Practice Essentials

Diabetic foot ulcers, as shown in the images below, occur as a result of various factors, such as mechanical changes in conformation of the bony architecture of the foot, peripheral neuropathy, and atherosclerotic peripheral arterial disease, all of which occur with higher frequency and intensity in the diabetic population.[[1](javascript:void(0);),[2](javascript:void(0);)]

[](javascript:refImgShow(1))Diabetic ulcer of the medial aspect of left first toe before and after appropriate wound care.

[View Media Gallery](javascript:refImgShow('001'))

[](javascript:refImgShow(2))Diabetic ulcer of left fourth toe associated with mild cellulitis.

[View Media Gallery](javascript:refImgShow('001'))

Nonenzymatic glycation predisposes ligaments to stiffness. Neuropathy causes loss of protective sensation and loss of coordination of muscle groups in the foot and leg, both of which increase mechanical stresses during ambulation.

Diabetic foot lesions are responsible for more hospitalizations than any other complication of diabetes.[[3](javascript:void(0);)]Diabetes is the leading cause of nontraumatic lower extremity amputations in the United States, with approximately 5% of diabetics developing foot ulcers each year and 1% requiring amputation.

Physical examination of the extremity having a diabetic ulcer can be divided into examination of the ulcer and the general condition of the extremity, assessment of the possibility of vascular insufficiency,[[4](javascript:void(0);)]and assessment for the possibility of peripheral neuropathy.

The staging of diabetic foot wounds is based on the depth of soft tissue and osseous involvement.[[5](javascript:void(0);),[6](javascript:void(0);),[7](javascript:void(0);)]A complete blood cell count should be done, along with assessment of serum glucose, glycohemoglobin, and creatinine levels.

The management of diabetic foot ulcers requires offloading the wound by using appropriate therapeutic footwear,[[8](javascript:void(0);),[9](javascript:void(0);)]daily saline or similar dressings to provide a moist wound environment,[[10](javascript:void(0);)]debridement when necessary, antibiotic therapy if osteomyelitis or cellulitis is present,[[11](javascript:void(0);),[12](javascript:void(0);)]optimal control of blood glucose, and evaluation and correction of peripheral arterial insufficiency.

A vascular surgeon and/or podiatric surgeon should evaluate all patients with diabetic foot ulcers so as to determine the need for debridement, revisional surgery on bony architecture, vascular reconstruction, or soft tissue coverage.

The hemorrheologic agent cilostazol is contraindicated in patients with congestive heart failure. See Medication regarding the product's black box warning.

## Pathophysiology

Atherosclerosis and peripheral neuropathy occur with increased frequency in persons with diabetes mellitus (DM).

### Diabetes-related atherosclerosis

Overall, people with diabetes mellitus (DM) have a higher incidence of [atherosclerosis](http://emedicine.medscape.com/article/1950759-overview), thickening of capillary basement membranes, arteriolar hyalinosis, and endothelial proliferation. Calcification and thickening of the arterial media (Mönckeberg sclerosis) are also noted with higher frequency in the diabetic population, although whether these factors have any impact on the circulatory status is unclear.

Diabetic persons, like people who are not diabetic, may develop atherosclerotic disease of large-sized and medium-sized arteries, such as aortoiliac and femoropopliteal atherosclerosis. However, significant atherosclerotic disease of the infrapopliteal segments is particularly common in the diabetic population. Underlying digital artery disease, when compounded by an infected ulcer in close proximity, may result in complete loss of digital collaterals and precipitate gangrene.

The reason for the prevalence of this form of arterial disease in diabetic persons is thought to result from a number of metabolic abnormalities, including high low-density lipoprotein (LDL) and very-low-density lipoprotein (VLDL) levels, elevated plasma von Willebrand factor, inhibition of prostacyclin synthesis, elevated plasma fibrinogen levels, and increased platelet adhesiveness.

### Diabetic peripheral neuropathy

The pathophysiology of diabetic peripheral neuropathy is multifactorial and is thought to result from vascular disease occluding the vasa nervorum; endothelial dysfunction; deficiency of myoinositol-altering myelin synthesis and diminishing sodium-potassium adenine triphosphatase (ATPase) activity; chronic hyperosmolarity, causing edema of nerve trunks; and effects of increased sorbitol and fructose.[[13](javascript:void(0);)]

The result of loss of sensation in the foot is repetitive stress; unnoticed injuries and fractures; structural foot deformity, such as hammertoes, bunions, metatarsal deformities, or Charcot foot (see the image below), as depicted in the image below; further stress; and eventual tissue breakdown. Unnoticed excessive heat or cold, pressure from a poorly fitting shoe, or damage from a blunt or sharp object inadvertently left in the shoe may cause blistering and ulceration. These factors, combined with poor arterial inflow, confer a high risk of limb loss on the patient with diabetes.

[](javascript:refImgShow(3))Charcot deformity with mal perf

## Etiology

The etiologies of diabetic ulceration include neuropathy,[[14](javascript:void(0);)]arterial disease,[[15](javascript:void(0);)]pressure,[[8](javascript:void(0);)]and foot deformity.[[16](javascript:void(0);)]Diabetic peripheral neuropathy, present in 60% of diabetic persons and 80% of diabetic persons with foot ulcers, confers the greatest risk of foot ulceration; microvascular disease and suboptimal glycemic control contribute.

A study by Naemi et al indicated that tissue mechanics may be associated with foot ulceration in patients with diabetic neuropathy, with an evaluation of 39 patients finding that the heel pad in nonulcerated feet tended to be stiffer than in ulcerated feet.[[17](javascript:void(0);)]. These results were further elucidated in another study by Naemi et al, which reported that the risk of diabetic foot ulcer is higher in diabetic neuropathy patients who have greater plantar soft tissue thickness and lower stiffness in the area of the first metatarsal head. The investigators found that adding the mechanical properties of plantar soft tissue (stiffness and thickness) to commonly evaluated clinical parameters improved specificity, sensitivity, prediction accuracy, and prognosis strength by 3%, 14%, 5%, and 1%, respectively.[[18](javascript:void(0);)]

The anatomy of the foot must be considered in risk calculation. A person with flatfoot is more likely to have disproportionate stress across the foot and may have an increased risk for tissue inflammation in high-stress regions.

### Charcot foot

Sensory neuropathy involving the feet may lead to unrecognized episodes of trauma due to ill-fitting shoes. Motor neuropathy, causing intrinsic muscle weakness and splaying of the foot on weight bearing, compounds this trauma. The result is a convex foot with a rocker-bottom appearance. Multiple fractures are unnoticed until bone and joint deformities become marked. This is termed a Charcot foot (neuropathic osteoarthropathy) and most commonly is observed in diabetes mellitus, affecting about 2% of diabetic persons.

If a Charcot foot is neglected, ulceration may occur at pressure points, particularly the medial aspect of the navicular bone and the inferior aspect of the cuboid bone. Sinus tracts progress from the ulcerations into the deeper planes of the foot and into the bone. Charcot change can also affect the ankle, causing displacement of the ankle mortise and ulceration, which can lead to the need for amputation.

## Epidemiology

According to the National Institute of Diabetes and Digestive and Kidney Diseases, an estimated 16 million Americans are known to have diabetes, and millions more are considered to be at risk for developing the disease. Diabetic foot lesions are responsible for more hospitalizations than any other complication of diabetes.[[3](javascript:void(0);)]Among patients with diabetes, 15% develop a foot ulcer, and 12-24% of individuals with a foot ulcer require amputation. Indeed, diabetes is the leading cause of nontraumatic lower extremity amputations in the United States. In fact, every year approximately 5% of diabetics develop foot ulcers and 1% require amputation.

### Age distribution for diabetic ulcers

Diabetes occurs in 3-6% of Americans. Of these, 10% have type 1 diabetes and are usually diagnosed when they are younger than 40 years. Among Medicare-aged adults, the prevalence of diabetes is about 10% (of these, 90% have type 2 diabetes). Diabetic neuropathy tends to occur about 10 years after the onset of diabetes, and, therefore, diabetic foot deformity and ulceration occur sometime thereafter.

### Prevalence of diabetic ulcers by race

The issue of diabetic foot disease is of particular concern in the Latino communities of the Eastern United States, in African Americans,[[19](javascript:void(0);)]and in Native Americans, who tend to have the highest prevalence of diabetes in the world.

## Prognosis

Mortality in people with diabetes and foot ulcers is often the result of associated large vessel arteriosclerotic disease involving the coronary or renal arteries.

Limb loss is a significant risk in patients with diabetic foot ulcers, particularly if treatment has been delayed.[[20](javascript:void(0);)]Diabetes is the predominant etiology for nontraumatic lower extremity amputations in the United States. Half of all nontraumatic amputations are a result of diabetic foot complications, and the 5-year risk of needing a contralateral amputation is 50%.[[21](javascript:void(0);)]

In diabetic people with neuropathy,[[22](javascript:void(0);)]even if successful management results in healing of the foot ulcer, the recurrence rate is 66% and the amputation rate rises to 12%.

A study by Chammas et al indicated that ischemic heart disease is the primary cause of premature death in patients with diabetic foot ulcer, finding it to be the major source of mortality on postmortem examination in 62.5% of 243 diabetic foot ulcer patients. The study also found that in patients with diabetic foot ulcer, the mean age of death from ischemic heart disease, as derived from postmortem examination, was 5 years below that of controls. Patients with neuropathic foot ulcers were determined to have the highest risk of premature death from ischemic heart disease.[[23](javascript:void(0);)]

A study by Chen et al indicated that following hospital treatment for diabetic foot ulcer, invasive systemic infection associated with the ulcer (DFU-ISI) is an important late complication that increases mortality risk. In the study’s patients, methicillin-resistant Staphylococcus aureus (MRSA) gave rise to 57% of the ISIs. Using Cox regression modeling, the investigators found that complicated ulcer healing and the presence of MRSA in the initial ulcer culture predicted the development of DFU-ISIs (hazard ratios of 3.812 and 2.030, respectively), with the hazard ratio for mortality risk in association with DFU-ISIs being 1.987.

## Patient Education

The risk of foot ulceration and limb amputation in people with diabetes is lessened by patient education stressing the importance of routine preventive podiatric care, appropriate shoes, avoidance of cigarette smoking, control of hyperlipidemia, and adequate glycemic control. For excellent patient education resources, visit eMedicineHealth’s [Diabetes Center](http://www.emedicinehealth.com/collections/CO1559.asp). Also, see eMedicineHealth’s patient education article [Diabetic Foot Care](http://www.emedicinehealth.com/articles/18002-1.asp).

### Diabetic Foot Care Symptoms

* Persistent [pain](https://www.emedicinehealth.com/pain_quiz_iq/quiz.htm) can be a symptom of sprain, strain, bruise, overuse, improperly fitting shoes, or underlying infection.
* Redness can be a sign of infection, especially when surrounding a [wound](https://www.emedicinehealth.com/puncture_wound/article_em.htm), or of abnormal rubbing of shoes or socks.
* Swelling of the feet or legs can be a sign of underlying inflammation or infection, improperly fitting shoes, or poor venous circulation. Other signs of poor circulation include the following:
  + Pain in the legs or buttocks that increases with walking but improves with rest (claudication)
  + Hair no longer growing on the lower legs and feet
  + Hard shiny skin on the legs
* Localized warmth can be a sign of infection or inflammation, perhaps from wounds that won't heal or that heal slowly.
* Any break in the skin is serious and can result from abnormal wear and tear, injury, or infection. Calluses and corns may be a sign of chronic trauma to the foot. Toenail [fungus](https://www.emedicinehealth.com/slideshow_skin_problems/article_em.htm), [athlete's foot](https://www.emedicinehealth.com/image-gallery/athletes_foot_1_picture/images.htm), and ingrown toenails may lead to more serious bacterial infections.
* Drainage of pus from a wound is usually a sign of infection. Persistent bloody drainage is also a sign of a potentially serious foot problem.
* A limp or difficulty walking can be sign of joint problems, serious infection, or improperly fitting shoes.
* [Fever](https://www.emedicinehealth.com/fever_in_adults/article_em.htm) or chills in association with a wound on the foot can be a sign of a limb-threatening or life-threatening infection.
* Red streaking away from a wound or redness spreading out from a wound is a sign of a progressively worsening infection.
* New or lasting numbness in the feet or legs can be a sign of nerve damage from diabetes, which increases a persons risk for leg and foot problems.

### When to Seek Medical Care

Write down the patient's symptoms and be prepared to talk about them on the phone with a doctor. Following is a list of common reasons to call a doctor if a person with diabetes has a diabetic foot or leg problem. For most of these problems, a doctor visit within about 72 hours is appropriate.

* Any significant trauma to the feet or legs, no matter how minor, needs medical attention. Even minor injuries can result in serious infections.
* Persistent mild-to-moderate pain in the feet or legs is a signal that something is wrong. Constant pain is never normal.
* Any new blister, wound, or ulcer less than 1 inch across can become a more serious problem. The patient will need to develop a plan with a doctor on how to treat these wounds.
* Any new areas of warmth, redness, or swelling on the feet or legs are frequently early signs of infection or inflammation. Addressing them early may prevent more serious problems.
* Pain, redness, or swelling around a toenail could mean the patient has an [ingrown toenail](https://www.emedicinehealth.com/ingrown_toenails/article_em.htm) - a leading cause of diabetic foot infections and amputations. Prompt and early treatment is essential.
* New or constant numbness in the feet or legs can be a sign of diabetic nerve damage ([neuropathy](https://www.emedicinehealth.com/neuropathy/article_em.htm)) or of impaired circulation in the legs. Both conditions put the patient at risk for serious problems such as infections and amputations.
* Difficulty walking can result from diabetic [arthritis](https://www.emedicinehealth.com/arthritis/article_em.htm) (Charcot's joints), often a sign of abnormal strain or pressure on the foot or of poorly fitting shoes, as well as the inability to perceive pain. Early intervention is key to preventing more serious problems including falls as well as lower extremity skin breakdown and infections.
* Constant itching in the feet can be a sign of fungal infection or [dry skin](https://www.emedicinehealth.com/dry_skin_quiz_iq/quiz.htm), both of which can lead to infection.
* Calluses or corns developing on the feet should be professionally removed. Home removal is not recommended.
* Fever, defined as a temperature over 98.6°F (37°C), in association with any other symptoms or even fever alone should prompt a call to a doctor's office. The degree of fever does not always correlate with the seriousness of infection. The patient could have no fever or a very low fever and still have a serious infection. People with diabetes need to be especially cautious of fever.

If time and the patient's condition permits, write down the patient's symptoms, a list of medications, [allergies](https://www.emedicinehealth.com/slideshow_10_common_allergy_triggers/article_em.htm) to medicines, and the doctor's name and phone number prior to coming to the hospital's emergency department. This information will greatly assist the emergency physician in the evaluation and treatment of the patient's problem.

Following are some common reasons to seek immediate medical attention for diabetic foot and leg problems.

* Severe pain in the feet or legs is often a sign of acute loss of circulation to the leg, serious infection, or may be due to severe nerve damage (neuropathy).
* Any cut to the feet or legs that bleeds significantly and goes all the way through the skin needs proper cleaning and repair to aid healing.
* Any significant [puncture wounds](https://www.emedicinehealth.com/puncture_wound/article_em.htm) to the feet (for example, stepping on a nail or being bitten by a dog or cat) carry a high risk of becoming infected.
* Wounds or ulcers that are more than about 1 inch across on the feet or legs are frequently associated with limb-threatening infections.
* Redness or red streaks spreading away from a wound or ulcer on the feet or legs are a sign of infection spreading through the tissues.
* Fever higher than 101.5°F (38.6°C) in association with redness, swelling, warmth, or any wound or ulcer on the legs may be a sign of a limb-threatening or life-threatening infection. If you are a person with diabetes and you simply have a fever more than 101.5°F (38.6°C), and no other symptoms, seek immediate care to determine the source of the fever and to initiate a plan of care. Because the degree of fever does not always correlate with the seriousness of the illness, people with diabetes should take even low-grade fevers [less than101.5°F (38.6°C)] very seriously and seek medical attention. The patient's doctor may or may not prescribe antibiotics, since fevers are often due to viral infections, which typically do not require antibiotics.
* Alteration in mental status (confusion) may be a sign of life-threatening infection that could lead to loss of a leg or foot, when associated with a leg wound or foot ulcer. Confusion may also be a sign of either very high or very low blood sugars, which are more common when infection is present
* **History and physical examination:**First, the doctor will ask the patient questions about their symptoms and will examine them. This examination should include the patient's vital signs (temperature, pulse, [blood pressure](https://www.emedicinehealth.com/image-gallery/blood_pressure_picture/images.htm), and respiratory rate), examination of the sensation in the feet and legs, an examination of the circulation in the feet and legs, a thorough examination of any problem areas. For a lower extremity wound or ulcer, this may involve probing the wound with a blunt probe to determine its depth. Minor surgical debridement of the wound (cleaning or cutting away of tissue) may be necessary to determine the seriousness of the wound.
* **Laboratory tests:**The doctor may decide to order a complete blood cell count, or [CBC](https://www.emedicinehealth.com/complete_blood_count_cbc/article_em.htm), which will assist in determining the presence and severity of infection. A very high or very low [white blood cell count](https://www.emedicinehealth.com/complete_blood_count_cbc/article_em.htm)suggests serious infection. The doctor may also check the patient's blood [sugar](https://www.emedicinehealth.com/slideshow_pictures_sugar_addiction/article_em.htm) either by fingerstick or by a laboratory test. Depending on the severity of the problem, the doctor may also order kidney function tests, blood chemistry studies ([electrolytes](https://www.emedicinehealth.com/electrolytes/article_em.htm)), [liver](https://www.emedicinehealth.com/liver/article_em.htm) enzyme tests, and heart enzyme tests to assess whether other body systems are working properly in the face of serious infection.
* **X-rays:**The doctor may order [x-rays](https://www.emedicinehealth.com/understanding_x-xays/article_em.htm) studies of the feet or legs to assess for signs of damage to the bones or arthritis, damage from infection, foreign bodies in the soft tissues. [Gas](https://www.emedicinehealth.com/flatulence_gas/article_em.htm) in the soft tissues, indicates gangrene - a very serious, potentially life-threatening or limb-threatening infection.
* **Ultrasound:** The doctor may order [Doppler ultrasound](https://www.emedicinehealth.com/ultrasound/article_em.htm) to see the blood flow through the arteries and veins in the lower extremities. The test is not painful and involves the technician moving a non-invasive probe over the blood vessels of the lower extremities.
* **Consultation:** The doctor may ask a vascular surgeon, orthopedic surgeon, or both to examine the patient. These specialists are skilled in dealing with diabetic lower extremity infections, bone problems, or circulatory problems.
* **Angiogram:** If the vascular surgeon determines that the patient has poor circulation in the lower extremities, an angiogram may be performed in preparation for surgery to improve circulation.
  + With an angiogram, a catheter is inserted through the artery in the groin and dye is injected while x-rays are taken. This allows the surgeon to see where the blockages are and plan an operation to bypass the blockages. This procedure is usually performed with local anesthesia and a light sedative given through a tube inserted in the patient's vein (an intravenous or IV line).

[**[https://sb.monetate.net/img/1/815/949044.png](https://www.healthline.com/health/diabetic-foot-pain-and-ulcers-causes-treatments)NEWSLETTER**](https://www.healthline.com/health/diabetic-foot-pain-and-ulcers-causes-treatments)

[](https://www.healthline.com/)

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# Diabetic Foot Pain and Ulcers: Causes and Treatment

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## Diabetic Foot Pain and Ulcers

Foot ulcers are a common complication of poorly controlled diabetes, forming as a result of skin tissue breaking down and exposing the layers underneath. They’re most common under your big toes and the balls of your feet, and they can affect your feet down to the bones.

All people with diabetes can develop foot ulcers and foot pain, but good foot care can help prevent them. Treatment for diabetic foot ulcers and foot pain varies depending on their causes. Discuss any foot pain or discomfort with your doctor to ensure it’s not a serious problem, as infected ulcers can result in amputation if neglected.

SYMPTOMS AND DIAGNOSIS

## Identifying Symptoms and Diagnosis

One of the first signs of a foot ulcer is drainage from your foot that might stain your socks or leak out in your shoe. Unusual swelling, irritation, redness, and odors from one or both feet are also common early symptoms of a foot ulcer.

The most visible sign of a serious foot ulcer is black tissue (called eschar) surrounding the ulcer. This forms because of an absence of healthy blood flow to the area around the ulcer. Partial or complete gangrene, which refers to tissue death due to infections, can appear around the ulcer. In this case, odorous discharge, pain, and numbness can occur.

Signs of foot ulcers are not always obvious. Sometimes, you won’t even show symptoms of ulcers until the ulcer has become infected. Talk to your doctor if you begin to see any skin discoloration, especially tissue that has turned black, or feel any pain around an area that appears callused or irritated.

Your doctor will likely identify the seriousness of your ulcer on a scale of 0 to 3 using the following criteria:

0: no ulcer but foot at risk

1: ulcer present but no infection

2: ulcer deep, exposing joints and tendons

3: extensive ulcers or abscesses from infection

CAUSES

## Causes of Diabetic Foot Pain and Ulcers

Diabetic ulcers are most commonly caused by:

* poor circulation
* high blood sugar (hyperglycemia)
* nerve damage
* irritated or wounded feet

Poor blood circulation is a form of vascular disease in which blood doesn’t flow to your feet efficiently. Poor circulation can also make it more difficult for ulcers to heal.

High glucose levels can slow down the healing process of an infected foot ulcer, so blood sugar management is critical. People with type 2 diabetes often have a harder time fighting off infections from ulcers.

Nerve damage is a long-term effect and can even lead to a loss of feeling in your feet. Damaged nerves can feel tingly and painful at first. Nerve damage reduces your sensitivity to foot pain and results in painless wounds that can cause ulcers.

Ulcers can be identified by drainage from the affected area and sometimes a noticeable lump that isn’t always painful.

Dry skin is common in diabetes. Your feet may be more prone to cracking. Calluses, corns, and bleeding wounds may occur.

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RISK FACTORS

## Risk Factors for Diabetic Foot Ulcers

All people with diabetes are at risk for foot ulcers, which can have multiple causes. Some factors can increase the risk of foot ulcers, including:

* poorly fitted or poor quality shoes
* poor hygiene (not washing regularly or thoroughly)
* improper trimming of toenails
* alcohol consumption
* eye disease from diabetes
* heart disease
* kidney disease
* obesity
* tobacco use (inhibits blood circulation)

Diabetic foot ulcers are also most common in older men.

TREATMENT

## Treating Diabetic Foot Ulcers

Stay off your feet to prevent pain and ulcers. This is called off-loading, and it’s helpful for all forms of diabetic foot ulcers. Pressure from walking can make an infection worse and an ulcer expand. For people who are overweight, extra pressure may be the cause of ongoing foot pain.

Your doctor may recommend wearing certain items to protect your feet:

* diabetic shoes
* casts
* food braces
* compression wraps
* shoe inserts to prevent corns and calluses

Doctors can remove diabetic foot ulcers with a debridement, the removal of dead skin, foreign objects, or infections that may have caused the ulcer.

An infection is a serious complication of a foot ulcer and requires immediate treatment. Not all infections are treated the same way. Tissue surrounding the ulcer may be sent to a lab to determine which antibiotic will help. If your doctor suspects a serious infection, he or she may order an X-ray to look for signs of bone infection.

Infection of a foot ulcer can be prevented with:

* foot baths
* disinfecting the skin around an ulcer
* keeping the ulcer dry with frequent dressing changes
* enzyme treatments
* dressings containing calcium alginates to inhibit bacterial growth

### Medications

Your doctor may prescribe antibiotics, antiplatelets, or anti-clotting medications to treat your ulcer if the infection progresses even after preventive or anti-pressure treatments. Many of these antibiotics attack Staphylococcus aureus, bacteria known to cause staph infections, or ß-haemolytic Streptococcus, which is normally found in your intestines.

Talk to your doctor about other health conditions you have that might increase your risk of infections by these harmful bacteria, including HIV and liver problems.

### Over-the-Counter Treatments

Many topical treatments are available for foot ulcers, including:

* dressings containing silver or silver sulphadiazine cream
* polyhexamethylene biguanide (PHMB) gel or solutions
* iodine (either povidone or cadexomer)
* medical grade honey in ointment or gel form

### Surgical Procedures

Your doctor may recommend that you seek surgical help for your ulcers. A surgeon can help alleviate pressure around your ulcer by shaving down the bone or removing foot deformities such as bunions or hammertoes.

You will likely not need surgery on your ulcer. However, if no other treatment option can help your ulcer heal or progress further into infection, surgery can prevent your ulcer from becoming worse or leading to amputation.

PREVENTION

## Preventing Diabetic Foot Problems

According to the [American Podiatric Medical Association](http://www.apma.org/Learn/FootHealth.cfm?ItemNumber=981), 14 to 24 percent of Americans with diabetic foot ulcers have amputations. Preventive care is crucial. Closely manage your blood glucose, as your chances of diabetes complications remain low when your blood sugar is stable. You can also help prevent diabetic foot problems by:

* washing your feet every day
* keep toenails adequately trimmed, but not too short
* keeping your feet dry and moisturized
* changing your socks frequently
* seeing a podiatrist for corn and callus removal
* wearing proper-fitting shoes

Foot ulcers can return after they’ve been treated. Scar tissue can become infected if the area is aggravated again, so your doctor may recommend you wear diabetic shoes to prevent ulcers from returning.

https://emedicine.medscape.com/article/460282-overview

<https://www.healthline.com/health/diabetic-foot-pain-and-ulcers-causes-treatments#overview1>

# Diabetic foot ulcer

From Wikipedia, the free encyclopedia

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| --- |
| **Diabetic foot ulcer** |
| [Neuropathic heel ulcer diabetic.jpg](https://en.wikipedia.org/wiki/File:Neuropathic_heel_ulcer_diabetic.jpg) |
| Neuropathic diabetic foot ulcer |
| [[edit on Wikidata](https://www.wikidata.org/wiki/Q52859)] |

**Diabetic foot ulcer** is a major [complication of diabetes mellitus](https://en.wikipedia.org/wiki/Complication_of_diabetes_mellitus), and probably the major component of the [diabetic foot](https://en.wikipedia.org/wiki/Diabetic_foot).

Wound healing is an innate mechanism of action that works reliably most of the time. A key feature of wound healing is stepwise repair of lost [extracellular matrix](https://en.wikipedia.org/wiki/Extracellular_matrix) (ECM) that forms the largest component of the dermal skin layer.[[1]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Iakovos-1) But in some cases, certain disorders or physiological insult disturbs the wound healing process. [Diabetes mellitus](https://en.wikipedia.org/wiki/Diabetes_mellitus) is one such metabolic disorder that impedes the normal steps of the wound healing process. Many studies show a prolonged inflammatory phase in diabetic wounds, which causes a delay in the formation of mature [granulation tissue](https://en.wikipedia.org/wiki/Granulation_tissue) and a parallel reduction in [wound](https://en.wikipedia.org/wiki/Wound) [tensile strength](https://en.wikipedia.org/wiki/Tensile_strength).[[2]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-McLennan-2)

Treatment of diabetic foot ulcers should include: [blood sugar](https://en.wikipedia.org/wiki/Blood_sugar) control, [removal of dead tissue from the wound](https://en.wikipedia.org/wiki/Debridement), [wound dressings](https://en.wikipedia.org/wiki/Dressing_(medical)), and removing pressure from the wound through techniques such as [total contact casting](https://en.wikipedia.org/wiki/Total_contact_casting).[[3]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Yaz2015-3)Surgery in some cases may improve outcomes.[[3]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Yaz2015-3) [Hyperbaric oxygen therapy](https://en.wikipedia.org/wiki/Hyperbaric_oxygen_therapy) may also help but is expensive.[[3]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Yaz2015-3)

It occurs in 15% of people with diabetes,[[4]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer" \l "cite_note-Harold-4) and precedes 84% of all diabetes-related lower-leg [amputations](https://en.wikipedia.org/wiki/Amputations).[[5]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-pmid24796080-5)

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  + [3.2Altered metabolism](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#Altered_metabolism)
  + [3.3Biomechanics](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#Biomechanics)
* [4Diagnosis](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#Diagnosis)
* [5Prevention](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#Prevention)
  + [5.1Footwear](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#Footwear)
* [6Treatment](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#Treatment)
  + [6.1Antibiotics](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#Antibiotics)
  + [6.2Wound dressings](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#Wound_dressings)
  + [6.3Total contact casting](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#Total_contact_casting)
  + [6.4Hyperbaric oxygen](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#Hyperbaric_oxygen)
  + [6.5Negative pressure wound therapy](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#Negative_pressure_wound_therapy)
  + [6.6Other treatments](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#Other_treatments)
* [7Epidemiology](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#Epidemiology)
* [8Research](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#Research)
* [9References](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#References)
* [10External links](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#External_links)

## Classification[[edit](https://en.wikipedia.org/w/index.php?title=Diabetic_foot_ulcer&action=edit&section=1" \o "Edit section: Classification)]

Diabetic foot ulcer is a complication of diabetes. Diabetic foot ulcers are classified as either [neuropathic](https://en.wikipedia.org/wiki/Neuropathic), [neuroischaemic](https://en.wikipedia.org/w/index.php?title=Neuroischaemic&action=edit&redlink=1" \o "Neuroischaemic (page does not exist)) or [ischaemic](https://en.wikipedia.org/wiki/Ischaemic" \o "Ischaemic).[[6]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-pmid21841646-6)

## Risk factors[[edit](https://en.wikipedia.org/w/index.php?title=Diabetic_foot_ulcer&action=edit&section=2" \o "Edit section: Risk factors)]

Risk factors implicated in the development of diabetic foot ulcers are infection, older age,[[7]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-pmid23123487-7) [diabetic neuropathy](https://en.wikipedia.org/wiki/Diabetic_neuropathy), [peripheral vascular disease](https://en.wikipedia.org/wiki/Peripheral_vascular_disease), cigarette smoking, poor glycemic control, previous foot ulcerations or amputations,[[5]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-pmid24796080-5) and [ischemia](https://en.wikipedia.org/wiki/Ischemia) of small and large blood vessels.[[8]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Examination-8)[[9]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Wu-9) Prior history of foot  disease, foot deformities that produce abnormally high forces of pressure,  [renal  failure](https://en.wikipedia.org/wiki/Renal_failure), [oedema](https://en.wikipedia.org/wiki/Oedema" \o "Oedema), impaired ability to look after personal care (e.g. visual impairment) are further risk factors for diabetic foot ulcer.[[7]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-pmid23123487-7)[[5]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-pmid24796080-5)

People with diabetes often develop diabetic neuropathy due to several metabolic and neurovascular factors. [Peripheral neuropathy](https://en.wikipedia.org/wiki/Peripheral_neuropathy) causes loss of pain or feeling in the toes, feet, legs and arms due to distal nerve damage and low blood flow. [Blisters](https://en.wikipedia.org/wiki/Blister) and [sores](https://en.wikipedia.org/wiki/Ulcer_(dermatology)) appear on numb areas of the feet and legs such as metatarso-phalangeal joints, heel region and as a result pressure or injury goes unnoticed and eventually become portal of entry for [bacteria](https://en.wikipedia.org/wiki/Bacteria) and [infection](https://en.wikipedia.org/wiki/Infection).

## Pathophysiology[[edit](https://en.wikipedia.org/w/index.php?title=Diabetic_foot_ulcer&action=edit&section=3" \o "Edit section: Pathophysiology)]

### Extracellular matrix[[edit](https://en.wikipedia.org/w/index.php?title=Diabetic_foot_ulcer&action=edit&section=4" \o "Edit section: Extracellular matrix)]

[Extra cellular matrix](https://en.wikipedia.org/wiki/Extra_cellular_matrix) (or "ECM") is the external structural framework that cells attach to in multicellular organisms. The [dermis](https://en.wikipedia.org/wiki/Dermis) lies below the [epidermis](https://en.wikipedia.org/wiki/Epidermis_(skin)), and these two layers are collectively known as the [skin](https://en.wikipedia.org/wiki/Skin). Dermal skin is primarily a combination of fibroblasts growing in this matrix. The specific species of ECM of [connective tissues](https://en.wikipedia.org/wiki/Connective_tissue)often differ chemically, but collagen generally forms the bulk of the structure.

Through the interaction of cell with its [extracellular matrix](https://en.wikipedia.org/wiki/Extracellular_matrix) (transmitted through the anchoring molecules classed as [integrins](https://en.wikipedia.org/wiki/Integrins" \o "Integrins)) there forms a continuous association between cell interior, [cell membrane](https://en.wikipedia.org/wiki/Cell_membrane) and extracellular matrix components that help drive various cellular events in a regulated fashion.[[10]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-10) [Wound healing](https://en.wikipedia.org/wiki/Wound_healing) is a localized event involving the reaction of cells to the damage sustained.

The cells break down damaged [ECM](https://en.wikipedia.org/wiki/Extracellular_matrix) and replace it, generally increasing in number to react to the harm. The process is activated, though perhaps not exclusively, by cells responding to fragments of damaged ECM, and the repairs are made by reassembling the matrix by cells growing on and through it. Because of this [extracellular matrix](https://en.wikipedia.org/wiki/Extracellular_matrix) is often considered as a 'conductor of the wound healing symphony'.[[11]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Sweitzer-11) In the Inflammatory phase, [neutrophils](https://en.wikipedia.org/wiki/Neutrophils) and [macrophages](https://en.wikipedia.org/wiki/Macrophages) recruit and activate [fibroblasts](https://en.wikipedia.org/wiki/Fibroblasts" \o "Fibroblasts)which in subsequent granulation phase migrate into the wound, laying down new [collagen](https://en.wikipedia.org/wiki/Collagen) of the subtypes I and III.

In the initial events of wound healing, [collagen III](https://en.wikipedia.org/wiki/Collagen_III) predominates in the granulation tissue which later on in remodeling phase gets replaced by collagen I giving additional [tensile strength](https://en.wikipedia.org/wiki/Tensile_strength) to the healing tissue.[[12]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Schultz-12)[[13]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Sussman-13) It is evident from the known collagen assembly that the tensile strength is basically due to fibrillar arrangement of collagen molecules, which self-assemble into microfibrils in a longitudinal as well as lateral manner producing extra strength and stability to the collagen assembly.[[13]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Sussman-13)[[14]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Thomas-14)Metabolically altered collagen is known to be highly inflexible and prone to break down, particularly over pressure areas. Fibronectin is the major glycoprotein secreted by fibroblasts during initial synthesis of extracellular matrix proteins. It serves important functions, being a chemo-attractant for macrophages, fibroblasts and endothelial cells.

Basement membrane that separates epidermis from the dermal layer and endothelial basement membrane mainly contain collagen IV that forms a sheet and binds to other extra cellular matrix molecules like laminin and proteoglycans. In addition to collagen IV, epidermal and endothelial basement membrane also contain laminin, perlecan and nidogen.[[13]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Sussman-13)[[14]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Thomas-14) Hyaluronic acid, a pure [glycosaminoglycan](https://en.wikipedia.org/wiki/Glycosaminoglycan) component is found in high amounts in damaged or growing tissues. It stimulates [cytokine](https://en.wikipedia.org/wiki/Cytokine" \o "Cytokine)production by [macrophages](https://en.wikipedia.org/wiki/Macrophages) and thus promotes [angiogenesis](https://en.wikipedia.org/wiki/Angiogenesis). In normal skin [chondroitin sulfate](https://en.wikipedia.org/wiki/Chondroitin_sulfate) [proteoglycan](https://en.wikipedia.org/wiki/Proteoglycan) is mainly found in the [basement membrane](https://en.wikipedia.org/wiki/Basement_membrane) but in healing wounds they are up regulated throughout the [granulation tissue](https://en.wikipedia.org/wiki/Granulation_tissue) especially during second week of wound repair, when they provide a temporary matrix with highly hydrative capacity.[[15]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Miriam-15) Binding of [growth factors](https://en.wikipedia.org/wiki/Growth_factors) is clearly an important role of [perlecan](https://en.wikipedia.org/wiki/Perlecan" \o "Perlecan) in [wound healing](https://en.wikipedia.org/wiki/Wound_healing) and [angiogenesis](https://en.wikipedia.org/wiki/Angiogenesis). Poor wound healing in diabetes mellitus may be related to [perlecan](https://en.wikipedia.org/wiki/Perlecan" \o "Perlecan) expression. High levels of glucose can decrease perlecan expression in some cells probably through transcriptional and [post-transcriptional modification](https://en.wikipedia.org/wiki/Post-transcriptional_modification).[[15]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Miriam-15)[[16]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Decarlo-16) Wound healing phases especially, granulation, re-epithelization and remodeling exhibit controlled turnover of [extracellular matrix](https://en.wikipedia.org/wiki/Extracellular_matrix) components.

### Altered metabolism[[edit](https://en.wikipedia.org/w/index.php?title=Diabetic_foot_ulcer&action=edit&section=5" \o "Edit section: Altered metabolism)]

[Diabetes mellitus](https://en.wikipedia.org/wiki/Diabetes_mellitus) is a metabolic disorder and hence the defects observed in diabetic wound healing are thought to be the result of altered protein and lipid metabolism and thereby abnormal [granulation tissue](https://en.wikipedia.org/wiki/Granulation_tissue) formation.[[17]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Tweedie-17) Increased glucose levels in the body end up in uncontrolled covalent bonding of [aldose](https://en.wikipedia.org/wiki/Aldose) sugars to a protein or lipid without any normal [glycosylation](https://en.wikipedia.org/wiki/Glycosylation) enzymes.[[18]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Goldin-18) These stable products then accumulate over the surface of cell membranes, structural proteins and circulating proteins. These products are called [advanced glycation endproducts](https://en.wikipedia.org/wiki/Advanced_glycation_endproducts) (AGEs) or Amadori products. Formation of AGEs occurs on [extracellular matrix](https://en.wikipedia.org/wiki/Extracellular_matrix) proteins with slow turnover rate. AGEs alter the properties of matrix proteins such as collagen, [vitronectin](https://en.wikipedia.org/wiki/Vitronectin" \o "Vitronectin), and [laminin](https://en.wikipedia.org/wiki/Laminin) through AGE-AGE intermolecular covalent bonds or cross-linking.[[18]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Goldin-18)[[19]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Singh-19)[[20]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Brownlee-20) AGE cross-linking on [type I collagen](https://en.wikipedia.org/wiki/Type_I_collagen) and [elastin](https://en.wikipedia.org/wiki/Elastin) results in increased stiffness. AGEs are also known to increase synthesis of [type III collagen](https://en.wikipedia.org/wiki/Type_III_collagen) that forms the [granulation tissue](https://en.wikipedia.org/wiki/Granulation_tissue). AGEs on laminin result in reduced binding to [type IV collagen](https://en.wikipedia.org/wiki/Type_IV_collagen) in the basement membrane, reduced polymer elongation and reduced binding of [heparan sulfate](https://en.wikipedia.org/wiki/Heparan_sulfate" \o "Heparan sulfate) [proteoglycan](https://en.wikipedia.org/wiki/Proteoglycan).[[18]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Goldin-18)

**Impaired NO synthesis**

[Nitric oxide](https://en.wikipedia.org/wiki/Nitric_oxide) is known as an important stimulator of cell proliferation, maturation and [differentiation](https://en.wikipedia.org/wiki/Differentiation_(cellular)). Thus, [nitric oxide](https://en.wikipedia.org/wiki/Nitric_oxide) increases [fibroblast](https://en.wikipedia.org/wiki/Fibroblast) proliferation and thereby collagen production in wound healing. Also, L-[arginine](https://en.wikipedia.org/wiki/Arginine) and [nitric oxide](https://en.wikipedia.org/wiki/Nitric_oxide) are required for proper cross linking of collagen fibers, via proline, to minimize scarring and maximize the tensile strength of healed tissue.[[21]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Kei-21) Endothelial cell specific [nitric oxide synthase](https://en.wikipedia.org/wiki/Nitric_oxide_synthase) (EcNOS) is activated by the pulsatile flow of blood through vessels. Nitric oxide produced by EcNOS, maintains the diameter of blood vessels and proper blood flow to tissues. In addition to this, nitric oxide also regulates [angiogenesis](https://en.wikipedia.org/wiki/Angiogenesis), which plays a major role in [wound healing](https://en.wikipedia.org/wiki/Wound_healing).[[22]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Dan-22) Thus, diabetic patients exhibit reduced ability to generate [nitric oxide](https://en.wikipedia.org/wiki/Nitric_oxide) from L-[arginine](https://en.wikipedia.org/wiki/Arginine). Reasons that have been postulated in the literature include accumulation of [nitric oxide synthase](https://en.wikipedia.org/wiki/Nitric_oxide_synthase) inhibitor due to high glucose associated kidney dysfunction and reduced production of [nitric oxide synthase](https://en.wikipedia.org/wiki/Nitric_oxide_synthase) due to [ketoacidosis](https://en.wikipedia.org/wiki/Ketoacidosis) observed in diabetic patients and pH dependent nature of [nitric oxide synthase](https://en.wikipedia.org/wiki/Nitric_oxide_synthase).[[18]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Goldin-18)[[23]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Linden-23)

**Structural and functional changes in fibroblasts**

Diabetic ulcer [fibroblasts](https://en.wikipedia.org/wiki/Fibroblasts) show various morphological differences compared to fibroblasts from age matched controls. Diabetic ulcer fibroblasts are usually large and widely spread in the culture flask compared to the spindle shaped morphology of the fibroblasts in age-matched controls. They often show dilated [endoplasmic reticulum](https://en.wikipedia.org/wiki/Endoplasmic_reticulum), numerous vesicular bodies and lack of microtubular structure in [transmission electron microscopy](https://en.wikipedia.org/wiki/Transmission_electron_microscopy) study. Therefore, interpretation of these observations would be that in spite of high protein production and protein turnover in diabetic ulcer fibroblasts, vesicles containing secretory proteins could not travel along the [microtubules](https://en.wikipedia.org/wiki/Microtubules) to release the products outside.[[24]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-fibroblasts-24)[[25]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Rowe-25) Fibroblasts from diabetic ulcer exhibit proliferative impairment that probably contributes to a decreased production of [extracellular matrix](https://en.wikipedia.org/wiki/Extracellular_matrix) proteins and delayed wound contraction and impaired wound healing.[[24]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-fibroblasts-24)

**Increased matrix metalloproteinases (MMP) activity**

In order for a wound to heal, [extracellular matrix](https://en.wikipedia.org/wiki/Extracellular_matrix) not only needs to be laid down but also must be able to undergo degradation and remodeling to form a mature tissue with appropriate [tensile strength](https://en.wikipedia.org/wiki/Tensile_strength).[[26]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Ravanti-26) Proteases, namely [matrix metalloproteinases](https://en.wikipedia.org/wiki/Matrix_metalloproteinases) are known to degrade almost all the [extracellular matrix](https://en.wikipedia.org/wiki/Extracellular_matrix) components. They are known to be involved in [fibroblast](https://en.wikipedia.org/wiki/Fibroblast) and [keratinocyte](https://en.wikipedia.org/wiki/Keratinocyte) migration, tissue re-organization, inflammation and remodeling of the wounded tissue.[[2]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-McLennan-2)[[26]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Ravanti-26) Due to persistently high concentrations of pro-inflammatory [cytokines](https://en.wikipedia.org/wiki/Cytokines) in diabetic ulcers, MMP activity is known to increase by 30 fold when compared to acute [wound healing](https://en.wikipedia.org/wiki/Wound_healing).[[27]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Vaalamo-27) MMP-2 and MMP-9 show sustained overexpression in chronic non-healing diabetic ulcers.[[2]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-McLennan-2)[[28]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Wysocki-28) Balance in the MMP activity is usually achieved by tissue inhibitor of metalloproteinases (TIMP). Rather than absolute concentrations of either two, it is the ratio of MMP and TIMP that maintains the proteolytic balance and this ratio is found to be disturbed in diabetic ulcer.[[29]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Lobman-29)[[30]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Muller-30) In spite of these findings, the exact mechanism responsible for increased MMP activity in diabetes is not known yet. One possible line of thought considers [Transforming growth factor](https://en.wikipedia.org/wiki/Transforming_growth_factor) beta (TGF-β) as an active player. Most MMP genes have TGF-β inhibitory element in their promoter regions and thus TGF–β regulates the expression of both MMP and their inhibitor TIMP.[[31]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Susan-31) In addition to the importance of cell-cell and cell-matrix interactions, all phases of wound healing are controlled by a wide variety of different [growth factors](https://en.wikipedia.org/wiki/Growth_factors) and [cytokines](https://en.wikipedia.org/wiki/Cytokines). To mention precisely, growth factors promote switching of early inflammatory phase to the [granulation tissue](https://en.wikipedia.org/wiki/Granulation_tissue) formation. Decrease in growth factors responsible for tissue repair such as TGF-β is documented in diabetic wounds. Thus, reduced levels of TGFβ in diabetes cases lower down the effect of inhibitory regulatory effect on MMP genes and thus cause MMPs to over express.[[4]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Harold-4)[[32]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Bennet-32)[[33]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Galkowska-33)

### Biomechanics[[edit](https://en.wikipedia.org/w/index.php?title=Diabetic_foot_ulcer&action=edit&section=6" \o "Edit section: Biomechanics)]

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| https://upload.wikimedia.org/wikipedia/en/thumb/f/f2/Edit-clear.svg/40px-Edit-clear.svg.png | This article **may be too**[**technical**](https://en.wiktionary.org/wiki/technical#Adjective)**for most readers to understand**. Please [help improve it](https://en.wikipedia.org/w/index.php?title=Diabetic_foot_ulcer&action=edit) to [make it understandable to non-experts](https://en.wikipedia.org/wiki/Wikipedia:Make_technical_articles_understandable), without removing the technical details. The [talk page](https://en.wikipedia.org/wiki/Talk:Diabetic_foot_ulcer) may contain suggestions. *(July 2012)* *(*[*Learn how and when to remove this template message*](https://en.wikipedia.org/wiki/Help:Maintenance_template_removal)*)* |

Complications in the Diabetic foot and foot-ankle complex are wider and more destructive than expected, and may compromise structure and function of several systems: vascular, nervous, somatosensory, musculoskeletal. Thus, a deeper comprehension of the alteration of gait and foot biomechanics in the Diabetic foot is of great interest, and may play a role in the design and onset of preventive as well as therapeutic actions.

Briefly, we can summarise the effect of diabetes on the main structures of the foot-ankle complex as:

* effects on skin: skin – and the soft tissues immediately underneath the skin – undergo greater compression and shear loading than usual, thus explaining the onset of tissue damage so deeply correlated to traumatic ulceration processes. Besides this, skin of the Diabetic foot suffers from loss of [autonomic nervous](https://en.wikipedia.org/wiki/Autonomic_nervous_system) control and consequently reduced hydration, making it less elastic and thus more vulnerable to the action of increased mechanical stress;
* effects on tendons and ligaments: protein [glycosylation](https://en.wikipedia.org/wiki/Glycosylation) and the resulting collagen abnormalities lead to greater transversal section – i.e. thickening – of tendons and ligaments and a greater coefficient of elasticity. Particularly impacted by this process are Plantar Fascia and Achilles Tendon. Both causes lead to an increased stiffness of those structures;
* effects on cartilage: similar to what happens to tendons and ligaments, cartilage changes its composition mainly due to the modification of collagen fibers; this increases its stiffness and decreases the range of motion of all joints in the foot and ankle;
* effects on muscles: Diabetes mellitus causes severe damage to nerve conduction, thus causing a worsening in the management of the related muscle fibers. As a consequence, both intrinsic and extrinsic muscles of the foot-ankle complex are damaged in structure (reduction of muscle volume) and function (reduction of muscle strength);
* effects on peripheral sensory system: impaired nerve conduction has a dramatic effect on the peripheral sensory system, since it leads to loss of protective sensation under the sole of the foot. This exposes the Diabetic foot to thermal or mechanical trauma, and to the late detection of infection processes or tissue breakdown;
* effects on foot morphology (deformities): due to most of the above alterations, a significant imbalance of peripheral musculature and soft tissue occur in the foot which seriously alters its morphology and determines the onset of foot deformities. Most common deformities of the Diabetic foot are represented by a high longitudinal arch (rigid cavus foot), hammer toes and hallux valgus. A completely different morphologic degeneration is represented by [neuropathic arthropathy](https://en.wikipedia.org/wiki/Neuropathic_arthropathy), whose analysis is not part of this discussion.[[34]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-34)[[35]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-35)[[36]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-36)[[37]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-pmid18442178-37)[[38]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-38)

## Diagnosis[[edit](https://en.wikipedia.org/w/index.php?title=Diabetic_foot_ulcer&action=edit&section=7" \o "Edit section: Diagnosis)]

Assessment of diabetic foot ulcer includes identifying risk factors such as diabetic peripheral neuropathy, noting that 50 percent of people are asymptomatic, and ruling out other causes of peripheral neuropathy such as alcohol abuse and  spinal injury.[[7]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-pmid23123487-7)

The location of the ulcer, its size, shape, depth and whether the tissue is granulating or sloughy needs to be considered. Further considerations include whether the there is [malodour](https://en.wikipedia.org/w/index.php?title=Malodour&action=edit&redlink=1" \o "Malodour (page does not exist)), condition of the border of the wound and [palpable](https://en.wikipedia.org/wiki/Palpable) bone and sinus formation should be investigated. Signs of infection require to be considered such as development of grey or yellow tissue, [purulent](https://en.wikipedia.org/wiki/Purulent) discharge, unpleasant smell, sinus, undermined edges and exposure of bone or [tendon](https://en.wikipedia.org/wiki/Tendon).[[6]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-pmid21841646-6)

Identification of diabetic foot in medical databases, such as commercial claims and prescription data, is complicated by the lack of a specific ICD-9 code for diabetic foot and variation in coding practices. The following codes indicate ulcer of the lower limb or foot:

* 707.1 Ulcer of lower limbs, except pressure ulcer
* 707.14 Ulcer of heel and midfoot
* 707.15 Ulcer of other part of foot
* 707.19 Ulcer of other part of lower limb

One or more codes, in combination with a current or prior diagnosis of diabetes may be sufficient to conclude diabetic foot:

* 250.0 Diabetes Mellitus
* 250.8 Diabetes with other specified manifestations

## Prevention[[edit](https://en.wikipedia.org/w/index.php?title=Diabetic_foot_ulcer&action=edit&section=8" \o "Edit section: Prevention)]

Steps to prevent diabetic foot ulcers include frequent review by a [foot specialist](https://en.wikipedia.org/wiki/Foot_specialist), good foot hygiene, [diabetic socks](https://en.wikipedia.org/wiki/Diabetic_sock)[[39]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-39)[[40]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-40) and [shoes](https://en.wikipedia.org/wiki/Diabetic_shoe), as well as avoiding injury.

* Foot-care education combined with increased surveillance can reduce the incidence of serious foot lesions.[[41]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-pmid8498761-41)

### Footwear[[edit](https://en.wikipedia.org/w/index.php?title=Diabetic_foot_ulcer&action=edit&section=9" \o "Edit section: Footwear)]

The evidence for special footwear to prevent foot ulcers is poor.[[37]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-pmid18442178-37)

*Clinical Evidence* reviewed the topic and concluded "Individuals with significant foot deformities should be considered for referral and assessment for customised shoes that can accommodate the altered foot anatomy. In the absence of significant deformities, high quality well fitting non-prescription footwear seems to be a reasonable option".[[42]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-pmid16620415-42) [National Institute for Health and Clinical Excellence](https://en.wikipedia.org/wiki/National_Institute_for_Health_and_Clinical_Excellence) concluded that for people at "high risk of foot ulcers (neuropathy or absent pulses plus deformity or skin changes or previous ulcer" that "specialist footwear and insoles" should be provided.[[43]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-webNICE-43)

People with loss of feeling in their feet should inspect their feet on a daily basis, to ensure that there are no wounds starting to develop.[[44]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-44)[[45]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-45) They should not walk around barefoot, but use proper footwear at all times.

## Treatment[[edit](https://en.wikipedia.org/w/index.php?title=Diabetic_foot_ulcer&action=edit&section=10" \o "Edit section: Treatment)]

Foot ulcers in diabetes require multidisciplinary assessment, usually by diabetes nurse specialist, a tissue viability nurse,[[6]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer" \l "cite_note-pmid21841646-6) [podiatrists](https://en.wikipedia.org/wiki/Podiatrists), diabetes specialists and [surgeons](https://en.wikipedia.org/wiki/Surgeon). An aim to improve glycaemic  control, if poor, forms part of the management, to slow disease progression.[[7]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-pmid23123487-7) Individuals who have sausage shaped toes, a positive 'probe to bone' test, evidence suggesting osteomyelitis, suspected [charcot neuroarthropathy](https://en.wikipedia.org/w/index.php?title=Charcot_neuroarthropathy&action=edit&redlink=1" \o "Charcot neuroarthropathy (page does not exist)), or those whose ulcers do not improve within 4 weeks of standard care and where there is evidence that [exudate](https://en.wikipedia.org/wiki/Exudate) is of [synovial membrane](https://en.wikipedia.org/wiki/Synovial_membrane) in origin. When osteomyelitis is suspected to be involved in the foot ulcer, but not evidenced on an [x-ray](https://en.wikipedia.org/wiki/X-ray), an [MRI scan](https://en.wikipedia.org/wiki/MRI_scan) should be obtained.[[6]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-pmid21841646-6)

With regards to infected foot ulcers, the presence of microorganisms is not in itself enough to determine whether an infection is present. Signs such as inflammation and [purulence](https://en.wikipedia.org/wiki/Purulence) are the best indicators of an active infection. The most common organism causing infection is [staphylococcus](https://en.wikipedia.org/wiki/Staphylococcus).[[5]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-pmid24796080-5) The treatment consists of [debridement](https://en.wikipedia.org/wiki/Debridement), appropriate bandages, managing [peripheral arterial disease](https://en.wikipedia.org/wiki/Peripheral_arterial_disease) and appropriate use of [antibiotics](https://en.wikipedia.org/wiki/Antibiotic)[[5]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-pmid24796080-5) (against [pseudomonas aeruginosa](https://en.wikipedia.org/wiki/Pseudomonas_aeruginosa), [staphylococcus](https://en.wikipedia.org/wiki/Staphylococcus), [streptococcus](https://en.wikipedia.org/wiki/Streptococcus) and [anaerobe](https://en.wikipedia.org/wiki/Anaerobe) strains), and arterial revascularisation.

### Antibiotics[[edit](https://en.wikipedia.org/w/index.php?title=Diabetic_foot_ulcer&action=edit&section=11" \o "Edit section: Antibiotics)]

The length of antibiotic courses depend on the severity of the infection and whether bone infection is involved but can range from 1 week to 6 weeks or more. Current recommendations are that antibiotics are only used when there is evidence of infection and continued until there is evidence that the infection has cleared, instead of evidence of ulcer healing. Choice of antibiotic depends on common local bacterial strains known to infect ulcers. Microbiological swabs are believed to be of limited value in identifying causative strain.[[7]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-pmid23123487-7) Microbiological investigation is of value in cases of [osteomyelitis](https://en.wikipedia.org/wiki/Osteomyelitis).[[6]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-pmid21841646-6) Most ulcer infections involve multiple microorganisms.[[5]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-pmid24796080-5)

### Wound dressings[[edit](https://en.wikipedia.org/w/index.php?title=Diabetic_foot_ulcer&action=edit&section=12" \o "Edit section: Wound dressings)]

There are many types of dressings used to treat diabetic foot ulcers such as absorptive fillers, hydrogel dressings, and hydrocolloids.[[46]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Hilton_2004-46) There is no good evidence that one type of dressing is better than another for diabetic foot ulcers.[[47]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-47) In selecting dressings for chronic non healing wounds it is recommended that the cost of the product be taken into account.[[48]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Dress13-48)

[Hydrogel](https://en.wikipedia.org/wiki/Hydrogel) dressings may have shown a slight advantage over standard dressings, but the quality of the research is of concern.[[49]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-49) Dressings and creams containing [silver](https://en.wikipedia.org/wiki/Silver) have not been properly studied[[50]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer" \l "cite_note-50) nor have [alginate dressings](https://en.wikipedia.org/wiki/Alginate_dressing).[[51]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-51) Biologically active bandages that combine hydrogel and hydrocolloid traits are available, however more research needs to be conducted as to the efficacy of this option over others.[[46]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Hilton_2004-46)

### Total contact casting[[edit](https://en.wikipedia.org/w/index.php?title=Diabetic_foot_ulcer&action=edit&section=13" \o "Edit section: Total contact casting)]

[Total contact casting](https://en.wikipedia.org/wiki/Total_contact_casting) (TCC) is a specially designed cast designed to take weight of the foot (off-loading) in patients with DFUs. Reducing pressure on the wound by taking weight of the foot has proven to be very effective in DFU treatment. DFUs are a major factor leading to lower leg amputations among the diabetic population in the US with 85% of amputations in diabetics being preceded by a DFU.[[52]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-ahrq.gov-52) Furthermore, the 5 year post-amputation mortality rate among diabetics is estimated at around 45% for those suffering from neuropathic DFUs.[[52]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-ahrq.gov-52)

TCC has been used for off-loading DFUs in the US since the mid-1960s and is regarded by many practitioners as the “reference standard” for off-loading the bottom surface (sole) of the foot.[[53]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-53)

TCC helps patients to maintain their quality of life. By encasing the patient’s complete foot — including the toes and lower leg — in a specialist cast to redistribute weight and pressure from the foot to the lower leg during everyday movements, patients can remain mobile.[[54]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-54) The manner in which TCC redistributes pressure protects the wound, letting damaged tissue regenerate and heal.[[55]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-55) TCC also keeps the ankle from rotating during walking, which helps prevent shearing and twisting forces that can further damage the wound.[[56]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Snyder.2C_R.J._2014._p._555-67-56)

Effective off loading is a key treatment modality for DFUs, particularly those where there is damage to the nerves in the feet (peripheral neuropathy). Along with infection management and vascular assessment, TCC is vital aspect to effectively managing DFUs.[[56]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Snyder.2C_R.J._2014._p._555-67-56) TCC is the most effective and reliable method for off-loading DFUs.[[57]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-57)[[58]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-58)[[59]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-59)

A 2013 [meta-analysis](https://en.wikipedia.org/wiki/Meta-analysis) by the [Cochrane Collaboration](https://en.wikipedia.org/wiki/Cochrane_Collaboration) compared the effectiveness of non-removable pressure relieving interventions, such as casts, with therapeutic shoes, dressings, removable pressure relieving orthotic devices, and surgical interventions. Non-removable pressure relieving interventions, including non-removable casts with an Achilles tendon lengthening component, were found to be more effective at healing foot ulcers related to diabetes that therapeutic shoes and other pressure relieving approaches.[[60]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-60)

### Hyperbaric oxygen[[edit](https://en.wikipedia.org/w/index.php?title=Diabetic_foot_ulcer&action=edit&section=14" \o "Edit section: Hyperbaric oxygen)]

In 2015, a [Cochrane review](https://en.wikipedia.org/wiki/Cochrane_review) concluded that for people with diabetic foot ulcers, [hyperbaric oxygen therapy](https://en.wikipedia.org/wiki/Hyperbaric_oxygen_therapy) reduced the risk of [amputation](https://en.wikipedia.org/wiki/Amputation) and may improve the healing at 6 weeks.[[61]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Kranke2015-61) However, there was no benefit at one year and the quality of the reviewed trials was inadequate to draw strong conclusions.[[61]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Kranke2015-61)

### Negative pressure wound therapy[[edit](https://en.wikipedia.org/w/index.php?title=Diabetic_foot_ulcer&action=edit&section=15" \o "Edit section: Negative pressure wound therapy)]

*Main article:*[*Negative pressure wound therapy*](https://en.wikipedia.org/wiki/Negative_pressure_wound_therapy)

This treatment uses [vacuum](https://en.wikipedia.org/wiki/Vacuum) to remove excess fluid and cellular waste that usually prolong the inflammatory phase of wound healing. Despite a straightforward mechanism of action, results of [negative pressure wound therapy](https://en.wikipedia.org/wiki/Negative_pressure_wound_therapy) studies have been inconsistent. Research needs to be carried out to optimize the parameters of pressure intensity, treatment intervals and exact timing to start negative pressure therapy in the course of chronic wound healing.[[62]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Armstrong-62)

### Other treatments[[edit](https://en.wikipedia.org/w/index.php?title=Diabetic_foot_ulcer&action=edit&section=16" \o "Edit section: Other treatments)]

[Ozone therapy](https://en.wikipedia.org/wiki/Ozone_therapy) – there is only limited and poor-quality information available regarding the effectiveness of ozone therapy for treating foot ulcers in people with diabetes.[[63]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-63)

[Growth factors](https://en.wikipedia.org/wiki/Growth_factors) - there is some low-quality evidence that growth factors may increase the likelihood that diabetic foot ulcers will heal completely.[[64]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-64)

## Epidemiology[[edit](https://en.wikipedia.org/w/index.php?title=Diabetic_foot_ulcer&action=edit&section=17" \o "Edit section: Epidemiology)]

Approximately 15 percent of people with diabetes experience foot ulcers.[[4]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-Harold-4) And approximately 84 percent of lower limb amputations have a history of ulceration with only approximately half of amputees surviving for more than 2 years. 56 percent of individuals with foot ulcers who do not have an amputations survive for 5 years. Foot ulcers and amputations significantly reduce the quality of life. Approximately 8.8 percent of hospital admissions of diabetic patients are for foot related problems, and such hospital admissions are about 13 days longer than for diabetics without foot related admissions.[[5]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-pmid24796080-5) Approximately 35 to 40 percent of ulcers recur within 3 years and up to 70 percent recur within 5 years. Diabetic foot disease is the leading cause of non-traumatic lower limb amputations.[[7]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-pmid23123487-7)

## Research[[edit](https://en.wikipedia.org/w/index.php?title=Diabetic_foot_ulcer&action=edit&section=18" \o "Edit section: Research)]

Stem cell therapy may represent a treatment for promoting healing of diabetic foot ulcers.[[65]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-65)[[66]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-66)[[67]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-67) Diabetic foot ulcers develop their own, distinctive [microbiota](https://en.wikipedia.org/wiki/Human_microbiota). Investigations into characterizing and identifying the [phyla](https://en.wikipedia.org/wiki/Phylum), [genera](https://en.wikipedia.org/wiki/Genera) and [species](https://en.wikipedia.org/wiki/Species) of [nonpathogenic bacteria](https://en.wikipedia.org/wiki/Nonpathogenic_organisms) or other microorganisms populating these ulcers may help identify one group of microbiota that promotes healing.[[68]](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_note-LavigneSotto2015-68)

## References[[edit](https://en.wikipedia.org/w/index.php?title=Diabetic_foot_ulcer&action=edit&section=19)]

* 1. [**Jump up^**](https://en.wikipedia.org/wiki/Diabetic_foot_ulcer#cite_ref-Iakovos_1-0)