Cutaneous Filariasis

Filariasis is a parasitic disease caused by thread-like filarial nematodes (roundworms) in the family Filarioidea (also known as ‘filariae’).[1] Of the hundreds of described filarial parasites, only eight species cause natural infections in humans (see separate articles Lymphatic Filariasis and Body Cavity Filariasis).[1] Cutaneous filariasis may be caused by Loa loa (the African eye worm), Onchocerca volvulus and Mansonella streptocerca. These worms occupy the subcutaneous layer of the skin, in the fat layer.

Loiasis

- Loiasis is a skin and eye disease caused by the nematode worm, Loa loa. Humans are the only known natural reservoir.
- Flies from two species of the genus Chrysops are the vector for loiasis.
- The female worms measure 40-70 mm in length and the males measure 30-34 mm in length.

Life cycle[2]
- During a blood meal, an infected fly introduces third-stage filarial larvae on to the skin of the human host, where they penetrate into the bite wound. The larvae develop into adults that often live in subcutaneous tissue.
- Adults produce microfilariae. During the day microfilariae are found in peripheral blood, but during the non-circulation phase, they are found in the lungs.
- The fly ingests microfilariae during a blood meal. After ingestion, the microfilariae migrate to the thoracic muscles of the arthropod, where they develop into third-stage infective larvae.
- The third-stage infective larvae migrate to the fly’s proboscis and so can then infect another human when the fly takes a blood meal.

Epidemiology
- It is estimated that 2-13 million humans are infected with the Loa loa larvae.
- Geographical distribution of human loiasis is restricted to the rainforest and swamp forest areas of West and Central Africa, especially Cameroon and on the Ogowe River.

Presentation
- Clinical features may appear up to several years after infection.
- Red itchy swellings (Calabar swellings) appearing, often on the forearms or wrists, sometimes after heavy exercise. They can appear on the face, breasts or legs.
- The swellings may last for 1-3 days, and may be associated with surrounding urticaria and pruritus.
- There may also be fever and irritability.
- The migrating worm can be seen under the skin.
- Migration of an adult worm to the eyes (subconjunctival) occurs frequently.
- Dead worms may cause chronic abscesses, which may lead to the formation of granulomatous reactions and fibrosis.

Investigations
- Eosinophilia is often prominent.
- Identification of microfilariae by microscopic examination is the most practical method of diagnosis. Daytime blood samples show microfilariae.
- Antigen detection using immunoassay is also useful because microfilaraemia can be low and variable.
- Polymerase chain reaction (PCR) and enzyme-linked immunosorbent assay (ELISA) methods are sensitive.[3]
- Antibody detection is of limited value because there is significant cross-reactivity between filaria and other helminths, and a positive serological test does not distinguish between past and current infection.
Identification of adult worms is possible from tissue samples collected during subcutaneous biopsies or worm removal from the eye.

Treatment

- Loiasis is treated with diethylcarbamazine, which kills microfilariae and many adult worms.
- In heavy infections there may be a febrile reaction and there is a small risk of encephalopathy. Treatment must be stopped at the first indication of cerebral involvement.
- Patients are also likely to have onchocerciasis, and careful monitoring for severe eye and skin inflammation is essential.

Prevention

Avoid Chrysops fly bites.

Onchocerciasis

- Onchocerciasis is caused by infestation with *O. volvulus*.
- The vector is then blackfly (genus *Simulium*).
- Adult female worms measure 33-50 cm in length and males measure 19-42 mm in length.
- When the worms die, *Wolbachia pipientis* (a bacterium which lives symbiotically in the worms and appears to be essential for the fertility and survival of the worms) is released, triggering a host response that causes intense itching and can destroy nearby tissues.

Life cycle

- During a blood meal, an infected blackfly introduces third-stage filarial larvae onto the skin of the human host, where they penetrate into the bite wound.
- The larvae develop into adults in palpable subcutaneous nodules, usually found over bony prominences of the thorax, pelvic girdle or knees (also found on the head of children). Adults can live in the nodules for approximately 15 years. Some nodules may contain many male and female worms.
- In the subcutaneous nodules, the female worms produce microfilariae, which have a lifespan that may reach two years. Microfilariae are usually found in the skin and in the lymphatics of connective tissues.
- A blackfly ingests the microfilariae during a blood meal. After ingestion, the microfilariae migrate to the thoracic muscles, where they develop into third-stage infective larvae. The third-stage infective larvae migrate to the blackfly's proboscis and can then infect another human when the fly takes a blood meal.

Epidemiology

- *O. volvulus* mainly causes infections in West, Central, and East Africa but also in South America and the Middle East.
- Onchocerciasis is the world’s second-leading infectious cause of severe sight impairment.

Presentation

- In the mild form there is localised maculopapular rash with itching. These may clear spontaneously or progress to a chronic and generalised form with severe itching.
- May heal with hyperpigmentation. Lichenified, hyperkeratotic lesions can be very distressing, as they are widespread and intensely itchy.
- A localised form in Arabia causes chronic papular dermatitis, often in one extremity only.
- In long-standing infection, destruction of elastic fibres in the skin makes it thin and wrinkled. The skin begins to sag and depigmentation of the pretibial areas is typical in older people living in endemic areas, (called 'leopard skin').
- Light-skinned patients infected on visiting a country may appear a year or so later with intensely itchy, red macular or maculopapular lesions that may be localised to one area of the body or be more generalised.
- There may also be fever, muscle or joint pain, weight loss and lymphadenitis.
- Rash sometimes lasts for several months after treatment.
- Ocular changes include intraocular microfilariae, punctate keratitis, sclerosing keratitis, anterior uveitis, chorioretinitis, optic neuritis, optic atrophy, glaucoma, and severe sight impairment (river blindness).

Investigation
Skin snips are immersed in normal saline and microfilariae can be seen swimming free within 24 hours. 
Examination of excised nodules shows adult worms.
More sensitive techniques include ELISA and PCR.

**Treatment**

- Ivermectin: a single dose clears microfilariae from the skin for several months. Repeating the dose every 6-12 months prevents progression.\(^6\)
- Treatment is often associated with increased itching, swelling of the face or extremities, headache and body pains, which usually occur after the first treatment.

**Prevention**

- Control of blackfly by spraying.
- Mass distribution of ivermectin.
- Doxycycline is effective at eliminating *W. pipiens* and its elimination may have a very important role in the treatment of onchocerciasis and other nematode infections in the future.\(^7\)

**Mansonellosis (Mansonella streptocerca)**\(^8\)

- *M. streptocerca* are found in Africa.
- Transmitted by *Culicoides* midges in tropical climates, they are of very limited clinical significance.
- Of the *Mansonella* species, only *M. streptocerca* causes recognised cutaneous symptoms.
- The females measure approximately 27 mm in length.

**Life cycle**

- During a blood meal, an infected midge introduces third-stage filarial larvae on to the skin of the human host, where they penetrate into the bite wound.
- Larvae develop into adults in the dermis, close to the skin surface. Adults produce microfilariae, which live in the skin but can also reach the peripheral blood.
- A midge ingests the microfilariae during a blood meal. The microfilariae migrate to the thoracic muscles, where they develop into third-stage larvae. The third-stage larvae migrate to the midge’s proboscis, and can then infect another human when the midge takes another blood meal.

**Presentation**

- Chronic papular lesions often with postinflammatory hyperpigmentation.
- Less commonly, it causes lichenification.

**Investigations**

- Microfilariae shown in blood or skin (a distinctive ‘walking stick’ shape to the tail).

**Treatment**

- If asymptomatic then no treatment is required.
- Otherwise, either diethylcarbamazine or ivermectin is effective.

**Further reading & references**

1. Wayanganka S et al; Filariasis, Medscape, May 2013
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8. Mansonellosis; Centers for Disease Control and Prevention
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