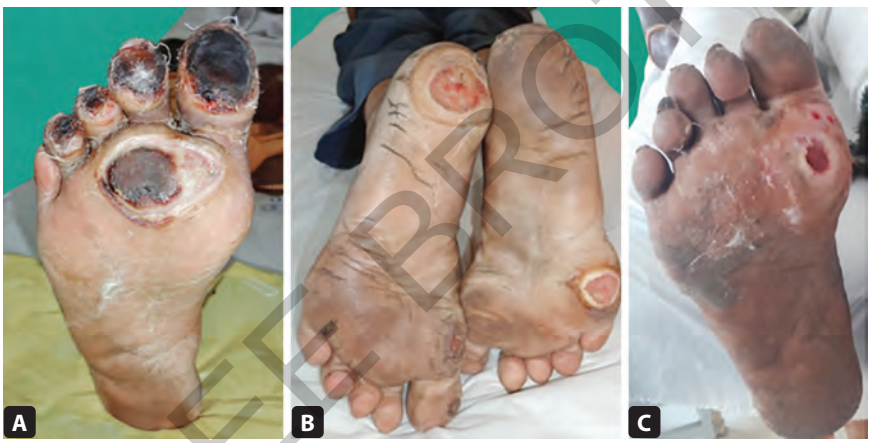
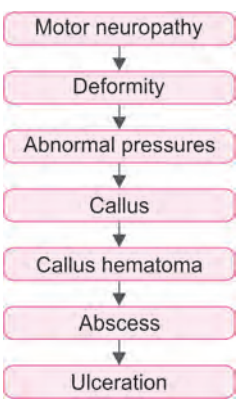


FIG. 2: Showing muscles of foot.



FIGS. 3A TO C: Showing sites of neuropathic ulcers—(A) Over plantar aspects of the toes, (B) Heel and fifth metatarsal head, and (C) First metatarsal head.



FLOWCHART 2: Mechanism of callosity developing to ulcer.

FIGS. 4A AND B: Showing—(A) Callosities present over the plantar aspects of both great toes, and (B) The underlying ulcer exposed on removal of the callosities.

Therefore, thick callus may press on the soft tissues beneath and cause ulceration (**Figs. 4A** and **B**).

A layer of whitish, macerated, moist tissue found under the surface of the callus indicates that the foot is close to ulceration, and urgent removal of the callus is required. If the callus is not removed, inflammatory autolysis and hematomas develop under the callus leading to tissue necrosis, resulting in a small cavity filled with serous fluid giving the appearance of a blister under the callus. Removal of the callus reveals an ulcer as seen in **Figure 4B**.

Ischemic and Neuroischemic Ulcers

Ischemic and neuroischemic ulcers are commonly located at the margins of the foot, often on the medial surface of the first and over the lateral aspect of the fifth metatarsophalangeal joint. In addition, they develop on the tips of the toes and beneath toe nails if these become overtly thick (**Figs. 5A** and **B**). The classic signs of preulceration in the neuroischemic foot are a red mark on the skin, often tight shoes due to small-sized shoe, leading to frictional forces on the vulnerable margins of the foot. The features of neuropathic, ischemic, and neuroischemic ulcers are shown in **Table 1**.

The cardinal sign of ischemic ulceration is a superficial blister, following persistent friction that develops into a shallow ulcer with a base of sparse pale granulation tissue or yellowish closely adherent slough. There can be associated features such as brittle nails and the absence of hair.

Despite delivering exemplary wound care, wounds may fail to heal due to a variety of reasons such as poor glycemic control, lack of blood flow, unrelieved pressure, poor care, infection, and coexisting systemic diseases.

FIGS. 5A AND B: A neuroischemic ulcer over the great toe.

TABLE 1: Features of neuropathic and ischemic ulcers.

Features	Neuropathic	Ischemic	Neuroischemic
Sensation	Usually painless	Painful	Degree of sensory loss
Callus/necrosis	Callus present and often thick	Necrosis common	Minimal callus prone to necrosis
Wound bed	Pink and granulating, surrounded by callus	Pale and sloughy with poor granulation	Poor granulation
Foot temperature and pulses	Warm with bounding pulses	Cool and absent pulses	Cool with absent pulses
Other	Dry skin and fissuring	Delayed healing	High risk of infection
Typical location	Weight-bearing areas of the foot such as metatarsal heads, the heel and over the dorsum of clawed toes	Tips of toes, nail edges and between the toes and lateral borders of the foot	Margins of the foot and toes
Prevalence	35%	15%	50%

Infected Ulcers

Individuals with DM have increased risk of hospitalization with soft tissue and bone infections of the foot compared to those without DM.[9] Following are the factors that predispose the ulcer for an infection:

- Chronic poor glycemic control
- A positive probe-to-bone (PTB) test
- Ulcer for >30 days

TABLE 2: Modified Dundee classification of cellulitis.

Modified "Dundee" classification	
Class I	No sepsis, no comorbidities, and SEWS [Standardized Early Warning Score (**Table 3**)] <4
Class II	Documentation of one or more significant comorbidities (e.g., obesity, peripheral vascular disease or venous insufficiency), no sepsis, and SEWS <4
Class III	Sepsis but SEWS <4
Class IV	Sepsis and SEWS ≥4

Source: Clinical Resource Efficiency Support Team (CREST). Guidelines on the Management of Cellulitis in Adults. 2005.

TABLE 3: SEWS (Standardized Early Warning Score) parameters and scoring systems.

Parameter	Score						
	3	2	1	0	1	2	3
Respiratory rate (breaths/min)	≤8			9–20	21–30	31–35	≥36
Oxygen saturation (%)	<85	85–89	90–92	≥93			
Temperature (°C)	<34	34–34.9	35–35.9	36–37.9	38–38.4	≥38.5	
Systolic blood pressure (mm Hg)	≤69	70–79	80–99	100–199		≥200	
Heart rate (bpm)	≤29	30–39	40–49	50–99	100–109	110–129	≥130
AVPU response (stimulus required to induce response)	Unrespon-sive	Pain	Verbal	Alert			

[AVPU: alert, verbal, pain, unresponsive (category of stimulus required to generate patient response)]

Source: SEWS Chart. [online] Available from: www.nhslothian.scot.nhs.uk/health_promotion/sewskey.pdf. [Last accessed November, 2021].

- Recurrent foot ulcers
- Ulcer following a trauma
- Underlying peripheral vascular disease
- Past history of lower extremity amputation
- Loss of protective sensation (LOPS)
- Associated renal insufficiency
- Behaviors such as walking barefoot
- Cigarette smoking

The modified Dundee classification of a patient with cellulitis is shown in **Table 2**. As per the International Working Group on Diabetic Foot (IWGDF) recommendations, the clinicians should evaluate a patient with an ulcer: The affected foot or limb and

FIG. 6: Showing ulcer over the medial aspect of the foot with redness and swelling suggestive of underlying infection and cellulitis.

the infected wound as well as the opposite limb. Clinicians should diligently look for the presence of symptoms or signs of inflammation (erythema, warmth, tenderness, pain, or induration) or purulent secretions (**Fig. 6**). One should also look for arterial and venous insufficiency, LOPS, and biomechanical problem. Subsequently, the severity of the infection should be determined depending on its extent and depth and the presence of any systemic findings of infection. It is recommended to debride any wound that has necrotic tissue or a surrounding callus; the required procedure may range from minor to extensive.

AN APPROACH TO A FOOT ULCER

The approach to a foot ulcer should target various levels, such as systemic signs, neurological, vascular, dermatological, musculoskeletal, radiological, and at the laboratory. Other factors such as socioeconomic status, psychosocial influence, and diabetes-related complications should also be considered.

Foot examination should include assessment of skin temperature since increased warmth is the first indicator of inflammation in the insensate foot. Skin color, thickness, dryness, cracking, perspiration, webspace infection, ulceration, calluses, blistering, hemorrhage, etc., should be observed while inspecting a diabetic foot. Deformities such as claw toes, hammer toe, mallet toe, bunion (**Figs. 7A** and **B**), prominent metatarsal heads, muscle wasting (guttering between metatarsals), and Charcot foot (**Fig. 7C**) should also be looked for in the foot.[10] The loss of sensation over the distal plantar surface to the 10 g Semmes Weinstein monofilament (5.08 g) is a significant and independent predictor of future foot ulceration and the possibility of lower-extremity amputation.

FIGS. 7A TO C: (A) Claw toe, (B) Bunion and hammer toes, and (C) Charcot foot with ulcer.

TABLE 4: The Society for Vascular Technology's interpretation of resting ABPI measurements.

Resting ABPI	Severity of disease
>1.4	Calcification may be present
>1.0	Probably no arterial disease
0.81–1.00	No significant arterial disease, or mild/insignificant disease
0.5–0.80	Moderate disease
<0.5	Severe disease
<0.4	Critical ischemia

(ABPI: ankle brachial pressure index)

Source: Al-Qaisi M, Nott DM, King DH, Kaddoura S. Ankle brachial pressure index (ABPI): An update for practitioners. Vasc Health Risk Manag. 2009;5:833-41.

In persons with DM and underlying ischemia, the distribution of peripheral arterial disease (PAD) is greater in the arteries below the knee. Simple bedside evaluation for PAD includes noninvasive assessments such as ankle brachial blood pressure index (ABPI), determination of systolic toe pressure by photoplethysmography (PPG), transcutaneous oximetry ($TcPO_2$), and Doppler arterial flow studies.

Although the ABPI is an easy and reliable tool, many a time it underestimates the degree of peripheral arterial occlusive disease (PAOD) amongst those with arterial calcification (**Table 4**).

Moreover, ulcers occur on the plantar surface of the foot in areas with increased pressure, due to the excessive repetitive and shear force. Almost half of the patients present with recurrent ulcer, either at the same foot or in the opposite foot if not intervened with appropriate footwear after the initial ulcer heals.

FIGS. 8A AND B: (A) An ulcer over the great toe with probe test being negative and (B) X-ray of the same patient showing osteomyelitis of the proximal and distal phalanges of the left great toe (Shown with a circle).

The most common site of ulcer is the base of the first metatarsal bone followed by the apex of the toes, bases of other metatarsals, and mid-foot ulcers.

Assessment of bone involvement is an important factor as it determines the ulcer healing. This has been explained in greater detail in the chapter on osteomyelitis. The involvement of the phalanges of left great toe with an ulcer is shown in **Figures 8A** and **B**.

Classification of Foot Ulcers

There are various classification systems which have been proposed (**Table 5**), most commonly cited ones are mentioned here.

The key features of various classifications are as follows:

- Classification systems grade ulcers according to the presence and extent of various physical characteristics, such as size, depth, appearance, and location.
- They can help in the planning and monitoring of treatment and in predicting outcome and can be used for research and audit.

Management of Foot Ulcers

Ulcer Dressing

Some studies show better healing rate with hydrogels in small ulcer comparing to gauze dressing. Whatever technique is used, achievement of the following goals is important in wound care:

- Promote granulation (new tissue containing all the cellular components for epithelialization)

TABLE 5: **Key features of various classification systems for foot ulcers.**

Classification system	Key points	Pros/Cons
Wagner (Table 8)	Assesses ulcer depth along with the presence of gangrene and the loss of perfusion using six grades (0–5)	• Well established • Does not fully address infection and ischemia
University of Texas (Table 6) (Armstrong)	Assesses ulcer depth, presence of infection and presence of the signs of lower-extremity ischemia using a matrix of four grades combined with four stages	• Well established • Describes the presence of infection and ischemia much better than the Wagner classification and may help in predicting the outcome of the DFU
PEDIS (Table 7) (PEDIS—perfusion, extent, depth, infection, and sensation)	Assesses Perfusion, Extent (size), Depth (tissue loss), Infection and Sensation (neuropathy) using four grades (1–4)	• Developed by IWGDF (International Working Group on Diabetic Foot) • User-friendly (clear definitions, few categories) for practitioners with a lower level of experience with diabetic foot management
SINBAD (Table 9) (site, ischemia, neuropathy, bacterial infection, area, and depth)	• Assesses site, ischemia, neuropathy, bacterial infection, and depth • Uses a scoring system to help predict outcomes and enable comparisons between different settings and countries	Simplified version of the S(AD) SAD classification system Includes ulcer site as data suggests this might be an important determinant of outcome

TABLE 6: **University of Texas classification.**

Stage	Grade			
	0	1	2	3
A (no infection or ischemia)	Pre- or post-ulcerative lesion completely epithelialized	Superficial wound not involving tendon capsule, or bone	Wound penetrating to tendon or capsule	Wound penetrating to bone or joint
B	Infection	Infection	Infection	Infection
C	Ischemia	Ischemia	Ischemia	Ischemia
D	Infection and ischemia	Infection and ischemia	Infection and ischemia	Infection and ischemia

Source: Armstrong DG, Lavery LA, Harkless LB. Validation of a diabetic wound classification system: the contribution of depth, infection and vascular disease to the risk of amputation. Diabetes Care. 1998;21(5): 855-9.

TABLE 7: PEDIS classification of severity of diabetic foot infections.

Clinical criteria	Grade/severity
No clinical signs of infection	Grade 1/uninfected
Superficial tissue lesion with at least two of the following signs: • Local warmth • Erythema >0.5–2 cm around the ulcer • Local tenderness/pain • Local swelling/induration • Purulent discharge Other causes of inflammation of the skin must be excluded	Grade 2/mild
Erythema >2 cm and one of the findings above or: • Infection involving structures beneath the skin/subcutaneous tissues (e.g., deep abscess, lymphangitis, osteomyelitis, septic arthritis, or fasciitis) • No systemic inflammatory response	Grade 3/moderate
Presence of systemic signs with at least two of the following: • Temperature >39°C or <36°C • Pulse >90 bpm • Respiratory rate >20/min • $PaCO_2$ <32 mm Hg • White cell count 12,000 mm^3 or <4,000 mm^3 • 10% immature leukocytes	Grade 4/severe

Source: Abbas Z, Lutale JK, Game FL, Jeffcoate WJ. Comparison of four systems of classification of diabetic foot ulcers in Tanzania. Diabet Med. 2008;25(2):134-7.

TABLE 8: Wagner–Meggitt classification.

Grades	Foot-related symptoms
Grade 1	Superficial ulcers
Grade 2	Deep ulcers
Grade 3	Ulcers with bone involvement
Grade 4	Partial gangrene
Grade 5	Complete gangrene

Source: Oyibo SO, Jude EB, Tarawneh I, Nguyen HC, Harkless LB, Boulton AJ. A comparison of two diabetic foot ulcer classification systems: the Wagner and the University of Texas wound classification systems. Diabetes care. 2001;24(1):84-8.

TABLE 9: SINBAD classification.

Category	Definition	Score
Site	• Forefoot • Midfoot	0 1
Ischemia	• Pedal pulses intact (at least one pulse palpable) • Clinical evidence of reduced pedal blood flow	0 1

Continued

Diabetic Foot

A Comprehensive Guide for Clinicians

Diabetic Foot: A Comprehensive Guide for Clinicians is the culmination of years of experience from a multidisciplinary approach toward an often overlooked complication in general diabetes care. The book serves as a practical guide to clinicians for the management of diabetes-related complications of the foot while detailing the various aspects in relation to the same, including anatomy, pathophysiology, surgery and rehabilitation. The use of algorithms and diagrams provide concise and clear insight into potential treatment strategies. A review of upcoming techniques and novel health technology used in the field has also been covered.

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