Podoconiosis: non-infectious geochemical elephantiasis

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Summary This article reviews peer-reviewed publications and book chapters on the history, epidemiology, genetics, ecology, pathogenesis, pathology and management of podoconiosis (endemic non-filarial elephantiasis). Podoconiosis is a non-infectious geochemical elephantiasis caused by exposure of bare feet to irritant alkalic clay soils. It is found in at least 10 countries in tropical Africa, Central America and northwest India, where such soils coexist with high altitude, high seasonal rainfall and low income. Podoconiosis develops in men and women working barefoot on irritant soils, with signs becoming apparent in most patients by the third decade of life. Colloid-sized silicate particles appear to enter through the skin, are taken up into macrophages in the lower limb lymphatics and cause endolymphangitis and obliteration of the lymphatic lumen. Genetic studies provide evidence for high heritability of susceptibility to podoconiosis. The economic burden is significant in affected areas dependent on subsistence farming. Podoconiosis is unique in being an entirely preventable non-communicable disease. Primary prevention entails promoting use of footwear in areas of irritant soil; early stages are reversible given good foot hygiene, but late stages result in considerable economic and social difficulties, and require extended periods of elevation and occasionally nodulectomy.

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1. Introduction

Podoconiosis (endemic non-filarial elephantiasis) has been recognized as a specific disease entity for over 1000 years and is widespread in tropical Africa, Central America and north India, yet it remains a neglected and under-researched condition. Manual and electronic literature review identified 19 peer-reviewed research articles with podoconiosis as their main topic published between 1970 and 1990, and only 10 since then.

2. History

From the time of the Roman Empire, travellers recorded anecdotes about people with progressive swelling of the feet. A more detailed reference to 'swollen legs' appears in
the Tibetan translations of a fourth century revelation originally recorded in Sanskrit as the second book of rGyud-bzhi (the ‘four tantras’). However, it was not until c.905 that the Persian physician Rhazes first distinguished elephantiasis ‘of the Greeks’ (lepromatous leprosy) from that ‘of the Arabs’ (most probably non-filarial elephantiasis) (Price, 1984a).

In the 1770s, the adventurer James Bruce gave a graphic description of the elephantiasis he saw in Gondar, northern Ethiopia:

‘The chief seat of this disease is from the bending of the knee downwards to the ankle; the leg is swelled to a great degree, becoming one size from bottom to top, and gathered into circular wrinkles…from between these circular divisions a great quantity of lymph constantly oozes. It should seem that the black colour of the skin, the thickness of the leg, its shapeless form and the rough tubercles or excrescences, very like those seen upon the elephant, gave the name to this disease…’

Bruce obtained permission from the emperor, Ras Mikhail, to treat a sufferer, using a range of regimes and medications, but beyond assuaging the patient’s thirst with a constant supply of whey, no treatment (including hemlock, mercury and tar-water) appeared effective (Pankhurst, 1990). Through the eighteenth and nineteenth centuries, the pathogenesis of elephantiasis was gradually elucidated through Hendy’s study of the lymphatic system in affected people. Wucherer (in Brazil), Lewis (in India), Manson and Bancroft all recognized the role of filarial parasites in elephantiasis, and for a time it was concluded that all elephantiasis was filarial. Towards the end of the nineteenth century, the discrepancy between distribution of elephantiasis and distribution of filaria in North Africa, Central America and Europe prompted revision of this theory. For a time, streptococci were considered to be causative agents, but detailed description of patients in Guatemala (and persistently negative tests for filaria and streptococci) led Robles to infer that the elephantiasis he was seeing was an endemic condition closely associated with walking barefoot (Price, 1984a).

Progress in recognizing the international distribution of non-filarial elephantiasis came as Cohen suggested the use of the term ‘idiopathic lymphoedema’ in place of the local terms ‘verrucosis lymphatica’ in Kenya and ‘mossy foot’ in Ethiopia (Cohen, 1960). The work of Oomen in the 1960s and Price in the 1970s was notable for distinguishing and concentrating on non-filarial elephantiasis. Price extended Oomen’s epidemiological studies (Price, 1973, 1974a), and described the aetiology (Price, 1974b), pathology (Price, 1977; Price and Henderson, 1978), and natural history (Price, 1983) of non-filarial elephantiasis in Ethiopia, establishing the term podoconiosis (from the Greek for foot: podos, and dust: konos) (Price, 1988), which has gained widespread acceptance.

3. Geographical distribution

Podoconiosis is found in highland areas of tropical Africa, Central America and northwest India. Areas of high prevalence have been documented in Uganda (Onapa et al., 2001), Tanzania (de Lalla et al., 1988), Kenya (Crivelli, 1986), Rwanda, Burundi, Sudan and Ethiopia (Price and Bailey, 1984), and in Equatorial Guinea (Corachan et al., 1988), Cameroon, the islands of Bioko, Sao Tome & Principe (Rui et al., 1994) and the Cape Verde islands, that is, approximately, between latitudes 15° N and 15° S.

The condition has been reported in the Central American highlands in Mexico and Guatemala south to Ecuador and Brazil in South America (Price, 1990; Tada and Marsden, 1993). Further east, on the north coast of South America in Suriname and French Guiana, the distinction between filarial and non-filarial elephantiasis has not been confirmed. Although filarial elephantiasis predominates in India, podoconiosis has been reported from northwest India, Sri Lanka and Indonesia. In the past, podoconiosis was common in North Africa (Algeria, Tunisia, Morocco and the Canary Islands) and Europe (France, Ireland and Scotland), but is longer found in these areas (Price, 1990), since use of footwear has become standard.

Prevalence estimates have been made exclusively in Ethiopia, where podoconiosis is present over approximately one-fifth of the land surface of Ethiopia. Early estimations of prevalence using counts of attendees at fifty-six markets ranged from 0.42 to 3.73% (Oomen, 1969), and further investigation in Wollamo zone, southern Ethiopia demonstrated prevalence of 5.38% across five markets. In the village of Ocholo, located at 2000 m altitude in the mountains west of Lake Abaya, southern Ethiopia, elephantiasis was present in 5.1% of long-term residents (Mengistu et al., 1987), while in two resettlement schemes in ilubabor, western Ethiopia, 9.1% of long-term residents were affected, and 5.2% of people resettled some 7–8 years previously (Kloos et al., 1992). More recent population-based surveys in northwest (Birrie et al., 1997) and southern Ethiopia (Desta et al., 2003), have documented prevalence of 6% and 5.4%, respectively.

4. Age, gender and occupation

Early reports based on clinic attendees cannot be relied upon to derive an accurate sex ratio. Price found a male:female ratio of 1:1.4 in market studies, which he attributed to greater use of footwear by men (Price, 1974b). Genene Mengistu et al. (1987) documented a male:female ratio of 1:4.2 in a survey in Ocholo, but many men were absent from the community at the time. By contrast, Kloos et al. (1992) noted higher prevalence among men in three of four resettlement communities in keffa Region. In a single village in Pawe, Birrie et al. (1992) found a male:female ratio of 1:1.4 among sufferers. The most recent community-based study recorded a gender ratio among podoconiosis sufferers (1:0.98, Table 1) that was not significantly different from the zonal gender ratio (1:1.02) (Desta et al., 2003).

All of the major community-based studies have shown onset in the first or second decade and a progressive increase in podoconiosis prevalence up to the sixth decade. Development of podoconiosis is closely associated with living and working barefoot on irritant soils. Farmers are at high risk, but the risk extends to any occupation with prolonged contact with the soil, and the condition has been noted among goldmine workers and weavers who sit at a ground level loom.
5. Genetics

Among many families, exposure to irritant soil is more or less uniform, yet not all family members will develop podoconiosis during their lifetime. Price performed segregation analyses on 80 families with more than one affected child, having adjusted appropriately for increased likelihood of a family with more than one affected individual being included. He calculated the proportion of siblings affected as approximately 0.2, with 95% confidence limits including 0.25, suggesting an autosomal recessive trait (Price, 1972). More recently, 59 multi-generational families were studied, and sibling recurrence risk calculated to be 5.07, and heritability 0.629. Segregation analysis showed the most parsimonious model to be that of an autosomal co-dominant major gene (Davey et al., 2007).

6. Geology and climate

An association between podoconiosis and exposure to the local soil was suspected by Robles at the end of the nineteenth century. However, it was not until Price superimposed maps of disease occurrence onto geological surveys that persuasive evidence of a link with red clays, rich in alkali metals like sodium and potassium and associated with volcanic activity, was provided (Price, 1976; Price and Bailey, 1984). The climatic factors necessary for producing irritant clays include high altitude (over 1000 m above sea level) and seasonal rainfall (over 1000 mm annually). These conditions contribute to the steady disintegration of lava and the reconstitution of the mineral components into silicate clays, colloid-sized particles of which have been demonstrated in the lower limb lymph node macrophages of those living barefoot on these clays (Price and Henderson, 1978). More recent comparison of soil from an endemic area with that from outside the area revealed high levels of beryllium and zirconium (both known to induce granuloma) (Frommel et al., 1993), but the role of these elements is not yet established.

7. Population movement

Studies among populations forcibly resettled during the Ethiopian military regime (1974—1991) give useful insights into the period of exposure to irritant soils necessary to provoke disease. People resettled from north Wollo and Tigray (where podoconiosis is rare) to Illubabor in 1984/5 were surveyed in 1990, and 5% found to have podoconiosis (Kloos et al., 1992). Likewise, of those people resettled from east Gojjam to the Tana Beles Project area around Pawe in 1984, almost all podoconiosis sufferers in 1996 reported development of the condition after moving to the area (Birrie et al., 1997).

8. Economic consequences

A comparative cross-sectional study was performed in 2005 to calculate the economic burden in a zone endemic for podoconiosis. Total productivity loss for a patient amounted to 45% of total working days per year, and in a zone of 1.5 million people, the total overall annual cost of podoconiosis was calculated to exceed US$ 16 million per year (Tekola et al., 2006).

9. Social stigma and access to health care

Social stigma against people with podoconiosis is rife, patients being excluded from school, denied participation in local meetings, churches and mosques, and barred from marriage with unaffected individuals (GebreHanna, 2005). Price (1974a) reports one podoconiosis sufferer as having remarked that 'it would be better to have leprosy', since stigma surrounding leprosy has diminished as a consequence of effective medicine and health care services. The belief that there is no effective medical treatment may act as a barrier to accessing health care. Recent evidence from the Mossy Foot Prevention and Treatment Association, a local non-government organization managing 30 000 patients in southern Ethiopia, suggests that sufferers attempting to access non-specialist health services encounter lack of expertise and prejudicial attitudes among health workers (Desta et al., 2003).

10. Pathogenesis

The pathogenesis of podoconiosis is not yet fully elucidated. At present, most evidence suggests an important role for mineral particles on a background of genetic susceptibility, but the possible role of other cofactors (for example chronic infection or micronutrient deficiencies) has not been explored. Colloid-sized particles of elements common in irritant clays (aluminium, silicon, magnesium and iron) are absorbed through the foot and have been demonstrated in the lower limb lymph node macrophages of those living barefoot on the clays (Price and Henderson, 1978). Electron microscopy shows local macrophage phagosomes to contain particles of stacked kaolinite (Al_{2}Si_{2}O_{5}(OH)_{4}), while light microscopy shows subendothelial oedema and subsequent collagenization of afferent lymphatics reducing and finally obliterating the lumen (Price, 1977). Experiments have shown that silica suspension injected into rabbit lymphatics can provoke similar intense macrophage proliferation followed by lymphatic fibrosis and blockage (Fyfe and Price, 1985).
11. Pathology

The pathology and natural history are well described in a range of articles (Cohen, 1960; Price, 1983, 1984b). Podoconiosis is characterized by a prodromal phase before elephantiasis sets in. Early symptoms commonly include itching of the skin of the forefoot and a burning sensation in the foot and lower leg. Early changes that may be observed are splaying of the forefoot, plantar oedema with lymph ooze, increased skin markings, hyperkeratosis with the formation of moss-like papillomata, and ‘block’ (rigid) toes. Later, the swelling may be one of two types: soft and fluid (‘water-bag’ type, Figure 1); or hard and fibrotic (‘leathery’ type, Figure 2), often associated with multiple hard skin nodules (Price, 1990). Very long-standing disease is associated with fusion of the interdigital spaces and ankylosis of the interphalangeal or ankle joints (Figure 3). Acute episodes occur in which the patients is pyrexial and the limb warm and painful. These episodes appear to be related to progression to the hard, fibrotic leg.

12. Differential diagnosis

The two conditions podoconiosis must most often be distinguished from are filarial and leprosy lymphoedema. Clinical features of podoconiosis that help distinguish it from filarial elephantiasis include the foot being the site of first symptoms (rather than elsewhere in the leg) and bilateral but asymmetric swelling usually confined to the lower leg (compared to the predominantly unilateral swelling extending above the knee in filariasis). Groin involvement in podoconiosis is extremely rare. A recent study using both midnight thick film examination and BinaxTM antigen cards has confirmed that in a podoconiosis-endemic area, community workers’ diagnoses are highly predictive of podoconiosis (Desta et al., 2007). Podoconiosis may be distinguished from leprosy lymphoedema by the preservation of sensation in the toes and forefoot, the lack of trophic ulcers, thickened nerves or hand involvement.

13. Prevention and management

Evidence suggests that primary prevention should consist of avoidance of prolonged contact between the skin and irritant soils. This may be achieved by use of robust footwear or covering of floor surfaces in areas of irritant soil. The Mossy Foot Prevention and Treatment Association trains treated patients to make low-cost durable leather boots and shoes for their communities in an attempt at primary prevention. In Kenya, sandals are made from old car tyres with a similar aim. However, footwear remains an unaffordable luxury for residents of most affected areas in the tropics.

Secondary prevention (prevention of the progression of early symptoms and signs to overt elephantiasis) takes the form of training in foot hygiene (washing daily with soap and water, using antiseptics and emollients), and use of socks and shoes. Compression bandaging is effective in reducing the size of the soft type of swelling. Progression can be completely averted if these measures are strictly adhered to, but compliance must be life-long. Relocation from an area of irritant soil (Price, 1983) or adoption of a non-agricultural
Tertiary prevention (the management of those with advanced elephantiasis) encompasses secondary prevention measures, elevation and compression of the affected leg, and, in selected cases, removal of prominent nodules. For elevation to be successful, at least 18 hours with the legs at or above the level of the heart are needed each day. Where electricity is available, intermittent compression machines may reduce swelling rapidly, but twice-daily application of elastic bandages is also effective (Price, 1975). The aim of elevation and compression is to reduce the swelling of the leg so that tall compression footwear can be worn, or nodulectomy undertaken. Previously, Charles’ operation (removal of skin, subcutaneous tissue and deep fascia to lay the muscles and tendons bare, followed by grafting of healthy skin), or a variant, was used (Cohen, 1960; Price, 1990), but long-term results are disappointing. Follow-up of patients suggests that those unable to scrupulously avoid contact with soil experience recurrent swelling which is more painful than the original disease because of scarring. Social rehabilitation is vital, and includes training treated patients in skills that enable them to generate income without contact with irritant soil. Successful training in shoemaking, bicycle repair, hairdressing and beauty care, electronics and carpentry has been given to several hundred treated patients by the Mossy Foot Association in southern Ethiopia.

14. Future directions

There are still many unresolved questions surrounding the pathogenesis of podoconiosis, in particular the pathways through which inorganic particles provoke inflammation and obliteration of the lymphatic lumen, and the roles of cofactors such as micronutrient deficiencies or chronic infections in these processes. Currently, a study investigating the role of oxidative stress in podoconiosis is underway, as is a linkage analysis using affected sibling pairs.

In terms of patient care, a clinical staging system, adapted from that developed for management of filarial lymphoedema (Dreyer et al., 2002), is being validated and tested for inter-observer agreement and test-retest repeatability. It is anticipated that this will enable clinicians to assess medical and surgical treatment, and researchers to document the effects of public health preventive interventions. Quality of life in new and treated patients is being assessed using the Cardiff Dermatological Life Quality Index (Findlay and Khan, 1994).

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