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REVIEW

Podoconiosis, a neglected tropical disease

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ABSTRACT

Podoconiosis or 'endemic non-filarial elephantiasis' is a tropical disease caused by exposure of bare feet to irritant alkaline clay soils. This causes an asymmetrical swelling of the feet and lower limbs due to lymphoedema. Podoconiosis has a curable pre-elephantiasic phase. However, once elephantiasis is established, podoconiosis persists and may cause lifelong disability. The disease is associated with living in low-income countries in the tropics in regions with high altitude and high seasonal rainfall. It is found in areas of tropical Africa, Central and South America and north-west India. In endemic areas, podoconiosis is a considerable public health problem. Social stigmatisation of patients is widespread and economic losses are enormous since it mainly affects the most productive people, sustaining the disease-poverty-disease cycle. Podoconiosis is unique in being an entirely preventable, non-communicable tropical disease with the potential for eradication. Low-cost preventive measures are a simple but effective solution. However, so far it has received little attention from health care policy makers and, until recently, research into the disease has been scarce and the pathogenesis and genetic basis are partly unclear. A better understanding of these aspects may lead to new prevention and treatment opportunities. In the past few years, several projects fighting podoconiosis have been started by non-governmental organisations. In February 2011, the World Health Organisation designated podoconiosis as one of the 20 neglected tropical diseases, marking an important step in the fight against the disease.

KEYWORDS

Elephantiasis, mossy foot disease, neglected tropical disease, non-filarial elephantiasis, podoconiosis

INTRODUCTION

Podoconiosis is a tropical disease characterised by an asymmetrical swelling of the feet and lower limbs due to lymphoedema. This swelling is called 'elephantiasis'. Although the most common cause of elephantiasis in the tropics is infection with filarial worms (*box 1*),

Box 1. Lymphatic filariasis

Lymphatic filariasis is a tropical disease caused by roundworms (nematodes). Three species of these worms are known to cause filariasis, of which the most important is *Wucheria bancrofti*. It is endemic in countries in the tropics and 1.39 billion people live in areas of risk. Approximately 40 million people have stigmatising and disabling clinical manifestations of the infection, of whom 15 million have elephantiasis.[20] More than 60% of those affected live in South-East Asia and over 30% live in Africa.

It is a communicable disease transmitted by many different mosquito vectors, including *Anopheles*, *Culex* and *Mansonia* species. Humans are definitive hosts. The transmission cycle begins with a bite of a mosquito which is infected with larvae. The larvae enter the body and mature into adult threadlike worms that inhabit the lymphatic vessels of the groin and scrotum or sometimes those of the arm. They produce thousands of microfilariae daily that circulate in the blood. Once a mosquito bites an infected person, the cycle begins again. Although many infections are asymptomatic, some patients suffer acute or chronic illness, including lymphoedema or elephantiasis. Various antihelminthic agents are effective, such as diethylcarbamazine (DEC), albendazole and ivermectin.[21]

In 2000, the WHO launched the 'Global Programme to Eliminate Lymphatic Filariasis'. Since then, considerable progress has been made, eliminating the disease in China (2007) and Korea (2008).

Figure 1. *Podoconiosis is also called 'mossy foot disease'*

Photo's: J. van der Zee (Expertise Centre Lymphology, Drachten, the Netherlands), with permission.

podoconiosis occurs in the absence of parasitic infection and is therefore also known as 'endemic non-filarial elephantiasis'. Podoconiosis (from the Greek word for foot: *podos*, and dust: *konos*) is unique in being an entirely preventable non-communicable tropical disease. In local communities, it is often called 'mossy foot disease', because the skin becomes rough and bumpy and its appearance resembles moss (*figure 1*). In February 2011, the World Health Organisation designated podoconiosis as one of the 20 neglected tropical diseases (*table 1*). Despite being widespread, so far research into the disease has been scarce and the pathogenesis is partly unclear.[1] In the 1980s Ernest Price, a British surgeon, discovered that podoconiosis is caused by an abnormal inflammatory reaction to persistent contact with irritant soils, especially red clays derived from alkaline volcanic rock.[2] The disease is associated with living and walking barefoot in low-income countries in the tropics in regions located higher than 1000 m (3300 ft) above sea level with an annual rainfall of more than 1000 mm, the climatic factors necessary for producing these irritant soils.[1] Mineral particles from these soils penetrate through the skin of the foot and are phagocytised by macrophages in the lymphatic vessels.[2,3] Here, they induce an inflammatory reaction leading to fibrosis and blockage of the vessel lumen, causing lymphoedema. However, the pathogenic events through which the particles provoke inflammation are unclear and only a minority of the people exposed to the irritant soils develop clinical symptoms. Evidence for a genetic basis of podoconiosis is emerging. There is familial clustering of the disease and the heritability is estimated to be 63%.[4] Siblings of patients have a five times higher risk of developing podoconiosis than people in general. A recent study, using a genome-wide approach, found an association of podoconiosis with genetic variants in the HLA class II loci, suggesting that it may be a T-cell-mediated inflammatory disease.[5] However, other genes involved have not yet been identified[4] and there has not been any research into the possible role of co-factors contributing to podoconiosis, such as chronic infection or micronutrient deficiencies.[1]

Table 1. *WHO neglected tropical diseases*

Buruli ulcer
Chagas diseases (American Trypanosomiasis)
Cysticericosis
Dengue
Dracunculiasis (Guinea-worm disease)
Echinococcosis
Fascioliasis
Human African trypanosomiasis
Leishmaniasis
Leprosy
Lymphatic filariasis (elephantiasis)
Onchocerciasis
Rabies
Schistosomiasis
Soil transmitted helminths
Trachoma
Yaws
Podoconiosis
Snakebite
Strongyloidiasis

More than one billion people are affected by one or more of the 20 neglected tropical diseases identified by the World Health Organisation. These diseases are neglected because they have been largely eliminated elsewhere and are often forgotten in wealthier places. Further information: http://www.who.int/neglected_diseases/.

PREVALENCE

It is estimated that 4 million people are affected by podoconiosis worldwide,[5] and 5 to 10% of the population in endemic areas where the use of footwear is uncommon.[6] In these areas, it can be even more prevalent than HIV/AIDS, tuberculosis or malaria. It is found in highland areas of tropical Africa, Central and South America and north-west

India. High prevalence has been documented in Ethiopia, Tanzania, Kenya, Uganda, Rwanda, Burundi, Sudan, Cameroon and Equatorial Guinea.[7] In these countries, podoconiosis is a considerable public health problem. The total number of cases seems to be highest in Ethiopia. Here, 11 million people, which is 18% of the population, are at risk through exposure to the irritant soils and estimates suggest that between 500,000 and 1 million people are affected countrywide.[6] Podoconiosis has been present in Ethiopia for centuries but has so far received little attention from health care policy makers, either because it is not an immediate threat to life, or because of a lack of information on the socioeconomic impact of the problem.[8] Men and women are usually equally affected. In the past, podoconiosis was also common in North Africa and European countries such as France, Ireland and Scotland.[9] However, the disease disappeared in these areas when the usage of footwear became standard.

CLINICAL FEATURES AND DIAGNOSIS

Early symptoms of podoconiosis include itching of the skin of the forefoot and recurrent episodes of burning and oedema of the foot or lower leg, especially after periods of intense physical activity.[10] As lymphatic vessel obstruction progresses, established lymphoedema sets in and elephantiasis occurs. This can clinically vary from soft subdermal lymphoedema to hard or leathery leg elephantiasis, consisting of fibrosis of the skin and subcutis which becomes remarkably thickened.[10] Over the years, the increase in the diameter of the leg persists and can progress to severe elephantiasis. The skin often shows hyperkeratosis, moss-like papillomas, and hard nodules.[11] Podoconiosis has a curable pre-elephantiasic phase. However, once elephantiasis is established, podoconiosis persists.[12]

Podoconiosis must clinically be distinguished from filarial and leprotic lymphoedema.[1] In contrast to lymphatic filariasis, podoconiosis is ascending, starting in the foot and progressing to the knee but rarely involving the upper leg or the groin. Furthermore, it is commonly bilateral yet asymmetric and occurs at altitudes higher than 1500 m (5000 ft), which exceeds that at which filarial transmission occurs. Research in a highland endemic area in southern Ethiopia demonstrated that these specific clinical features combined with establishing that a patient has not migrated from a lowland area is a valid way of ruling out filarial disease.[13] If doubt remains, blood tests such as the filariasis *in vitro* immunodiagnostic essay for the detection of *Wucheria bancrofti* antigen can be used to rapidly distinguish podoconiosis from filariasis. In contrast to leprosy lymphoedema, sensation in the toes and foot is maintained, tropic ulcers are absent and there is no hand involvement.[1]

IMPLICATIONS

Podoconiosis has enormous social, psychological and economic implications for affected individuals. Social stigmatisation of people with the disease is widespread and patients are banned from schools, local meetings and churches, and not allowed to marry into unaffected families.[14] Patients going to non-specialist health services often encounter a lack of expertise and prejudicial attitudes among health workers.[6] A study among 275 health professionals in public and private health institutions in southern Ethiopia showed that nearly all held at least one significant misconception about the cause of podoconiosis.[15] Furthermore, around half incorrectly considered podoconiosis to be an infectious disease and were afraid of acquiring podoconiosis while providing care. All of the health professionals held at least one stigmatising attitude towards affected persons.

The stiffness of the skin and the increased diameter of the legs result in severe disability of the patient. Therefore, podoconiosis threatens economic development because it mainly affects the most productive people (16 to 45 years of age),[7] sustaining the disease-poverty-disease cycle. Research has demonstrated a loss of productivity equivalent to 45% of working days per patient annually.[8] This costs a single zone of 1.5 million inhabitants more than US$ 16 million per year, significantly contributing to poverty. The annual economic losses for Ethiopia are estimated to exceed US$ 200 million in lost productivity and medical costs.

PREVENTION AND MANAGEMENT

European history has shown that podoconiosis has the potential for eradication. Theoretically, the disease can be completely prevented by simple and low-cost measures. In endemic areas, the majority of the community hold significant misconceptions about causation, care, treatment and prevention of the disease.[16] Therefore, primary prevention should consist of education on the aetiology and how to avoid prolonged exposure to irritant soils, most importantly by using appropriate and protective footwear, covering floor surfaces and applying skincare. Early stages of podoconiosis are reversible and secondary prevention consists, again, of encouraging shoe wearing and daily foot-washing with soap, water and, if possible, antiseptics in order to prevent bacterial infection. Wound care is important and infections should be treated with antibiotics. Furthermore, compression therapy by bandaging and hosiery is essential to prevent further swelling (*figure 2*). In compliant patients, these measures are able to completely avert progression.[10] The tertiary prevention of podoconiosis is similar to the management

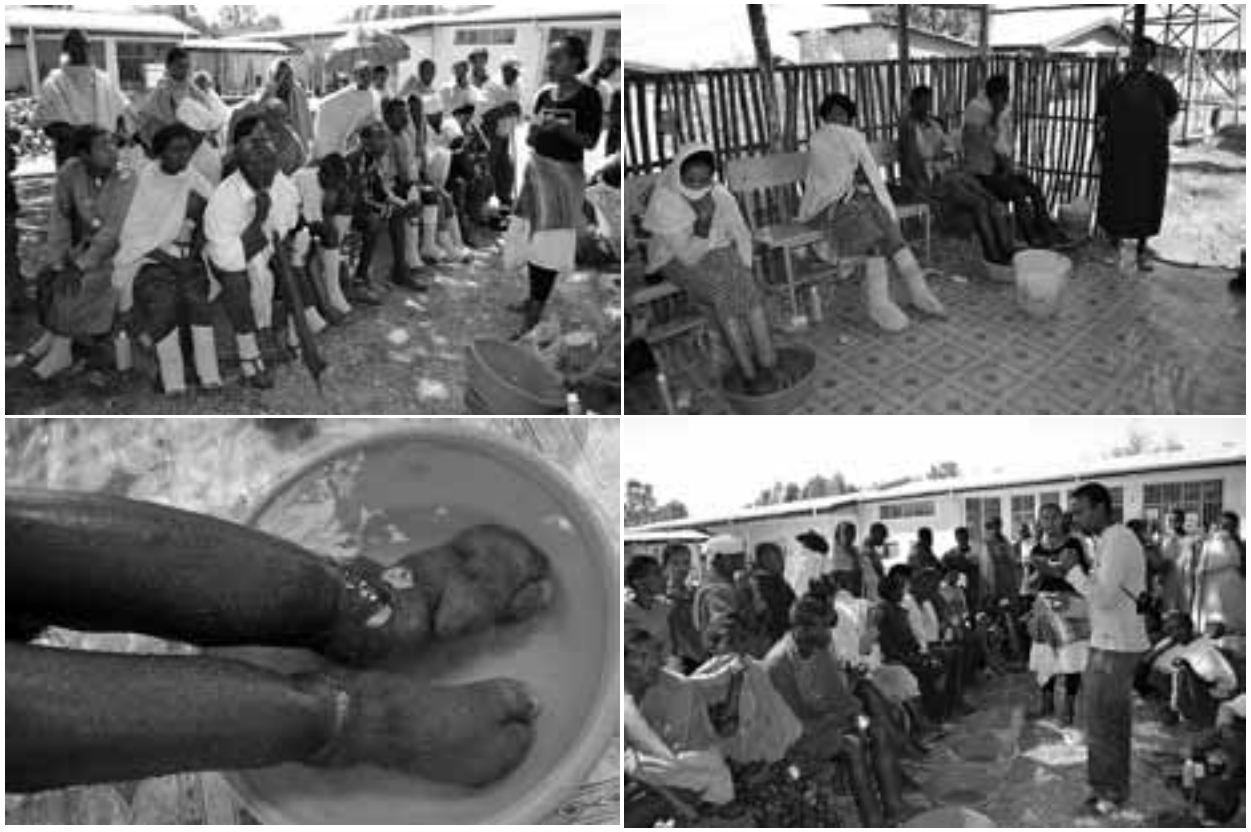
of patients with lymphoedema due to another cause. It is an extension of the secondary preventive measures and also includes elevation of the limb above hip level. This leads to reduction in limb size by improving venous and lymphatic return. A recent study showed that these measures in patients with podoconiosis have a considerable impact both on clinical progression and self-reported quality of life.[17] However, since many patients live far from a treatment centre, educating them on how to apply these measures is a fundamental part of the treatment. Although long-term results of more radical surgery are disappointing, prominent nodules can be removed in selected cases.[1] Most of these treatments seem simple but in the majority of the endemic areas shoes, socks and soap, let alone bandages, antibiotics and surgeons, are unaffordable luxuries.

In the past few years, several projects fighting podoconiosis have been started by non-governmental organisations. For example, in 1997 the 'Mossy Foot Project' was established in Ethiopia. This organisation aims to raise awareness of the disease in the Western World and works towards its treatment and eradication in affected countries. The main strategy of this program consists of prevention, for example by providing shoes and socks. Special oversized shoes are distributed among patients. Furthermore, microfinance initiatives have been created to assist patients to start their own business and become economically independent. The launch of 'Foot*work*', the International Podoconiosis Initiative, in March 2012 marks the next step in the increasing advocacy and awareness of podoconiosis.[18,19] The aims of this organisation include bringing together private and public partners to prevent and treat podoconiosis.

CONCLUSION

In endemic areas, podoconiosis is a considerable public health problem with severe social, psychological and economic implications. Despite being widespread and the lifelong disability it causes in affected individuals, research into the disease has been scarce and the pathogenesis is partly unclear. A better understanding of the pathogenesis might lead to new prevention and treatment opportunities. Low-cost preventive measures, especially raising awareness on the aetiology and prevention of podoconiosis, are a simple but effective solution and therefore must be promoted by health care policy makers. History has shown that podoconiosis has

Figure 2. *Secondary preventive measures include foot-washing and bandaging*



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the potential for eradication. Perhaps the largest challenge for the future will be to fight misconceptions and social stigmatisation in endemic areas.

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