Lower Extremity Ulcers: Venous, Arterial, or Diabetic?

Determining the answer to this question is crucial to avoid administering treatment that only makes a serious condition worse. After pointing out where to look for the keys in the history and physical, the authors review how the etiology of an ulcer should influence the therapeutic approach.

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When a patient presents to the emergency department with a lower extremity cutaneous ulcer, many etiologies must be considered. These include venous and arterial disease, diabetes mellitus, connective tissue disorders, rheumatoid arthritis, vasculitis, and malignancies. One goal of the initial assessment is to determine whether the ulcer is chronic (defined as taking a significant amount of time to heal, failing to heal, or recurring), as such ulcers are associated with significant morbidity.[1,2]

Most prominent in the differential diagnosis should be venous reflux, arterial insufficiency, pressure ulcer, and ulcer secondary to diabetic neuropathy (Table 1).[2-16] With emphasis on those causes, this article will review emergency department evaluation, diagnosis, treatment, and referral options for the patient with a lower extremity cutaneous ulcer.

>>FAST TRACK<<

The ankle-brachial index should be measured in all patients.

INITIAL ASSESSMENT

Proper management begins with a complete medical and surgical history and physical examination. A thorough history that includes the location, onset, duration, progression, prior treatments, and clinical course of the ulcer can suggest its etiology. Possible considerations to rule out include diabetes; hypertension; hyperlipidemia; coronary artery disease; alcohol and tobacco use; thyroid, pulmonary, renal, neurologic and rheumatic diseases; peripheral vascular disease; deep vein thrombosis; and specifically cutaneous factors including cellulitis, trauma, and recent surgery. The patient should be asked about lower extremity pain, paresthesia, anesthesia, and claudication.

Physical examination, too, may suggest the etiology of an ulcer. Wound characteristics that should be noted include size, location, margins, presence of granulation tissue, necrosis, weeping, odor, and pain. Pulses must be palpated in the distal extremities. The surrounding region should be examined for pain, edema, erythema, warmth, induration, discoloration, maceration, dryness, scarring from previous wounds, hair pattern, gangrenous digits, clubbing, cyanosis, capillary refill, and varicose veins. It is important to bear in mind that venous and arterial disease may coexist in the same patient.

Ulcers that form at ankle, calf, or pretibial sites are likely secondary to venous reflux (Figure 1). Any ulcer in a diabetic patient is by convention considered a diabetic ulcer. Pressure ulcers are known to occur on those areas subject to pressure, such as over the heel in a bedridden patient or over the side of the foot as a result of wearing tight shoes (Figure 2).

The ankle-brachial index (ABI) should be measured in all patients, as this value may alter management (see "Arterial Ulcers," page 22). The index is

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TABLE 1. Differential Diagnosis of Lower Extremity Ulcers

	Venous	Arterial	Diabetic
History	• rapid onset • edema • trauma • thrombophlebitis (20%)	• slowly progressive • arteriosclerosis • claudication • age usually > 45 years • significant smoking history • hypertension • hyperlipidemia	• diabetes • peripheral neuropathy
Pain	• some pain • increases with dependency • decreases with elevation	• moderate to severe • intermittent claudication • decreases with dependency • increases with elevation (at night) or leg exercises	• neuropathy (not painful) • anesthesia • paresthesia
Location	• medial malleolus • ankle • lower calf • stocking distribution	• lateral malleolus • anterior tibia • toes, heels, bony prominences	• pressure sites • plantar surface • heels, bony prominences • metatarsal head
Appearance	• irregular border • base with granulation tissue • exudative • weeping	• well demarcated, punched out • pale or white base	• thin, undetermined border • black, gray, or yellow base
Surrounding skin	• brown pigmentation • hyperkeratotic borders • edema • mottling • stasis dermatitis	• dry eschar • pale, cyanotic • cool • thin • shiny • dependent rubor • hairless	• pale • reticular vascular pattern • palpable purpura • hemorrhagic vessels • callus around wound • bullae formation • Charcot's deformity • hammertoes
Vascular exam	• pulses may be normal • normal ABI (≥ 0.9) • abnormal findings on venous Doppler ultrasound	• pulses deceased to absent • low ABI (< 0.9) • pallor with elevation, rubor with dependency • delayed venous filling • delayed capillary refill	• pulses usually present • unreliable ABI • mixed neuropathic and vascular (usually arterial) disease

Data extracted from London and Donnelly. 2000[2]; Carr. 2008[3]; Choucair and Fivenson. 2001[4]; Tam and Moschella. 1991[5]; Abu-Own, et al. 1994[6]; Goldman and Fronek. 1989[7]; Ayello. 2005[8]; Dean. 2008[9]; Calianno and Holton. 2007[10]; Federman and Kravetz. 2007[11]; Hampton. 2000[12]; Hooi, et al. 2002[13]; Boulton. 2004[14]; Brem and Tomic-Canic. 2007.[15]

determined by dividing the blood pressure in the upper arm by the blood pressure in the ankle. Due to the effects of gravity, the ratio is generally greater than 1. With peripheral arterial disease, the ratio is less than 1 and becomes progressively lower with more severe obstruction. A patient with an abnormal

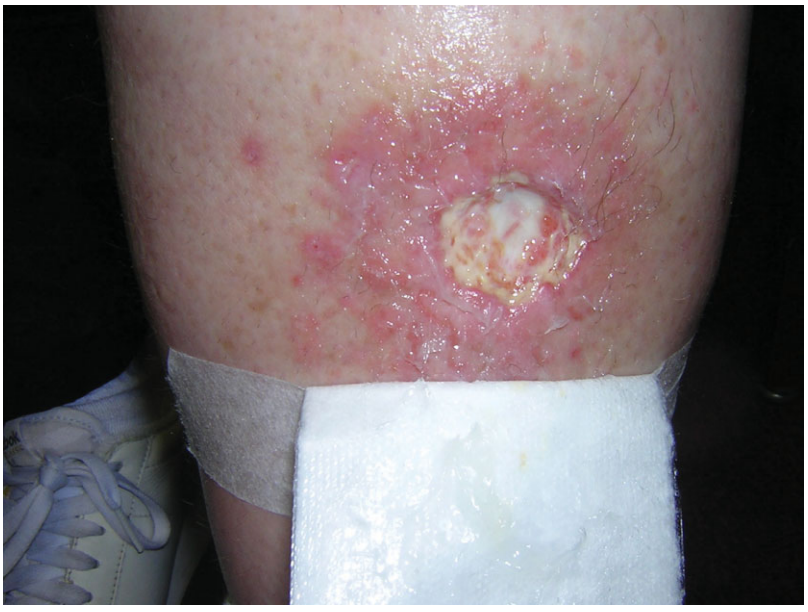

Photo courtesy of Stephen M. Schleicher, MD.

FIGURE 1. Venous Stasis Ulcer. Note the presence of significant edema and the location of the ulcer above the ankle.

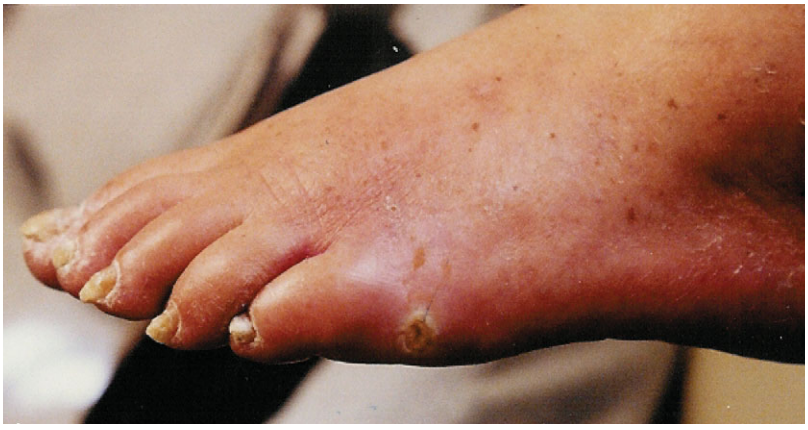

Photo courtesy of Stephen M. Schleicher, MD.

FIGURE 2. Pressure Ulcer. Note that the ulcer is located on the lateral surface of the foot where the shoe applies pressure.

ABI, even in the presence of normal pulses, requires a vascular surgery consult.

Imaging should be ordered in patients in whom osteomyelitis or an underlying foreign body is considered. In the emergency setting, plain radiography is often chosen, but it may be augmented by MR or CT scan. Patients with ulcers of unknown etiology should undergo outpatient color venous duplex scanning to better define the underlying venous abnormality.[2,4] For a summary of therapeutic considerations as indicated by ulcer type, see Table 2.[3,11,15,17-26]

VENOUS ULCERS

Venous circulation of the lower extremities progresses from the superficial to perforating to deep veins, with valves in each system to ensure unidirectional blood flow. As the calf muscles contract, the pumping action causes the blood to flow from the deep veins into the inferior vena cava. Disease of these pathways results in venous insufficiency.

Venous insufficiency is thought to occur when the valves of the perforating and deep veins no longer function properly, or become incompetent, allowing retrograde flow and stasis. This chronic insufficiency and stasis leads to venous hypertension.

The earliest signs of chronic insufficiency and stasis are pigmentation of the skin and edema. The latter is initially postural, worsens with prolonged standing, and progresses to a persistent edema, independent of position. The hyperpigmentation associated with this condition is thought to be secondary to the breakdown of hemoglobin to hemosiderin in the region, as well as transudation of serous fluid. A weepy, pruritic stasis dermatitis can result from a generalized hypersensitivity, or id reaction. Finally, the chronic nature of the edema and recurrent cellulitis can lead to induration of the lower extremities.[3,5] When this induration causes contraction of the subcutaneous tissue, the characteristic deformity of the lower extremities referred to as "bottle leg," "champagne bottle," or "inverted bowling pin" may develop.

There are many theories on how venous insufficiency and stasis lead to ulcers. For example, Tam and Moschella argue that insufficiency leads to venous hypertension, which in turn causes tissue hypoxia.[5] Another possible contributor to tissue hypoxia is pericapillary fibrin deposition impeding oxygen diffusion. Prolonged hypoxia, in

TABLE 2. Treatment Options for Lower Extremity Ulcers

	Venous	Arterial	Diabetic
Education	• teach patients about peripheral vascular diseases	• teach patients about peripheral vascular diseases • smoking cessation • control of hypertension, hyperlipidemia, diabetes	• teach patients about peripheral vascular diseases • diabetic education • daily foot assessment by patient • podiatry referral
Mechanical	• exercise program • weight reduction • leg elevation above the level of the heart (30 min, 3-4 times/day) • compression (30 mm Hg) - elastic stockings - Unna boots - pneumatic compression	• exercise program • weight reduction • *compression therapy contraindicated*	• exercise program • weight reduction • off-load pressure - shoes - casting - bed rest
Dressings	• topical medications - silver sulfadiazine cream - iodine ointment - mupirocin cream • occlusive dressings - hydrocolloid - hydrogels - semipermeable films	• occlusive dressings - hydrocolloid - hydrogels	• moist, nonadherent dressing
Drugs	• antibiotics - cellulitis - wound infection • anticoagulation - DVT • topical intermediate-strength corticosteroids and antihistamines: - stasis dermatitis	• antibiotics - infection • defer to management by vascular specialist - pentoxifylline - cilostazol	• diabetes medications • antibiotics - infection • hyperbaric oxygen
Surgery	• necrosis debridement • grafts • ligation of perforating veins • saphenous vein stripping	• revascularization prior to debridement • bypass grafts, amputation • skin grafts	• debridement • amputation

Data extracted from Carr. 2008[3]; Federman and Kravetz. 2007[11]; Brem and Tomic-Canic. 2007[15]; Labropoulos and Leon. 2005[17]; Rice. 2005[18]; Coleridge-Smith. 2009[19]; Douglas and Simpson. 1995[20]; O'Meara, et al. 2009[21]; O'Donnell and Lau. 2006[22]; O'Meara, et al. 2009[23]; Gohel, et al. 2007[24]; Caruana, et al. 2005[25]; Roeckl-Wiedmann, et al. 2005.[26]

combination with even minor trauma and impaired wound healing, is thought to lead to the formation of ulcers.[3,5]

Diagnosis. In patients who present with bilateral lower extremity edema, skin changes, and ulcers, it is important to consider the diagnosis of venous disease. To better diagnose venous disease, bilateral Doppler ultrasonography of both extremities should be ordered to assess the blood flow and rule out obstructive pathology, such as deep vein thrombosis and venous reflux.[17,27] In addition, as mentioned earlier, it is important to check the ABI to rule out the presence of arterial or mixed disease prior to treatment of venous disease.[18]

Treatment. The first-line treatment of venous ulcers, supported by level IA evidence in medical research, is compression.[8,20,21] Compression therapy not only improves ulcer healing by increasing venous flow and enhancing the pump action of the calf in motion, but it also prevents ulcer recurrence with continued use.[3,19,21] Outcome is significantly influenced by ulcer size, but overall, nearly 70% of ulcers heal within 6 months with the use of compression bandages.[2] Multilayer compression wraps containing an elastic layer are more effective than an inelastic single-layer wrap, studies have found.[21,23]

There are several types of compression devices on the market. Patients with small, noninfected venous ulcers should receive a prescription for compression stockings (30 mm Hg)[3,19] and referral to a vascular surgeon or dermatologist for follow-up and further treatment.

The dermatologic conditions associated with venous stasis and venous hypertension must be addressed. For example, cellulitis associated with lower extremity ulcers is often missed in the emergency department; comparative assessment of both legs will make it more apparent, especially in patients with darker skin tones. Consider obtaining a deep biopsy to rule out resistant bacteria that may otherwise escape detection in ulcers with considerable drainage, and treat with systemic antibiotics as appropriate. Surrounding stasis dermatitis can often be controlled with a topical antihistamine or corticosteroid.[3-5] Deep vein thrombosis should be treated with anticoagulation, where no contraindication exists. Special attention must be given to the direct treatment of the ulcer. Ulcers that appear infected are often contaminated predominantly with gram-positive *Staphylococcus aureus* and *Streptococcus pyogenes.* Either erythromycin or dicloxacillin is an appropriate treatment if resistance in the local patient population is taken into account. In particular, there has recently been a significant increase in the incidence of skin and soft tissue infections caused by community-acquired methicillin-resistant *S aureus*. These organisms are generally sensitive to co-trimoxazole, rifampin, linezolid, and vancomycin. *Pseudomonas aeruginosa*, the most common gram-negative organism in these ulcers, can be treated with ciprofloxacin, but again, one should consult hospital resistance rates.[3-5]

>>FAST TRACK<<

Nearly 70% of venous ulcers heal within 6 months with the use of compression bandages.

Ulcers with drainage can be treated with daily wet to dry saline dressing changes. Once the edema is better controlled and with minimal drainage, a hydrocolloid occlusive dressing should be placed over the ulcer. Alternatively, a topical agent such as silver sulfadiazine cream, mupirocin cream, or iodine ointment can be applied.[3] Ulcers with tissue necrosis should be debrided, as necrosis inhibits local healing. If the emergency physician is inexperienced with such debridement, the patient should be referred to a surgeon.

All patients with lower extremity venous ulcers should be referred to the care of a peripheral vascular surgeon, as several surgical options exist for further management. For example, the ESCHAR study noted that while venous surgery along with compression therapy was not superior to compression therapy alone in achieving healing, surgically treated patients did have a lower rate of recurrence.[24] Patients exhibiting significant edema or a large, nonhealing, or recurrent ulcer should be referred more emergently.

ARTERIAL ULCERS

Many diseases and disorders can cause peripheral arterial ulcers, including Raynaud's disease, arteriosclerosis obliterans, Buerger's disease, arterial emboli or thrombi, and obliterative or cutaneous vasculopathies. While the specific diagnosis may be elusive during the emergency department visit, it is important for the physician to broadly consider arterial disease in the differential diagnosis of lower extremity ulcers.

As noted in Table 1,[2-15] arterial ulcers are often associated with a history of hypertension, hyperlipidemia, diabetes, and smoking. Unlike patients with venous ulcer, those with arterial ulcers will complain of leg pain with exertion (also known as claudication) or while supine. Most patients will report pain relief with dependency (hanging their legs off the bed while sleeping, for example).[1,4,5,10-12] Claudication is thought to occur secondary to atherosclerotic changes in the arteries and arterioles of the lower extremities. While most patients can tolerate up to 70% occlusion of their vessels, the increased metabolic demand of exercise can cause pain with use of the limb. If this pain is relieved with rest, it is termed intermittent claudication. When pain occurs while the patient is supine, this denotes that circulation is sluggish unless aided by gravity.

Diagnosis. According to Khan and colleagues, physical examination alone is insufficient to exclude the presence of peripheral arterial disease.[28] To better diagnose the etiology of these ulcers, additional studies must be ordered. As previously noted, venous duplex ultrasound scans of both extremities are needed to exclude the presence of venous disease, and all patients with lower extremity ulcers should undergo ABI measurement.

An ABI of less than 0.9 is associated with the presence of arterial disease. An experienced practitioner should determine the ABI, as the results will influence treatment options. Although arteriography remains the diagnostic gold standard, this simple calculation has been thoroughly studied and found to be not only a valid, reliable assessment tool but also an independent marker for cardiovascular mortality in patients with peripheral arterial disease.[13,25,29]

>>FAST TRACK<<

Physical examination alone is insufficient to exclude the presence of peripheral arterial disease.

Treatment. An important distinction exists in the treatment of ulcers of venous and arterial origin, as alluded to above. While the first-line treatment of venous ulcers is compression therapy, such treatment is contraindicated in the presence of arterial disease and must not be applied to mixed arterial-venous ulcers, as it can exacerbate ischemia.

Control of hypertension, hyperlipidemia, and

diabetes, as well as smoking cessation, will prevent worsening of arterial disease. These lifestyle modifications should begin in the emergency department. Federman and Kravetz argue that smoking cessation, for instance, not only slows the progression of peripheral arterial disease but can also lead to relief from claudication symptoms.[11]

In contrast to venous ulcer necrosis, arterial ulcers should not be debrided prior to revascularization, but simply kept covered with a moist dressing to promote ulcer debridement.[5,16] After revascularization, hydrocolloid dressings can be used to maintain an environment favorable to healing. While there are other treatments available for peripheral arterial disease, such as pentoxifylline and cilostazol, such measures should be left to the specialists. An ABI of less than 0.9 warrants referral to a peripheral vascular specialist, as many patients below that threshold may require surgical intervention.[11]

DIABETIC ULCERS

Diabetic patients are at higher risk for arterial diseases and therefore can develop ulcers due to both entities. In addition, hyperglycemia poses the risk of ulcers secondary to neuropathic impairment of sensory, motor, and autonomic function, typically in the hand and foot, or "stocking and glove" distributions. The treatment of ulcers that have developed as a consequence of such impairments differs from that of venous or arterial ulcers.

Sensory neuropathy results from damage to the nerves in the lower extremities and can range from decreased perception to completely absent sensation. Patients may complain of "pins and needles" or may have little to no feeling in their legs. Consequently, injuries may go unnoticed.

>>FAST TRACK<<

For ulcers with purulent discharge or other signs of infection, it is important to obtain a deep culture.

Motor neuropathy results from wasting of the muscles in the lower extremities, which may lead to such deformities as hammertoes (toes in permanent flexion) and Charcot's deformity (flattening of the medial longitudinal arches). Such changes can cause gait abnormalities that increase the risk of injuries.

Autonomic neuropathy alters the blood flow to the extremities and can alter the sweat and oil production. Therefore, the skin may be thin and cracked, and wounds are less likely to heal.

Diagnosis. Neuropathy places the diabetic patient at increased risk of injury and deters healing. However, neuropathy is only one cause of diabetic ulcers.[15] The etiologic investigation of ulcers in diabetic patients should begin with a thorough history and physical examination, including documentation of the neurologic examination and any foot deformities. A venous duplex ultrasound scan should be ordered in these patients, as simultaneous macrovascular or microvascular disease may be present. More likely, diabetic patients will also have some component of arterial disease. However, the ABI may be falsely elevated in these patients and is therefore often unreliable.[10,12,14,30] Magnetic resonance angiography is recommended; a CT angiography is also an option. Toe blood pressure may be measured, and values less than 30 mm Hg are indicative of arterial disease. Transcutaneous oxygen tension can also be measured, with values less than 40 mm Hg notable for impaired wound healing and ischemic disease. Finally, radiographic imaging is recommended to rule out osteomyelitis and assess for wound tracking below the surface.[10,12,14,30]

Treatment. Wagner created a classification system, later revised by Brodsky, as a guide to the treatment of cutaneous ulcers in diabetic neuropathy. The depth of the lesion is graded from 0 (no breaks in the skin) to 3 (exposed bone, abscess, or osteomyelitis). Ischemic changes are graded from A (no ischemia) to D (complete gangrene).[30] The initial treatment of a diabetic patient with an ulcer is glycemic control. For ulcers with purulent discharge or other signs of infection, it is important to obtain a deep culture that avoids sampling of superficial skin contaminants.[10,12,14,30] Such infected lesions should be treated with systemic antibiotics.

Grade 0 lesions, or those with no breaks in the skin, require regular foot examinations and referral to a podiatrist. The goal in patients with such wounds is to relieve pressure on the lower extremity to prevent harm and injury.

Grade 1 lesions are superficial ulcers, and unfortunately, consensus is lacking on the appropriate dressings for these wounds. Relief of weight-bearing pressure, which can include plastazote shoes and casts, is necessary for treatment. Patients are allowed minimal

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weight bearing after the first 48 hours, and the cast, if placed, should be changed after 1 week.[10,12,30]

Grade 2 lesions have exposed tendons or joints, which often necessitate surgical debridement. Grade 3 ulcers, which involve osteomyelitis, exposed bone, or abscess, require antibiotics plus abscess drainage and removal of affected bone as needed.[10,12,14,30]

There is some evidence that chronic diabetic lesions that are resistant to common treatments may benefit from hyperbaric oxygen treatment.[26]

Appropriate emergency department disposition of diabetic patients with foot ulcers is governed by several key principles. The concomitant presence of arterial disease must be ruled out; debridement with deep culture should be considered; infections must be treated aggressively, and any deep neuropathic lesions or those that involve arterial or venous disease should be referred to a vascular surgeon. All patients in this population should be educated about their disease and referred to a physician who can help them establish better glycemic control. Those with superficial lesions should be taught to care for their lower extremity and referred to a podiatrist. □

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