INVITED REVIEW

TUNGIASIS

Jorg HEUKELBACH (1)

SUMMARY

Tungiasis is a neglected parasitic skin disease caused by the permanent penetration of the female sand flea (also called jigger flea) *Tunga penetrans* into the skin of its host. After penetration, most commonly on the feet, the flea undergoes an impressive hypertrophy, and some days later the abdominal segments of the flea have enlarged up to the size of about 1 cm. The flea infestation is associated with poverty and occurs in many resource-poor communities in the Caribbean, South America and Africa. In this review, a historical overview on tungiasis is given. The natural history, pathology, epidemiology, diagnosis, therapy and control of the parasitic skin disease are discussed. It is concluded that tungiasis is an important parasitosis causing considerable morbidity in affected populations. Future studies are needed to increase the knowledge on the biology, pathophysiology, epidemiology, therapy and control of the ectoparasite.

KEYWORDS: Tungiasis; *Tunga penetrans*; Sand flea; Jigger flea.

INTRODUCTION

Tungiasis is a neglected parasitic skin disease caused by the permanent penetration of the female sand flea or jigger flea *Tunga penetrans* into the skin. After penetration, which most commonly takes place on the feet, the flea undergoes an impressing hypertrophy, and some days later the abdominal segments of the flea have enlarged up to the size of about 1 cm. The flea infestation is associated with poverty and occurs in many resource-poor communities in the Caribbean, South America and Africa. In Brazil, tungiasis is called popularly *bicho de pé*, *pulga de bicho* or *pulga de porco*.

HISTORICAL OVERVIEW

Interestingly, *T. penetrans* is one of the few parasites which have spread from the western to the eastern hemisphere. The sand flea has been introduced several times in the 17th, 18th and 19th century to West Africa as a result of the slave trade; however, the flea did not spread over the continent and disappeared after some time (JEFFREYS, 1952; JANSELME, 1908; HENNING, 1904). Finally, *T. penetrans* came to Africa with ballast sand carried by a ship that left from Brazil to Angola in 1872 (HOEPPLI, 1963; HESSE, 1899). Within a few years, the parasite spread from Angola along trading routes and with soldiers in the entire sub-Saharan Africa (HEUKELBACH et al., 2001; HENNING, 1904; HESSE, 1899; GORDON, 1941). In the 19th century travellers to South America, Africa and the Caribbean reported about native communities suffering from severe jigger infestation, eventually leading them to abandon entire villages (HOEPPLI, 1963; HEUKELBACH et al., 2001; BRUCE et al., 1942). They already noted the intense inflammation leading to suppuration, ulcer and gangrene; difficulties in walking were commonly reported (WATERTON, 1973; COTES, 1899; KONCZAKI, 1985; GREY, 1901; HESSE, 1899; BRUCE et al., 1942). The participants of expeditions into Africa at the end of the 19th and the beginning of the 20th century reported natives and also themselves with severe infestation that made many of them almost unable to walk (GREY, 1901; KONCZAKI, 1985). Some military operations in colonial times were prejudiced because the feet of the soldiers were so heavily infested, that they could hardly walk (JOLLY, 1926; GORDON, 1941; HOEPPLI, 1963). At the end of the 19th century
the sand flea had reached East-Africa, Zanzibar and Madagascar (BLANCHARD, 1899; HESSE, 1899). In 1899, returning British troops brought *T. penetrans* to the Indian Subcontinent. However, the parasite never established there (GORDON, 1941; TURKHUD, 1928; SANE & SATOSKAR, 1985; COTES, 1899).

DECLE (1900) reported vividly the problems encountered in the late 19th century caused by tungiasis in Africa: “In this village there was not a man, woman or child who was not covered with ulcers”. He continues: “I found the people starving, as they were so rotten with ulcers from jiggers that they had been unable to work in their fields, and could not even go to cut the few bananas that had been growing.” These and other observations made him conclude: “My experience makes me look upon jigger as the greatest curse that has ever afflicted Africa”. Clearly, today the situation is not as dramatic as described in this historical text. However, the historical reports demonstrate the pathology that severe tungiasis can cause. Even today, in resource-poor communities, infestation with individuals harboring hundreds of fleas occurs and severe pathology is common (HEUKELBACH *et al.*, 2001; FELDMEIER *et al.*, 2003).

**NATURAL HISTORY AND CLINICAL PATHOLOGY**

*Tunga penetrans* is the smallest flea species known with only 1 mm of size (Fig. 1). Both males and females are blood-feeding (WITT *et al.*, 2004), but eventually the female sand fleas penetrate permanently into the skin of its hosts and undergoes an important hypertrophy, expelling hundreds of eggs during a period of two to three weeks (EISELE *et al.*, 2003). Already during penetration the hypertrophy of the flea’s abdomen begins, and after some days the abdominal segments reach the size of up to 1 cm (EISELE *et al.*, 2003; GEIGY & HERBIG, 1949). After expulsion of the eggs, the involution of the lesion begins. About three weeks after penetration, the fleas die and eventually are sloughed from the epidermis by skin repair mechanisms (EISELE *et al.*, 2003).

It is important to understand that infestation with *T. penetrans* is a dynamic process with lesions altering their morphological aspect continuously. The natural history of tungiasis has been divided into five stages, the so-called Fortaleza Classification (EISELE *et al.*, 2003). In stage I the flea is in *statu penetrandi* (30 min to several hours), and a reddish spot of about 1 mm appears. In stage II the hypertrophy begins and the parasite becomes more obvious as a growing whitish or mother-of-pearl-like nodule (one to two days after penetration). In the protruding rear cone of the flea, the anal-genital opening appears as a central black dot. The lesion is surrounded by an erythema. In stage III the hypertrophy is maximal and becomes macroscopically visible: two days to three weeks after penetration (Fig. 2). A round, watch-glass-like patch appears which is frequently accompanied by hyperkeratosis and desquamation of the surrounding skin. Expulsion of eggs and faeces are typical in this stage (Fig. 3). The lesions are usually painful and
produce the sensation of foreign bodies expanding under the skin. In stage IV a black crust covers an involuted lesion with a dead parasite (three to five weeks after penetration). A residual scar in the stratum corneum is characteristic for stage V (six weeks to several months after penetration). The usual sequence of development of the neosome, involution of the lesion and stage V formation may be changed by superinfection and manipulation of the lesion by the patient or a carer.

Typically, *T. penetrans* affects the periungual area of the toes, the heels and the soles. However, embedded sand fleas can be found on almost every part of the body, such as the hands, elbows, neck, buttocks and the genital region (Fig. 4) (HEUKELBACH et al., 2002b; HEUKELBACH et al., 2004d; BEZERRA, 1994; VERALDI et al., 1996). If several lesions occur simultaneously they are usually located in clusters. Severe infestations with hundreds of embedded sand fleas are not rare. In single cases lesions may take the aspect of a tumourous growth and in histological sections appear as pseudoepitheliomatous hyperplasia (HEUKELBACH et al., 2004d).

Although tungiasis is a self-limited infestation, complications are common in the endemic area (FELDMEIER et al., 2003; HEUKELBACH et al., 2001). Many patients report severe pain, and inflammation and fissures commonly hinders individuals from walking normally (FELDMEIER et al., 2004). Sequels include deformation and loss of toenails, as well as deformation of digits (Fig. 5). The sore in the skin caused by the protruding rear end of the flea is an entry point for pathogenic microorganisms (FELDMEIER et al., 2002). Superinfected lesions lead to formation of pustules, suppuration and ulcers. *Staphylococcus aureus* and streptococci most frequently occur, but other aerobic and anaerobic bacteria (including clostridia) are also found (FELDMEIER et al., 2002). In non-vaccinated individuals tungiasis may lead to tetanus (OBENGUI, 1989; TONGE, 1989; LITVOC et al., 1991; GRECO et al., 2001; SORIA & CAPRI, 1953).

**DIAGNOSIS**

The diagnosis of tungiasis is made clinically (HEUKELBACH et al., 2001). Even the untrained physician can diagnose the ectoparasitosis taking into account the typical topographic localisations and the natural history of the disease. The patient typically complains about local itching, pain and the sensation of a foreign body. Patients commonly report having walked in infested places such as beaches and farms.

Most lesions occur on the nail rim. Eggs being expelled or eggs attached to the skin and the release of brownish threads of faeces are pathognomonic signs (Fig. 3 and 5). Faeces threads are of a helical structure and often spread into the dermal papillae. A biopsy of the lesion and histopathological examination is not indicated. However, histological sections are often done to confirm the diagnosis in European and North American travellers after their return from the endemic area (FRANCK et al., 2003; SMITH & PROCP, 2002). The sections usually demonstrate the presence of the parasite, eggs or chitinous fragments (FRANCK et al., 2003; FIMIANI et al., 1990; DOUGLAS-JONES et al., 1995; BURKE et al., 1991; REISS, 1966; POPPITI Jr. et al., 1983; MACIAS & SASHIDA, 2000; SMITH & PROCP, 2002). In single cases of atypical tungiasis, a biopsy may be indicated, for example lesions with a pseudoepitheliomatous appearance at ectopic sites (HEUKELBACH et al., 2004d).

Differential diagnoses include verrucae, myiasis, pyogenic infection/abscess, foreign bodies, acute paronychia, cutaneous larva migrans, dermoid cysts, dracontiasis, melanoma, deep mycosis and bites or stings of other injurious arthropods (FRANCK et al., 2003; HEUKELBACH et al., 2001; WARDHAUGH & NORRIS, 1994; GOLOUH & SPILER, 2000; SANUSI et al., 1989).

**TREATMENT AND PREVENTION**

The standard treatment is surgical extraction of the flea under sterile conditions (HEUKELBACH et al., 2001). Fleas should be extracted as
early as possible to avoid secondary infections. However, this is not an easy task, as it requires a skilled hand and good eye-sight. The opening in the epidermis should be carefully widened with an appropriate instrument such as a sterile needle to enable the extraction of the entire flea. If the flea is torn during extraction or if parts are left in the sore, severe inflammation is the rule. After extraction the sore should be treated with a topical antibiotic. In resource-poor settings, strict hygiene is often not applied and appropriate instruments are unavailable with the consequence that attempts removing the fleas often do more harm than good (FELDMEIER et al., 2003). Tetanus immune status has to be checked, and in case of inappropriate immunization, prophylaxis is indicated.

Daily inspection of the feet and immediate extraction of embedded fleas protect against complications. Closed shoes and socks seem to prevent tungiasis to a certain degree although complete protection cannot be achieved by these means.

At this moment, there is no drug on the market with satisfactory clinical efficacy. A randomized controlled trial realized more than 20 years ago showed a good efficacy of oral niridazole, an anti-schistosomal compound with severe adverse events which has been taken from the market since long (ADE-SERRANO et al., 1982). In the cited study, the therapeutic efficacy of niridazole was claimed to be very good. However, the outcome measures were not well defined and the study showed other methodological problems which limit the interpretation of results. In northeast Brazil many dermatologists claim a good efficacy of ivermectin in tungiasis and support their notion by anecdotal observations. In fact, a case report suggests oral ivermectin given at a single dose (200 µg/kg body weight) to be effective against embedded sand fleas (SARACENO et al., 1999). Additionally, there are several anecdotal reports of health care providers about the efficacy of oral ivermectin for the treatment of tungiasis (HEUKELBACH et al., 2004c). However, a recently conducted randomized controlled trial with oral ivermectin at a relatively high dose (2x300 µg/kg body weight) did not show any efficacy as compared to placebo (HEUKELBACH et al., 2004c). Another trial reported some efficacy of topical ivermectin, metrifonate and thiabendazole as compared to a topical placebo lotion and a control group without treatment (HEUKELBACH et al., 2003b). Other authors suggested oral thiabendazole as an effective drug against embedded sand fleas, but controlled studies are unavailable (CARDOSO, 1981; VALENÇA et al., 1972).

Recently, a case series using a natural repellent based on coconut oil showed an impressive regression of clinical pathology in severely infested patients by prevention of re-infestation (SCHWALFENBERG et al., 2004). The twice-daily application of this plant-based repellent reduced the infestation rate in an area with extremely high transmission rates by almost 90% (FELDMEIER et al., submitted 2005). In endemic communities the use of an effective repellent would probably be a better approach to reduce tungiasis-associated morbidity than treatment after infestation.

**Epidemiology and control**

Tungiasis occurs on the American continent from Mexico to northern Argentina, on several Caribbean islands, as well as throughout sub-Saharan Africa (HEUKELBACH et al., 2001; FRANCK et al., 2003). Single cases are reported from India and southern Italy (SANE & SATOSKAR, 1985; VERALDI et al., 2000). The ectoparasitosis occurs in underdeveloped communities in the rural hinterland, in fishing villages along the coast and in the slums of urban centres. Similar to many other parasitic diseases, the occurrence of severe tungiasis is linked to poverty (HEUKELBACH et al., 2004a; HEUKELBACH et al., 2002a). A study assessing risk factors for heavy infestation in a fishing community in Brazil indicated that poor housing is the most important independent factor (MUEHLEN et al., 2005).

In poor communities in Brazil, Trinidad and Nigeria, prevalences ranged between 16% and 54% (ADE-SERRANO & EJEZIE, 1981; CHADEE, 1998; MUEHLEN et al., 2003; WILCZEK et al., 2002; CARVALHO et al., 2003; CHADEE, 1994; CHADEE et al., 1991; NTE & EKE, 1995; EJEZIE, 1981). Prevalence and parasite burden are correlated, and commonly individuals harbour dozens - even hundreds - of fleas (Fig. 6) (FELDMEIER et al., 2003). The disease is associated with the presence of sandy soils, but may also be found in banana plantations and in the tropical forest. In Brazil, tungiasis occurs throughout the country, from Yanomami populations in the Roraima State in the far north to rural areas in Rio Grande do Sul State in the far South. Several historical and anecdotal reports indicated a higher incidence of tungiasis in the dry season (COTES, 1899; ATUNRASE et al., 1952; SILVADO, 1908). In fact, there is a clear seasonal variation of infestation with only few cases occurring during the rainy season and a high incidence and consequently prevalence during the dry season (HEUKELBACH et al., 2005).

**Fig. 6** - Commonly seen in resource-poor communities in endemic areas: the feet of a 10-year-old girl with dozens of penetrated sand fleas.

The animal reservoir plays an important role for transmission dynamics. Domestic animals such as dogs (RIETSCHEL, 1989; HEUKELBACH et al., 2004b; FRANCO DA SILVA et al., 2001b), cats (HEUKELBACH et al., 2004b) and pigs (COOPER, 1967; COOPER, 1976; VERHULST, 1976), but also rats are important reservoirs (HEUKELBACH et al., 2004b). In a slum in Fortaleza (Northeast Brazil), 67% of dogs, 50% of cats and 59% of captured rats were found infested (HEUKELBACH et al., 2004b). In the rural area, pigs and cattle are known reservoirs for *T. penetrans* (VERHULST, 1976; FRANCO DA SILVA et al., 2001a; VAZ & ROCHA, 1946), but its importance seems to have diminished in the last years. Tungiasis
has also been observed in a variety of other host animals such as monkeys (HESSE, 1899; FALKENSTEIN, 1877), sheep (WOLFFHÜGEL, 1910), goats (TRENTINI et al., 2000), sylvatic rodents (KARSTEN, 1865), coatis (WOLFFHÜGEL, 1910) and armadillos (DA FONSECA, 1936; FÜLLEBORN, 1908). The clinical picture and natural history in the animal hosts does not differ considerably from human tungiasis.

Due to the presence of a variety of domestic and sylvatic animals possibly serving as reservoirs, control of tungiasis is difficult to achieve (HEUKELBACH et al., 2002a). Additionally, eggs, larvae and pupae of *T. penetrans* may persist in the environment for a prolonged time, and the reduction of the human and animal reservoir would result in rapid re-infection (HEUKELBACH et al., 2002a). Surface spray ing with insecticides has been claimed to be effective, but there is no controlled study to confirm this assumption (MATIAS, 1991), and due to the particular biology of *T. penetrans*, environmental application of insecticides may not be effective. As the flea seems to prefer sandy and shady soil for breeding, floors of houses could be cemented and streets be paved to reduce attack rates (HEUKELBACH et al., 2002a). Improved sanitation and regular waste collection will contribute to reduce incidence and morbidity. These means are clearly very cost-intensive and in many communities not feasible. Health education should focus on secondary prevention, i.e. educating people and the carers of children to inspect daily their feet and take out embedded fleas with an appropriate and sterile instrument (HEUKELBACH et al., 2003a). However, this issue is complicated as many people in the endemic areas consider tungiasis as a nuisance rather than a disease and therefore tend to neglect this ectoparasitosis (HEUKELBACH et al., 2003c).

**CONCLUSION AND FUTURE OUTLOOK**

In the last few years, knowledge on tungiasis has increased considerably. The natural history has been described in detail, several therapy studies have been conducted, and the epidemiology and morbidity in resource poor settings has been described.

However, there are still many issues to be resolved. The biological habit of premature stages of the flea and the susceptibility of these stages to insecticides is still not known. The epidemiology of tungiasis in indigenous populations remains enigmatic. The histopathological mechanisms in the inflammatory reaction of the host after infestation is not understood. Studies have to be performed to assess the efficacy and efficiency of various control measures as well as to analyse health care seeking behaviour of different populations. A new flea species, *Tunga trimamillata*, that also parasitizes man has been described recently from Ecuador (PAMPIGLIONE et al., 2004; FIORAVANTI et al., 2003). The lack of data on epidemiology and pathology of this new ectoparasite species calls for future studies.

Recent studies have shown that *T. penetrans* harbour *Wolbachia* bacteria in large numbers (FISCHER et al., 2002; HEUKELBACH et al., 2004a). It may be assumed that the *Wolbachia* of *T. penetrans* are obligatory symbionts similar to those described from other parasites. The role of *Wolbachia* in the biology of *T. penetrans* and in the pathogenesis of tungiasis is not known, but it is likely that *Wolbachia* endobacteria of sand fleas contribute to the severe inflammation constantly found in tungiasis (HEUKELBACH et al., 2004a). Future studies will have to show whether antigens released from parasites actually contribute to the inflammatory reaction commonly observed in patients with tungiasis. Clearly, the presence of *Wolbachia* in sand fleas offers new perspectives for therapy and control. Using appropriate study designs, it remains imperative to increase further the knowledge on the biology, pathophysiology, epidemiology, therapy and control of the sand flea *T. penetrans*.

**REFERENCES**


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