Dr. José Antonio Rubio García.
Specialist Physician. Endocrinology and Nutrition Service.
Diabetic Foot Unit. Hospital Príncipe de Asturias. Alcalá de Henares.
Associate Professor in Health Sciences. Department of Medicine and Medical Specialties. UAH. (Madrid, Spain).

Sara Jiménez González.
Podiatrist. Endocrinology and Nutrition Service.
Diabetic Foot Unit.
Hospital Príncipe de Asturias. Alcalá de Henares (Madrid, Spain).

What is diabetic foot?

Why does it occur?
What can its consequences be?

People with diabetes mellitus, especially after poor control of their disease, can suffer from chronic complications. The most well-known are retinal involvement (retinopathy) and kidney damage (nephropathy). In this article, we will address diabetic foot, a chronic complication that is generally less understood regarding its causes and consequences.

Diabetic foot (DF) is defined by the presence of infection, ulceration (an open skin lesion), or destruction of deep tissues of the foot, caused by the presence of **peripheral neuropathy** (damage to peripheral nerves) **and/or peripheral arterial disease (PAD)** and can occur in any type of diabetes. It is more frequent with longer disease duration, and therefore with age, being unusual to appear before the age of 40.

Neuropathy leads to a loss of protective sensitivity, putting patients with this complication at risk of developing ulceration. If PAD is also present, it can result in reduced arterial blood flow to the foot (insufficient blood supply to oxygenate and nourish tissues), leading to non-healing wounds that may progress unfavorably. DF not only includes the situation associated with ulceration, infection, or tissue destruction but also encompasses patients at risk of having lesions due to the presence of neuropathy and/or PAD. We refer to this latter group as at-risk diabetic foot.

WHAT FACTORS CONTRIBUTE TO HAVING DIABETIC FOOT?

Since neuropathy and PAD are the fundamental conditions, factors that favor either one of them will be responsible for the appearance of at-risk DF. We know that chronic hyperglycemia, what we refer to as poor glycemic control, as estimated by glycated hemoglobin (HbA1c), is a key factor in the development of both. For individuals with diabetes who use interstitial glucose sensors, glycemic control is estimated by the percentage of time in range, i.e., the time spent between 70 and 180 mg/dL.

In the case of neuropathy, in addition to hyperglycemia, other contributing factors include the presence of hypertension, dyslipidemia (abnormal blood fat levels), and abdominal obesity, the latter being more typical of type 2 diabetes mellitus. In the development of PAD, in addition to the above-mentioned factors, tobacco plays an important role. Remember that PAD occurs due to the occlusion of the arteries in the lower limbs, caused by the accumulation of fatty plaques (atherosclerosis) in the walls of blood vessels. With all of the above, we can deduce that if we act on the factors responsible for the development of diabetic neuropathy and PAD, we can prevent the occurrence of at-risk DF. We should not forget, as its name indicates, that these are chronic complications resulting from years of poor disease control, and once they appear, they are irreversible. From this, the importance of prevention is derived, but we will leave that to discuss in more detail in a different article.

WHY CAN PEOPLE WITH AT-RISK DIABETIC FOOT DEVELOP ULCERS?

Between 25% and 50% of people with diabetes, depending on the studied population, have at-risk DF, and between 15% and 25% of people could develop an ulcer in their lifetime. For more than 4 decades, we have known that **neuropathy** ***(figure 1)*** in »

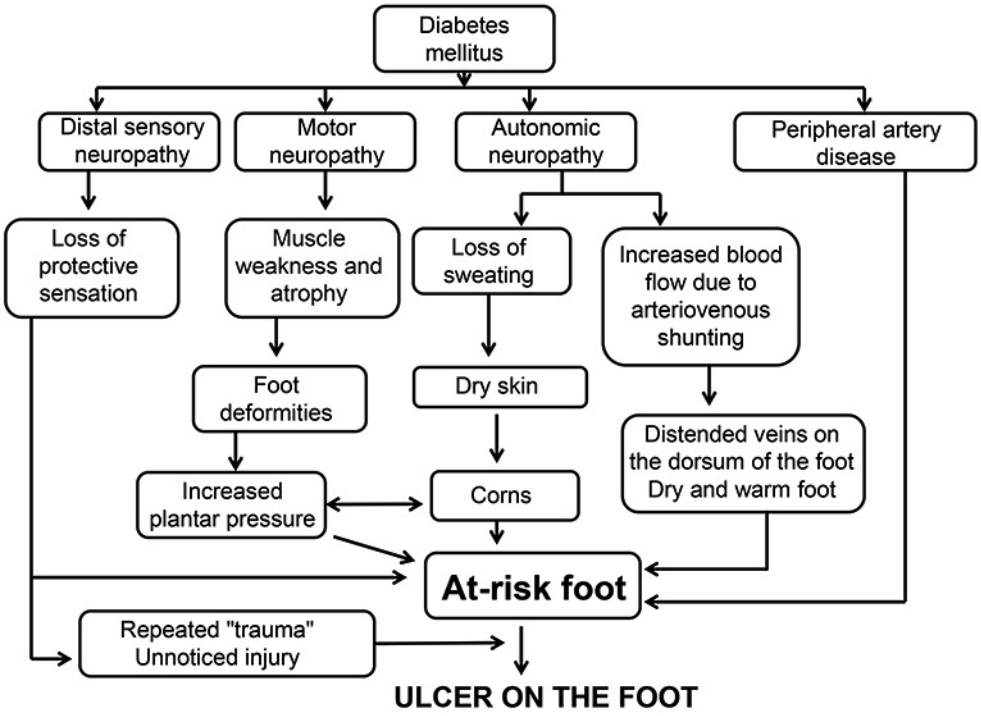

FIGURE 1. Pathways to ulceration in diabetic foot. Adapted from: Boulton AJM, Whitehouse RW. The Diabetic Foot. [Updated 2023 Jul 28]. In: Feingold KR, Anawalt B, Blackman MR, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. [Accessed March 11, 2024] Available online: https://www.ncbi.nlm.nih.gov/books/

» its various forms causes the following alterations in the feet, making them prone to ulceration:

- Sensory neuropathy reduces pain perception and other sensory stimuli.
- Motor neuropathy causes muscle atrophy and weakness, leading to foot deformities.
- Autonomic neuropathy affects the nerves of the autonomic nervous system (sympathetic and parasympathetic), causing the skin of the foot to become drier and more brittle, in addition to reducing nutrient exchange due to arteriovenous shunts.

We can often predict areas of the foot that are vulnerable to ulceration. Thus, it is not uncommon for hyperkeratosis, calluses, or hard spots to appear before ulceration. These areas are often on the dorsum and tips of the toes, frequently over clawed toes, on the soles of the feet, and over the heads of the metatarsal bones.

If **PAD** coexists in the patient, it will hinder healing (the continuous process by which our tissues regenerate and repair when they ulcerate), and the ulcer could worsen. Currently, nearly 70% of patients with DF ulcers have PAD, and thus face problems with arterial flow. When we add that approximately 50% of ulcers become infected, the situation can become even more complicated.

WHAT WOULD TRIGGER THE LESION?

Among the local factors we can find, one stands out above the others due to its frequency: footwear ***(figure 2)***. We all have experienced new shoes that are too tight or sometimes in poor condition, causing us pain or discomfort. If we lose this sensitivity, it should not be surprising that we are "unprotected." This is what happens to people with at-risk diabetic foot. Other times, the trigger is increased activity during regular walking (walking), going barefoot in pools or on beaches, warming the feet on a radiator/stove, or simply cutting a nail that grows poorly, pulling on a skin tag, trying to remove a callus on our own, using a callus remover, and a long etcetera. These manipulations that the patient performs on their own have been termed bathroom surgery, a practice that may seem insignificant at first but can have disastrous consequences. If we understand how ulcerations occur, we will have established the foundation for prevention.

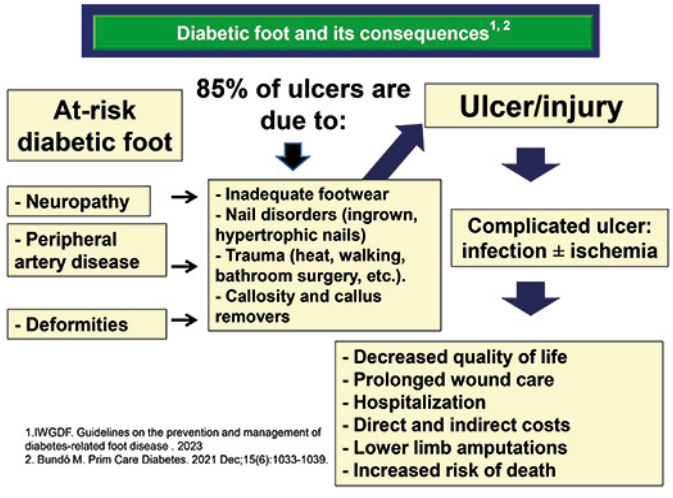

FIGURE 2. Schematic representation of the factors that constitute the at-risk diabetic foot, the factors that can trigger ulceration, and the final consequences of diabetic foot.

To these pre-existing conditions, we must add high-risk factors for ulceration, such as the presence of previous amputations and/or ulcers. Both situations, prior amputation and ulceration, are associated with increased risk.

We cannot overlook general factors that lead to ulceration. The presence of advanced microvascular complications, such as proliferative retinopathy and/or vision reduction, severe chronic kidney disease requiring dialysis or a kidney transplant, the presence of poor current glycemic control, active smoking, and low socioeconomic status are factors associated with increased risk of ulceration.

WHAT ARE THE CONSEQUENCES?

The presence of an ulcer complicated by infection or lack of arterial flow (what we call ischemia) can prevent healing and worsen the condition. Additionally, if there is significant tissue loss that is "irrecoverable," including bone, it may necessitate amputation of a toe or part of the foot, or of the leg, termed minor and major amputation respectively, and even lead to death (figure 2). One in five people who seek care for DF ulcers at a Diabetic Foot Unit end up with lower limb amputation or death, making appropriate management at this stage of the complication very important.

Less known is how the ulcer affects our body. The presence of an ulcer, with or without infection, reduces the patient's quality of life and subjects them to prolonged treatment, generally requiring, at least, 3 days a week for no less than 4 to 6 weeks. In many cases, the patient requires hospitalization, either for ulcer management or for cardiovascular decompensation due to the foot injury, thereby increasing medical costs and costs from lost productivity. More importantly, there are intangible costs that reflect greater suffering for people with diabetes, as well as for their caregivers and family members.

We must also consider the higher long-term mortality risk for individuals with this complication, which increases 4-fold vs someone with diabetes but without DF. Finally, as a reflection of the suffering experienced by a patient with diabetic foot, it should be noted that the presence of an ulcer or undergoing minor amputation causes more fear for the patient than lo- »

BETWEEN 25% AND 50% OF PEOPLE WITH DIABETES, DEPENDING ON THE STUDIED POPULATION, HAVE AT-RISK DF, AND BETWEEN 15% AND 25% OF INDIVIDUALS COULD DEVELOP AN ULCER OVER THEIR LIFETIME

» sing their vision or undergoing dialysis. Thus, understanding the multifactorial nature of why diabetic foot occurs, its ulceration, and the extent of its consequences are key points for its management and prevention.

In conclusion, diabetic foot occurs due to the presence of 2 chronic complications: diabetic neuropathy and peripheral arterial disease. Both factors cause changes in the foot, primarily loss of sensitivity and reduced blood flow, placing the feet of people with diabetes at greater risk for ulceration. The pathways to ulceration are known and can be prevented. **Controlling triggering factors, such as having appropriate footwear among others, would be an important aspect in preventing ulceration.** The consequences of diabetic foot, such as ulceration, lead to suffering for patients and their social and family surroundings, prolonged treatments, hospitalization, increased economic costs, loss of part or the entire lower limb, and even death, representing a significant burden for both patients and society.

Properly addressing DF, both in terms of prevention and treatment of established ulcers, has proven effective in reducing its burden, but we will leave this point for our next article. D

REFERENCES

- International Working Group on the Diabetic Foot. IWGDF Guidelines on the prevention and management of diabetes-related foot disease [accedido el 11 de marzo de 2024]. Disponible en: https://iwgdfguidelines.org/guidelines-2023/all-guidelines-2023/
- Armstrong DG, Tan TW, Boulton AJM, Bus SA. Diabetic Foot Ulcers: A Review. JAMA. 2023 Jul 3;330(1):62-75. https://doi.org/10.1001/jama.2023.10578.
- Boulton AJM, Whitehouse RW. The Diabetic Foot. [Updated 2023 Jul 28]. In: Feingold KR, Anawalt B, Blackman MR, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. [accedido el 11 de marzo de 2024] Disponible en: https://www.ncbi.nlm.nih.gov/books/NBK409609/
- Ministerio de Sanidad. Abordaje del pie diabético. Estrategia de Diabetes del Sistema Nacional de Salud. Edita y distribuye: © Ministerio de Sanidad. Centro de publicaciones. Paseo del Prado, 18 - 28014 Madrid. NIPO en línea: 133-22-045-9. 2022. [accedido el 11 de marzo de 2024] Disponible en: https://cpage.mpr.gob.es/producto/abordaje-al-pie-diabetico/