Filariasis

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Filarial infections are caused by parasitic, tissue-dwelling filarial nematode worms that are transmitted by biting insects. The three main filarial diseases in humans are:

- lymphatic filariasis
- onchocerciasis
- loiasis.

Lymphatic filariasis

The infecting parasite is usually *Wuchereria bancrofti*, though *Brugia malayi* or *B. timori* may be responsible in South East Asia and Indonesia. A wide range of mosquitoes transmit the parasites; *Culex quinquefasciatus* is the major vector.

Adult female worms inhabit lymph nodes and produce sheathed microfilarial larvae that circulate in the peripheral blood (Figure 1). Microfilariae are generally nocturnally periodic (circulating in the blood only at night, with no detectable circulating microfilariae at other times). However, the periodicity of microfilarial circulation varies geographically and may be subperiodic (constantly circulating in blood with peaks at certain times of day or night) or non-periodic (constantly circulating with no peaks).

Epidemiology

More than 1 billion individuals in more than 80 countries are at risk of infection and 120 million are infected, one-third in Africa, one-third in India and others throughout Asia, the Pacific and the Americas. Associated disability occurs in 40 million individuals.

Clinical features

Larvae migrate to lymph nodes and mature into adult worms over about 6 months. During this period, no microfilariae are found in blood, though subclinical disease and lymphatic damage may occur. Adult worms are relatively harmless; major symptoms result from the host's immune response to infection, which varies between individuals. Most patients present with acute attacks of 'filarial fever' up to 15 months after infection; headache and malaise are accompanied by swelling, erythema and aches around lymph vessels and glands, caused by lymphangitis and lymphadenitis. These attacks typically last 3–15 days and are accompanied by high eosinophilia and microfilaraemia. Epididymo-orchitis with scrotal oedema is also common.

Manifestations of chronic infection occur in a minority of individuals, usually after 10–15 years of infection in endemic areas, but within 1–2 years in patients from non-endemic areas. They are probably caused by a combination of obstruction and dilatation of lymphatic vessels by adult worms, and host immune responses. Microfilariae are not detectable in blood at this stage.

- Swelling and growth of thickened skin often leads to secondary bacterial or fungal infection in the affected area.
- Hydrocele occurs in up to 50% of males.
- Blockage of lymph vessels around the bladder occasionally leads to chyluria (lymph causing milky urine, Figure 2).
- Elephantiasis (lymphoedema causing gross enlargement and fibrosis of the limbs, breasts or genitalia) is an irreversible late stage (Figure 3).

The course of brugian filariasis is similar, but elephantiasis usually involves only the limbs.

Hyper-reactive syndromes occur occasionally. The most common is tropical pulmonary eosinophilia, which is seen predominantly in South India and South East Asia, and in individuals from non-endemic regions exposed to short-term, intense transmission. Asthma-like symptoms, including a paroxysmal, severe dry cough and wheezing, predominate. Fever and splenomegaly may occur. These features resolve after about 1 year, with no elephantiasis and only rarely microfilaraemia.

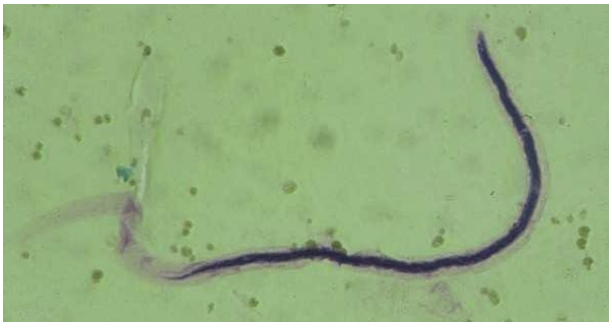
Diagnosis

Acute and chronic manifestations can usually be diagnosed clinically, particularly in endemic areas.

Microfilariae can be detected microscopically in peripheral blood films after passing 20 ml of citrated blood taken between 11 p.m. and 1 a.m. through a polycarbonate filter (20 mm pore size). This method is difficult, because of the periodicity of microfilarial circulation. Provocation can be used in regions where onchocerciasis (see below) does not occur; diethylcarbamazine (DEC), 6 mg/kg, is administered to induce a peak of microfilaraemia 15 minutes later (60 minutes in *B. malayi* infection).

Filarial antigen card testing has recently been developed. This is highly sensitive and specific for *W. bancrofti* circulatory antigen, avoiding the need for collection of blood at night.

Eosinophilia – high eosinophilia occurs in all filarial infections; however, this is of diagnostic use only in patients with tropical pulmonary eosinophilia, who also have very high serum IgE levels (usually more than 10,000 ng/ml) and specific IgG and IgE antifilarial antibodies.



1 *Wuchereria bancrofti* microfilaria in a blood slide.

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2 Chyluria on the left caused by lymphatic filariasis.

Ultrasonography has been used to detect the movement of living adult *W. bancrofti* in lymph nodes ('filaria dance sign'). This is useful for evaluating the efficacy of macrofilaricidal drugs, but is relatively insensitive as a general diagnostic indicator.

Management

In early-stage disease, treatment is ideally undertaken through referral to a specialist tropical medicine unit for diagnosis and management, and is important to prevent lymphatic damage and progression to chronic disease. Treatment with DEC, 6 mg/kg daily for 21 days in *W. bancrofti* infection and 15 days in *Brugia* infection, kills microfilariae and adult worms. To minimize adverse reactions, lower doses can be used initially and increased each day. Hyperreactive syndromes resolve rapidly after treatment with high-dose DEC, 10 mg/kg daily. DEC can cause a severe reaction in patients co-infected with onchocerciasis (see below) and therefore cannot be used on a large scale in most of West Africa.

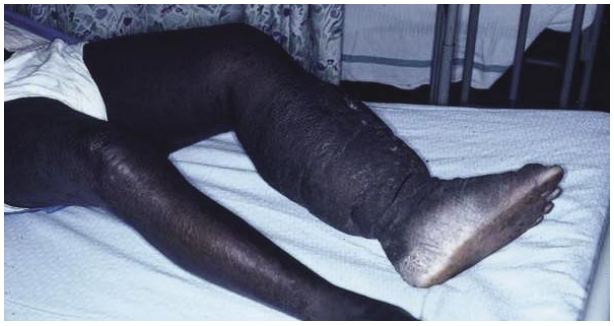
In the later stages of infection, with largely irreversible lymphatic damage and elephantiasis, management focuses on hygiene and prevention of secondary bacterial and fungal infection. Elevation of affected limbs, washing with soap and water, treatment and prevention of secondary infections with topical antifungal drugs and antibiotics, and physiotherapy when possible are important and may partially reduce elephantiasis. Surgery can be considered in some cases.

Control

The long course of DEC treatment required for radical cure is not feasible for control programmes in endemic areas. A Global Alliance to Eliminate Lymphatic Filariasis has been established, aided by public–private partnerships and the provision of free or subsidized drugs by manufacturers. Current strategies focus on annual mass treatment with single-dose combination therapy for 4–6 years (the lifespan of adult worms); in 2003, more than 70 million individuals in 36 countries were treated. DEC-fortified cooking salt has been used in a highly successful control campaign in China.

Single-dose combination therapy aims to kill microfilariae and interrupt transmission. Single doses of albendazole, 400 mg, and DEC, 6 mg/kg, can completely clear microfilariae for up to 1 year. A single dose of ivermectin, 150–200 μg/kg, is useful in West Africa where DEC cannot be used, particularly in combination with albendazole.

Education to reduce the stigma associated with elephantiasis is important to improve the quality of life of affected individuals.



3 Elephantiasis of the left leg caused by chronic lymphatic filariasis.

Onchocerciasis

'River blindness' is caused by *Onchocerca volvulus* and transmitted by day-biting *Simulium* blackflies. The greatest disease burden occurs near fast-flowing rivers, where adult blackflies lay their eggs. Blackflies bite exposed skin only, because their broad mouthparts cannot penetrate clothing.

Larvae take about 1 year to mature into adults and start producing microfilarial larvae. Adult female worms live for 10–15 years and release up to 10,000 microfilariae per day. Heavily infected individuals may carry 50–200 million larvae, 90% of which are in the skin.

Epidemiology

Onchocerciasis occurs mainly in Sub-Saharan Africa, with foci in Central and South America and Yemen; 90 million individuals live in endemic zones, of whom 17 million are infected and 0.5 million blind. There are forest and savannah strains in West Africa; typically, eye disease is more common in those infected with savannah strains.

Clinical features

Infection with adult worms produces non-painful, subcutaneous nodules that are usually less than 2 cm in diameter and situated over bony prominences. The site of nodules varies geographically; in Africa, they are commonly found on the pelvic girdle. Head nodules are more common in children (Figure 4).

Infection is often asymptomatic. The most common symptoms are pruritus and skin disease from immune responses to microfilariae. The main dermatological presentations are itchy, papular dermatitis, dermal atrophy and depigmentation (Figure 5). Hyperreactive skin disease (Sowda) is most common in the Yemen and usually affects a single limb, with no microfilariae or nodules.

Eye disease is the most devastating clinical feature, occurring mainly in individuals with high microfilarial loads. Microfilariae can enter all eye tissues, leading to punctate and sclerosing keratitis, iritis, chorioretinitis, optic atrophy, and eventually blindness. In hyperendemic regions, 5% of the population may be blind, with severe socioeconomic consequences for affected communities.

Diagnosis

Microfilariae – definitive diagnosis is by detection of microfilariae in two to six skin snips (Figure 6). Microfilariae emerge from the skin fragment after 30 minutes' to 24 hours' incubation in saline solution. If skin snips are negative, a Mazzotti provocation test can be performed. After administration of DEC, 50 mg,

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