With Bare Feet in the Soil: Podoconiosis, a Neglected Cause of Tropical Lymphoedema

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Abstract

Podoconiosis is a form of lymphoedema that occurs in tropical highland areas in genetically susceptible individuals who are exposed to irritant volcanic soils. The disease is preventable through consistent use of footwear and attention to foot hygiene; however, in endemic areas there is a strong barefoot tradition, and many cannot afford shoes. Patients with podoconiosis face significant physical disability, psychological comorbidity, reduced quality of life and experience frequent episodes of systemic illness due to acute dermatolymphangioadenitis. This review provides an overview of this important and neglected tropical skin disease and summarizes the latest research findings.

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Introduction

Tropical lymphoedema, or elephantiasis, is generally caused by either lymphatic filariasis (LF) or podoconiosis, also known as endemic non-filarial elephantiasis. LF is one of the 20 neglected tropical diseases (NTDs) recog-

nized by the World Health Organisation (WHO). It is an infectious disease caused by the parasitic nematodes *Wuchereria bancrofti*, *Brugia malayi* or *Brugia timori*, which are transmitted by mosquitoes in endemic areas [1]. Table 1 summarizes the major skin manifestations for 18 of the 20 diseases in the WHO NTD portfolio where skin involvement is a recognized feature. Podoconiosis is a chronic inflammatory, geochemical skin disease caused by prolonged exposure to irritant red clay soils derived from volcanic rocks [2] and causes bilateral asymmetrical swelling of the lower legs. Podoconiosis is a neglected disease, although currently it does not appear on the WHO list of NTDs. Podoconiosis is often not recognized and can be misdiagnosed as LF. It is prevalent among the world's poorest, remote and underprivileged populations in tropical and subtropical areas, particularly in African countries [3]. Podoconiosis affects people who live and work barefoot and cannot afford shoes, such as subsistence farmers. It causes physical impairments, stigmatization and inability to work, imposing a social and economic burden in already marginalized communities, and yet the disease can easily be prevented by encouraging the use of appropriate footwear. Established lymphoedema

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Table 1. Clinical features of the skin NTDs

Disease	Causative agent	Typical skin manifestations
Bacterial infections		
1. Leprosy	<i>Mycobacterium leprae</i>	Hypopigmented anaesthetic patches or plaques, neuropathic ulcers, widespread papules/nodules, leprosy reactions (oedema)
2. Buruli ulcer	<i>Mycobacterium ulcerans</i>	Painless ulcer with undermined edge, oedema, scarring, usually lower limb
3. Yaws (endemic treponematoses)	<i>Treponema pallidum (pertenu)</i>	Nodules, ulceration
Viral infections		
4. Dengue and chikungunya	Dengue and chikungunya viruses (arboviruses)	Maculopapular rash Chikungunya: bullous rash, centrofacial pigmentation, transient nasal erythema
Mycetoma, chromoblastomycosis and other deep mycoses		
5. Mycetoma	Various fungi (eumycetoma) and bacteria (actinomycetoma)	Papules, nodules, plaques Mycetoma: sinus tracts which discharge grains
Chromoblastomycosis and other deep mycoses	Various fungi	
Helminth (parasitic worm) infections		
<i>Nematodes (roundworms)</i>		
6. Lymphatic filariasis	<i>Wuchereria bancrofti</i> , <i>Brugia malayi</i> , <i>Brugia timori</i>	Limb oedema, nodules, hyperkeratosis and skin fissuring
7. Onchocerciasis	<i>Onchocerca volvulus</i>	Pruritus, papules, nodules (onchocercomas), plaques, depigmentation, skin atrophy, oedema
8. Dracunculiasis (Guinea worm disease)	<i>Dracunculus medinensis</i>	Pruritus, burning, vesicles, oedema
9. Soil-transmitted helminthiasis	<i>Ascaris lumbricoides</i> , <i>Trichuris trichiura</i> , <i>Necator americanus</i> and <i>Ancylostoma duodenale</i>	Urticaria
<i>Platyhelminths (flatworms)</i>		
10. Schistosomiasis	<i>Schistosoma</i> sp.	Cercarial dermatitis (swimmer's itch), urticaria, purpura, oedema, skin granulomas
11. Foodborne trematodiasis	<i>Clonorchis</i> sp., <i>Fasciola</i> sp., <i>Opisthorchis</i> sp., <i>Paragonimus</i> sp.	Urticaria, migratory subcutaneous nodules
12. Taeniasis/cysticercosis	<i>Taenia solium</i>	Cysticercosis: subcutaneous nodules and cysts (cysticerci)
13. Echinococcosis	<i>Echinococcus</i> sp.	Subcutaneous nodules and cysts
Kinetoplastid diseases		
14. Leishmaniasis	<i>Leishmania</i> sp.	Cutaneous: ulcers, papules, nodules, plaques, destruction of mucosa and cartilage Post kala azar dermal leishmaniasis: papules
15. Human African trypanosomiasis (sleeping sickness)	<i>Trypanosoma brucei gambiense</i> , <i>Trypanosoma brucei rhodesiense</i>	Chancre, oedema, maculopapular (trypanid) rash
16. Chagas disease (American trypanosomiasis)	<i>Trypanosoma cruzi</i>	Periorbital swelling (Romana's sign), nodule/oedema (chagoma)
Scabies and other ectoparasitic infections		
17. Scabies	<i>Sarcoptes scabiei</i>	Pruritus, serpiginous burrows, papules, nodules, excoriations, hyperkeratotic plaques
Tungiasis (sand flea disease)	<i>Tunga penetrans</i>	Pruritus, pain, papules and ulceration, usually on the feet
Cutaneous larva migrans	Hookworm larvae, various species	Serpiginous eruption, pruritus, vesicles
Non-communicable		
18. Snakebite envenoming	n.a.	Ulceration, oedema, haemorrhage, tissue necrosis

Neglected tropical diseases (NTDs) with recognized skin involvement, grouped according to the class of causative organism. No. 1, 2, 6–8 and 10 are diseases that can cause oedema, and which might be considered in the differential diagnosis of podoconiosis. Other conditions causing enlargement of the lower limb must also be distinguished, such as chromoblastomycosis and mycetoma. n.a., not applicable.

can be significantly improved with simple management measures taught as part of educational community programmes [4]. The aim of the current review is to give an updated overview on podoconiosis describing the epidemiology, pathophysiology, clinical features and management of this poorly understood and underresearched non-communicable disease.

History

Throughout history the description of “swollen legs” has been reported and can be traced back to the Roman Empire. The distinction between podoconiosis and LF was probably made at the end of the 19th century, when Dr. Rodolfo Robles inferred that patients from Guatemala, who suffered from lymphoedema and repeatedly tested negative for microfilaria and streptococci, were associated with walking barefoot [5]. In the 1960s, Oomen [6] described a type of tropical lymphoedema that was found at an altitude of 1,000–2,000 m and was not caused by LF or onchocerciasis. Price [7–9] extended these epidemiological studies in the 1970s exploring the aetiology and pathophysiology of podoconiosis in Ethiopia, which to date remains the most severely affected country. The term podoconiosis was established by Price and is derived from the Greek words “podos” (foot) and “konos” (soil) [10]. Until the 1990s, there were few additions to the existing literature, most of which were led by Price. Subsequently, a significant body of research has emerged, and many of the key findings will be discussed further in this review.

Epidemiology

The global prevalence of podoconiosis is largely unknown, and available numbers are likely to be underestimated. In many countries its presence is based on cross-sectional surveys and individual case reports. This scarcity in knowledge may, in part, be explained by poor awareness and lack of interest of health care providers and by the reduced mobility and associated stigma of the affected people. But it is also attributable to global health communities and local governments failing to prioritize podoconiosis in research programmes and using inconsistent methodologies to assess the geographical distribution. Another important limiting factor is the absence of an accurate diagnostic point-of-care test to confirm the disease. To address some of these challenges, Deribe et al. [11] have recently launched the Wellcome Trust-funded

global atlas project with the aim of mapping the geographical distribution and prevalence of podoconiosis in countries where there is a coexistence of predisposing factors. The group has recently published data from Cameroon [12, 13] and Rwanda [14] and is planning additional maps for high-risk African and Asian countries.

Globally podoconiosis affects an estimated 4 million people in 32 endemic countries, many of which are in the highlands of tropical sub-Saharan Africa, but also in parts of Central and South America and South East Asia [3]. In Africa, podoconiosis has been reported in Angola, Burundi, Cameroon, Cape Verde, Chad, the Democratic Republic of Congo, Equatorial Guinea, Ethiopia, Kenya, Madagascar, Mozambique, Niger, Nigeria, Rwanda, Sao Tome and Principe, Sudan, Tanzania and Uganda; in Latin America, in Brazil, Colombia, Costa Rica, Ecuador, El Salvador, French Guiana, Guatemala, Honduras, Mexico, Peru and Suriname; and in Asia, in India, Sri Lanka and Indonesia [11, 15]. The countries with the highest reported regional prevalence are Ethiopia (2.7–7.5%) [16], Cameroon (0.5–8.1%) [17] and Uganda (0.1–4.5%) [18]. In Ethiopia, an estimated 1.5 million adults are affected [19] and a further 35 million people are at risk [20]. Equally, in Rwanda, despite a relatively low prevalence, podoconiosis is widely distributed throughout the country [14].

Podoconiosis is limited to people living and working barefoot who have been exposed from early childhood, over many years, to irritant volcanic soils, such as subsistence farmers, gold miners, weavers and potters [21]. Naturally, the risk extends to any profession or activity in which there is prolonged contact with irritant soils. Podoconiosis is present among remote and underprivileged communities where people cannot afford shoes, have lack of access to clean water and poor sanitation. Men and women are equally affected. The majority of people develop signs and symptoms of the disease in the second or third decade, but prevalence increases up to the sixth decade [22].

The distribution of podoconiosis is limited to tropical volcanic areas where alkalic red clay soils are formed under specific environmental circumstances, including high altitude (1,000–1,500 m above sea level), high seasonal rainfall (1,000–1,500 mm annually) and a mean annual land surface temperature between 19 and 21 °C [2, 23]. It is thought that these climatic conditions contribute to the weathering and disintegration of lava and the reconstitution of mineral components into silicate clays, which are capable of penetrating the skin inducing an abnormal inflammatory reaction in the lymphatic system [24]. The irritant colloid-sized particles typically

found in these derived soils are silicon, aluminium, magnesium, potassium, iron, kaolinite, beryllium and zirconium [21, 25–27].

Pathophysiology

Large gaps still remain in our understanding of the immunopathophysiology of podoconiosis. The condition results from a complex interaction between favourable environmental conditions and host susceptibility combined with poverty-related circumstances. Price and colleagues hypothesized that the different colloid-sized particles breach through the bare skin, either through microtrauma, which, for example, in farmers inevitably occurs when digging and hoeing manually on the land, or through the numerous sweat ducts that are present on the soles of the feet [24]. The particles are then absorbed by the phagosomes of dermal tissue macrophages in the lower limb lymphatics and attract other pro-inflammatory immune cells towards the injured region [28]. The resulting inflammatory process is thought to trigger subendothelial oedema, endolymphangitis and collagenization and occlusion of afferent lymph vessels leading to permanent deposition of silicates in dermal tissues, increased fibrosis and ultimately blockage of the lymph drainage system resulting in lymphoedema [25, 29, 30].

Although podoconiosis is the result of an abnormal reaction to irritant soil particles, it is not precisely known which mediators are involved in this process. A study performed by Addisu et al. [31] suggested that transforming growth factor- β and oxidative stress may play a role in the early phases of the disease. In other forms of chronic lymphoedema, it has been suggested that the mobilization of lymphocytes and Langerhans cells from skin to regional lymph nodes is impaired and causes insufficient clearance of foreign antigens providing the substrate for chronic inflammatory changes [32]. Ultimately, adipocytes, keratinocytes and fibroblasts accumulate transforming the soft oedematous dermal tissue into a hard, fibrotic and hyperkeratotic mass [31]. It is conceivable that similar mechanisms play a role in the pathogenesis of podoconiosis. Patients with podoconiosis may also have an impaired skin barrier function. A recent study found that the quality of the stratum corneum of the lower legs and feet of affected patients was compromised compared to negative controls making it more likely for mineral colloid-sized particles and micro-organisms to enter through the skin barrier [33]. The significance of

this finding, whether the deficiency in skin barrier is a cause or a consequence of lymphoedema, and to what extent it has a role in the pathogenesis of podoconiosis, is not clear.

Soil-transmitted helminth (STH) infections are common in the (sub)tropics, especially in sub-Saharan Africa and Asia, regions which are also co-endemic for podoconiosis. A study in Ethiopia reported a significant higher prevalence of STH infections among individuals with podoconiosis compared to healthy controls [34]. A reduced immunity due to an underlying inflammatory disorder, such as podoconiosis, may facilitate the establishment of STH infections. By contrast, STH infections are known to dysregulate the host immune response that may also facilitate disease progression of podoconiosis or possibly impair the effectiveness of current available treatments [35]. Likewise, these studies illustrate the burden and geographical overlap of multiple NTDs in resource-constrained settings and highlight the importance of integrated disease control and management.

Genetic Susceptibility

Host genetic factors play an important role in the susceptibility of podoconiosis. Price [21, 36] and his predecessors had observed that familial clustering occurs and that a small proportion of individuals exposed to irritant soils developed disease, even though affected and unaffected people had similar mineral particles within their lymphatic system. These microparticles corresponded to the elemental content of the soil on which the investigated individuals resided and suggested that affected people respond differently to the absorbed particles [25, 37]. In a series of 90 Ethiopian families with more than one affected family member, the existence of an autosomal recessive mode of inheritance was suspected with an estimated gene frequency of 30% (range of 15–40% in the general population) [36]. Thirty years later a similar pedigree study was performed by the group of Davey in southern Ethiopia and predicted that the heritability of podoconiosis was around 60% with a risk ratio of occurrence of 5.07 among siblings of the index patient [22]. Recently, the same group has performed a genome-wide, family-based association study and identified an association between genetic variants in HLA class II loci with podoconiosis. They also found that certain single-nucleotide polymorphisms increased the likelihood of contracting the disease by two- to threefold [38].

Fig. 1. Early mossy foot changes involving the toes. Clinical images provided by Action on Podoconiosis and Integrated Development Organization, www.actiononpodo.com.

Fig. 2. Advanced disease with hyperkeratosis and nodules. Clinical images provided by Action on Podoconiosis and Integrated Development Organization, www.actiononpodo.com.

Clinical Features

Podoconiosis causes progressive bilateral, though asymmetrical, swelling of the lower legs, only rarely reaching above the knee. The condition is characterized by a prodromal phase which may start during early childhood or adolescence and includes mild swelling of the medial toes, itching of the dorsum of the forefoot and/or a burning sensation in the foot and lower leg. The latter typically occurs at night and may follow a period of intense activity during the day (such as walking to the market), excessive alcohol ingestion or at the beginning of a menstrual cycle [39]. Subsequent episodes affect the same leg, may be associated with a tender femoral lymph node and mild fever, and usually subside spontaneously after a few days of rest and elevation of the affected leg. The other limb may only become involved after many months or years. The itching may be persistent leading to repetitive scratching, lichenification (reactive thickening of the skin) and cracks/breaches in the skin. This may prompt secondary bacterial infection (i.e., cellulitis) and further complicate the condition [40, 41]. Early, relatively subtle clinical signs that can be observed are splaying of the forefoot (widening of the forefoot with slight swelling and separation of toes), plantar oedema with slight lymphatic oozing onto the skin attracting the characteristic presence of flies, increased skin markings, hyperkeratosis, the development of a mossy foot (papillomatous skin) and “block” toes (toes resemble sausages, lacking their usual curvature) [42]. These early changes are demonstrat-

ed in Figure 1. As the disease progresses over the years, the chronic irreversible stage sets in. The clinical features can vary from a predominantly soft, squashy and lymphoedematous type (referred to as “water-bag”) to the thickened, leathery, fibrotic type often accompanied by multiple hard skin nodules (Fig. 2) and is referred to as elephantiasis [15]. Many patients show a combination of these two variants.

In addition, the disease trajectory is punctuated by episodes of acute dermatolymphangioadenitis (ADLA), which occur as frequently as 23 times per year [43]. The clinical presentation of ADLA resembles cellulitis, with diffuse swelling and erythema of the limb, inflamed tender lymphatic vessels and lymph nodes, and systemic symptoms including fever. These acute inflammatory episodes occur with other causes of lymphoedema as well, such as LF, and the aetiology is thought to be similar involving bacterial entry through skin fissures or other breaks in the epidermis [40]. Typical changes of hyperkeratosis with fissuring are shown in Figure 3. In particular the presence of interdigital lesions (any web space without normal intact skin) was shown to be an important risk factor for ADLA in patients with LF in Guyana [44]. In this study, only 1 in 5 of these interdigital lesions had positive microscopy or culture for fungal organisms. Each attack leads to further progression of the lymphoedematous limb to the hard, fibrotic type. The chronic stage of disease can be associated with fusion of the interdigital spaces and ankylosis of the interphalangeal or ankle joints [45]. Bacterial and fungal superinfections may produce a foul smell adding to the stigmatization and social isolation of the patient.

Fig. 3. Hyperkeratosis and fissuring creating bacterial entry points. Clinical images provided by Action on Podoconiosis and Integrated Development Organization, www.actiononpodo.com.

Diagnosis

Podoconiosis is a clinical diagnosis, relying on recognition of typical clinical features in the correct geographical context. Other causes of (tropical) lymphoedema must be excluded, the main two being leprosy and LF.

Leprotic lymphoedema is rarely discussed in the literature, and the frequency with which this complication occurs is not clear. However in Ethiopia, where lower limb lymphoedema is common, leprosy is the second most common cause of lymphoedema behind podoconiosis, accounting for more cases of lymphoedema than LF [46]. Nerve impairment, loss of sensation in the feet, neuropathic ulcers, involvement of the hands, and a number of characteristic skin changes will distinguish leprosy from podoconiosis.

LF is the most common cause of lymphoedema in the tropics; however, in areas where podoconiosis is prevalent, LF accounts for a minority of cases (for example less than 1% of cases in Ethiopia). Filarial lymphoedema tends to be unilateral but frequently extends above the knee and can involve the groins and genitals causing hydrocele.

Other causes of secondary lymphoedema to be considered include rheumatic heart disease, endemic Kaposi sarcoma, onchocerciasis (river blindness), chronic recur-

rent erysipelas/cellulitis and liver failure. Clinical algorithms are available to aid the diagnosis of podoconiosis, combining history and physical examination with disease-specific tests to exclude the differential diagnoses [46, 47]. The differential will also vary with geographic location of the patient. Finger-prick blood samples can be used to test for circulating filarial antigen using immunochromatographic card tests; an additional blood sample can be taken for filarial antibody testing. However, both tests may become negative in patients with chronic manifestations of LF.

The diagnosis of podoconiosis is often delayed. Access to health care is a problem for many patients, particularly in rural areas due to the time and costs involved in seeking treatment, and patients may be reluctant to present to health services due to widespread beliefs that there is no effective medical treatment [17, 48]. In addition, it has been shown that patients presenting to non-specialist health services frequently encounter lack of expertise and stigmatizing attitudes from health professionals [49, 50]. In a highland area of Ethiopia endemic for podoconiosis, clinical assessment by appropriately trained community health workers (ensuring the patient has not migrated from a lowland area and performing physical examination) was shown to be a valid means of diagnosing podoconiosis [51].

Disease Burden: Physical Impairment and Disability

Podoconiosis is a cause of chronic disability in endemic areas. Physical impairment is a significant part of this problem and results from progressive lower limb lymphoedema and its complications. This progression is captured in the clinical staging system for podoconiosis, developed by Tekola et al. [52] in Ethiopia, which was adapted from the Dreyer system for staging filarial lymphoedema [53]. It consists of 5 stages, starting with reversible oedema (stage 1), progressing to more extensive and non-reversible oedema with dermal nodularity and hyperkeratosis (stages 2–4), ultimately resulting in fixation of the ankle and toe joints (stage 5).

Increasing size and weight of the lower limbs makes it difficult (or impossible in some cases) to perform normal daily activities, in particular those related to standing and mobilizing. This has a significant impact on an individual's ability to work or find employment, especially in rural areas where subsistence farming and manual labour are the major occupations. Individuals also face difficulty participating in other important societal roles and events.

Impairments in body function and structure are intimately connected with an individual's ability to perform essential activities and participate in important life roles, as emphasised in the International Classification of Functioning, Disability and Health model of disability. Environmental and personal factors also influence health and functioning within this framework. Anecdotally the physical and social issues faced by those with podoconiosis are understood, although population level data on activity limitation and social participation are lacking. A small number of studies have included the WHO Disability Assessment Schedule questionnaire in their assessment of patients with podoconiosis. In one study, having podoconiosis was associated with a higher WHO Disability Assessment Schedule score, as were a number of other factors including living in a rural area, having a high depression score and being poor on the wealth index [54].

Disease Burden: Mental Health and Stigma

Podoconiosis is a highly stigmatizing condition, associated with significant psychological morbidity and reduced quality of life, adding considerably to the overall disease burden.

Depression is common in those with podoconiosis, with reported prevalence of depressive symptoms ranging from 12.6% in one study conducted in Northern Ethiopia [54] to 37% in a recent study in Cameroon [55]. In the latter study by Semrau et al. [55], unemployment was (the only factor) found to be predictive of higher depression scores. Similar results are reported for lymphoedema of other cause; Obindo et al. [56] identified depression in 20% of patients with LF in Nigeria, with more than half of these having moderate or severe depressive symptoms.

In the case of chronic NTDs, particularly those causing disfigurement, the psychosocial impact is long-lasting [57, 58]. Furthermore, the psychological and emotional impact of the disease extends beyond the patient, to include family members and caregivers [59], as is the case for other skin-related NTDs such as leprosy and cutaneous leishmaniasis [60–62].

Social stigma is one of the most significant problems faced by those with podoconiosis. In podoconiosis endemic areas most members of the community are aware of the disease and can recognize it [48]. However, misconceptions are common, relating to a number of areas from aetiology to treatment, with significant consequences. In Cameroon, 12% of those interviewed believed the disease to be the result of witchcraft whilst 4% attributed it to des-

tiny/fate [17]. Unfortunately, false beliefs regarding the aetiology of the condition are common among health professionals; in one study, more than half of those interviewed thought the disease was infectious and all expressed one or more stigmatizing attitudes towards podoconiosis patients [50].

Affected persons have been removed from school, excluded from local meetings and religious events, and prevented from marrying unaffected individuals [48, 63, 64]. Many people would not eat with someone with podoconiosis [48].

Franklin et al. [65] were the first to develop and validate a standardized measure of podoconiosis stigma, consisting of subscales for felt and enacted stigma. They demonstrated good psychometric properties and a significant correlation between felt and enacted stigma scales. The scales have subsequently been used to quantify the burden of stigma in patients with confirmed podoconiosis in Ethiopia, and to identify factors associated with higher stigma scores which include advanced disease stage and above average monthly income [66].

Physical and psychological health, social participation and ability to function productively within the environment are some of the factors which contribute to an individual's overall sense of well-being or quality of life. Not surprisingly, quality of life is significantly reduced in patients with podoconiosis. A study conducted in Northern Ethiopia using the validated Amharic version of the WHO Quality of Life questionnaire (WHOQoL-BREF) showed that patients with podoconiosis had a lower quality of life, including in all four subdomains (physical, psychological, social and environmental), compared with matched healthy controls [67]. Experiencing high levels of stigma was also associated with below-average quality of life scores in this study. The Dermatology Life Quality Index (DLQI), a tool widely used by dermatologists in many countries, has been translated into Amharic and validated for patients with podoconiosis in Ethiopia [68]. The median DLQI scores in this study were 13 for new (untreated) patients and 3 for treated patients. This is comparable to mean DLQI scores reported for other debilitating skin conditions including acne (11.9), chronic urticaria (9.9), hidradenitis suppurativa (8.9) and scabies (8.6) [69]. The maximum DLQI score is 30, and a score between 11 and 20 indicates a very large effect on a patient's life [70]. In the context of psoriasis and atopic eczema, where the DLQI is used routinely in clinical practice, a score greater than 10 indicates severe disease and justifies the use of systemic agents including biological therapies.

Economic Impact

Podoconiosis has a significant economic impact in endemic areas, on affected families and the wider economy. Households affected by podoconiosis in Cameroon incur a total out-of-pocket expenditure (direct cost) of 142 USD per year, which amounts to more than one third of the total household income [71]. This includes payment for medical treatment and associated non-medical costs such as food and transport. By contrast, leprosy-affected households in Cameroon do not incur any direct costs. Additional financial burden arises through loss of productivity; as most patients are from an economically productive age group and engaged in farming or manual labour, ill health renders them unable to earn money. Similar results have been demonstrated in Ethiopia, where podoconiosis-affected households spend a total of 143 USD per year [4]. This study was conducted in Wolaita zone, southern Ethiopia, where the cost of podoconiosis was in excess of 16 million USD per year. Applying these results to the whole of Ethiopia, the estimated total cost of podoconiosis would be at least 208 million USD per year.

This level of catastrophic spending creates a strong argument for controlling podoconiosis. Interventions should focus on reducing treatment costs to patients and protecting against productivity losses.

Management

Prevention is better than treatment, and podoconiosis is entirely avoidable if susceptible individuals wear shoes that protect the skin against the irritant soil. Education is therefore of paramount importance, and this is expanded on in the next section.

For established disease there are a number of simple and low-cost treatment measures that can be adopted to prevent disease progression and disability. Attention to skin hygiene is a priority. Water, sanitation and hygiene (WASH) interventions have recognized benefits for patients with lymphoedema conditions, including LF and podoconiosis, resulting in improvement in both clinical parameters and patient-reported quality of life [72, 73]. Daily washing of the affected skin requires that patients have access to clean water, soap and antiseptic agents (bleach for diluting), and many organizations caring for patients with podoconiosis in endemic areas will provide these materials, along with emollients and bandages. As we have stated, the skin barrier function is impaired in

podoconiosis [33]. Emollients help to improve and maintain the integrity of the skin barrier, by preventing skin fissuring and limiting the entry of harmful microsilica particles and microbes; Whitfield's ointment is often favoured due to its keratolytic and antiseptic properties. Additionally, it has been shown that washing with a smaller volume of water (1 litre compared with 6 litres), with the addition of 20 mL of glycerol (as a humectant) to produce a 2% (v/v) dilution, results in significant improvements in stratum corneum hydration and reduced transepidermal water loss [74]. Compression hosiery, bandaging and manual lymph drainage are useful approaches to reducing lymphoedema; however, they are not always available.

Prevention of acute ADLA, arguably the most important complication of podoconiosis, is challenging. Lymphoedema self-care has been shown to reduce the frequency and duration of ADLA episodes [43]. In this study, the use of a simple self-care package, consisting of information on foot hygiene, skin care, bandaging, foot and calf exercises, and use of socks and shoes, resulted in 4.5 fewer episodes of ADLA per person-year, compared with those who received no treatment. There is some evidence that long-term systemic antibiotic treatment is beneficial in preventing ADLA in patients with advanced stages of lymphoedema [75]; however, antibiotics are not widely available in rural settings of podoconiosis patients.

Community-based lymphoedema self-care has been shown to reduce the incidence of ADLA and limit disease progression among patients with filarial lymphoedema in a variety of settings [76–78]. Integrated approaches to skin care, combining simple hygiene measures, exercise (yoga and deep breathing techniques) and traditional Indian medicine (Ayurveda), have also been used for the management of LF, demonstrating improvements in lymphoedema severity and reduced incidence of “inflammatory episodes” [79].

The evidence base on traditional medicines, in terms of efficacy and adverse effects, needs to be expanded; these treatments are widely available in rural settings where tropical lymphoedema conditions are endemic and are commonly used due to their cultural acceptability.

Towards Elimination of Podoconiosis

Elimination of podoconiosis should be feasible and could possibly be achieved within one generation. Key preventive strategies include use of footwear, regular foot hy-

giene, and covering floor surfaces in areas of irritant soil; however, the implementation of these strategies is not straightforward.

For example, there are a number of barriers to the consistent use of shoes. These include financial constraints, unsuitability of shoes for farming activities, fear of stigma and labelling, and low perception of risk [80]. In rural areas, access to quality footwear can be limited, and there is a strong barefoot tradition. Those who do own shoes may not wear them, frequently reserving them for special occasions or simply not prioritizing their use. Women face additional social barriers to use of shoes and are more likely than men to be ridiculed for wearing shoes [81].

Shoes must be affordable, acceptable to patients and appropriate to the environment and climate (fit for purpose). Providing education on the aetiology of podocooniosis and the need to wear shoes is essential, both for affected individuals and those at risk. Knowledge and understanding of podocooniosis is significantly lower in unaffected households compared with affected households [82]. Interestingly, among those who do wear shoes, prevention of podocooniosis is rarely the motivating factor. Most people want to wear shoes for other social and cultural reasons, and it could be helpful for future interventions to take this into consideration.

Simple lymphoedema management is effective in preventing disease progression and associated disability, although these services are not always easy to access. In Ethiopia, there is a lack of expertise relating to podocooniosis within government health services, and foot care is provided by a number of community-based non-government organizations. The Mossy Foot Treatment and Prevention Association is one such example; based in southern Ethiopia they have been treating patients and providing education, training in foot hygiene and socioeconomic rehabilitation since 1998 when they were founded.

Interventions that address poverty and socioeconomic development are also important; urbanization and the use of shoes probably explain why podocooniosis disappeared from parts of North Africa (Algeria, Morocco and Tunisia) and the Canary Islands, where it was once common.

In recent years there have been several notable achievements. In 2011, podocooniosis was recognized by the WHO as an NTD, and in the same year the National Podocooniosis Action Network was established with the support of the Ethiopian Federal Ministry of Health. The National Podocooniosis Action Network consortium brings together organizations working on podocooniosis from across Ethiopia, with the aim of preventing podocooniosis and improving access to treatment. One of these member organizations

is the Action on Podocooniosis and Integrated Development Organization, an implementing partner of the Preventing Podocooniosis Project. In 2017 the Action on Podocooniosis and Integrated Development Organization moved from providing care directly to patients to training health extension workers and health professionals and supporting them to treat podocooniosis patients in the government health service. “Footwork” (www.podo.org), the International Podocooniosis Initiative, enables collaboration between public and private partners to support advocacy, research and the integration of control activities for podocooniosis with those of other NTDs. Footwork has produced a range of educational materials aimed at raising awareness of podocooniosis. An excellent example is “Best Foot Forward,” a short animated video that illustrates the cause, treatment and prevention of podocooniosis.

There are numerous opportunities to integrate control activities for NTDs that affect the skin [83, 84]. This is particularly the case for podocooniosis and other causes of tropical lymphoedema, which are frequently co-endemic and benefit from a similar approach to management as described earlier. An integrated mapping exercise conducted in Ethiopia by Kebede et al. [85] identified more than 25,000 cases of leg lymphoedema across 20 districts known to be co-endemic for podocooniosis and LF; understanding this will help to ensure effective implementation of morbidity management and disability prevention services for these diseases. In addition to the physical aspects of care, there is increasing recognition of overlap in the mental health impact of NTDs [86] including the psychosocial consequences of stigma [87]. There is thus an additional opportunity to include mental health and stigma interventions within existing integrated activities for skin NTDs. This could be facilitated by the use of generic “cross-cutting” approaches to stigma measurement and intervention, as highlighted by van Brakel et al. [87].

Conclusions

Podocooniosis is a chronic, debilitating neglected disease affecting genetically susceptible people who are continuously exposed to irritant red clay volcanic soils. The condition causes significant physical morbidity, has a devastating impact on mental health and quality of life, and has catastrophic economic consequences for patients and their communities. Podocooniosis has great potential for elimination, as the disease can be prevented by consistent use of footwear from early childhood and by practicing proper foot hygiene.

Podoconiosis is a challenge to public health care in some of the poorest and marginalized communities across the world. Research activities have gained momentum, with ongoing efforts to define the global distribution and burden of podoconiosis, although fundamental aspects of disease aetiology including genetic susceptibility are poorly understood. Despite awareness of the condition in endemic areas, those suffering from podoconiosis are highly stigmatized and disadvantaged. Globally coordinated efforts are required to support research and develop a robust health policy, and to educate and empower those living in endemic areas.

Key Message

Podoconiosis is a common but poorly understood cause of lymphoedema in tropical highland areas.

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Statement of Ethics

Ethical approval was not required.

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Author Contributions

D.J.C. and M.L.G. contributed equally to writing the article. L.C.F. made contributions throughout and reviewed the drafts. D.J.C. was responsible for correspondence and revisions.

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