

# Lymphatic Filariasis

## A neglected disease

Sanne Jongma

*A 30-year-old man is admitted to a local hospital in rural Kenya. His right leg is extremely swollen up to his knee, the skin cracked. People ignore him as they walk by. His leg hurts so much he is unable to walk, let alone that he can work as a farmer. The doctors told him worms had invaded his body and nothing could be done to improve his condition. He is now permanently disabled, unable to look after his six children. Recently, the pain got worse and he got a fever. He decided to head back to the hospital to ask for medicine once again.*

### Introduction

Lymphatic filariasis, also known as “elephantiasis” in the advanced stage, is a parasitic tropical disease caused by thread-like nematodes (roundworms). It is thought to have affected humans since approximately 2000 BC as artefacts from ancient Egypt show possible elephantiasis symptoms. The first reference to the disease is found in ancient Greek literature, where scholars differentiated the often similar symptoms of lymphatic filariasis from those of leprosy. Three species of filarial worms are known to cause lymphatic filariasis, of which *Wuchereria Bancrofti* is the most significant. The other two are *Brugia malayi* and *Brugia timori*. Lymphatic filariasis is a communicable disease transmitted by many different mosquito vectors, including Anopheles, Culex and Mansonia species, with humans as definitive hosts.

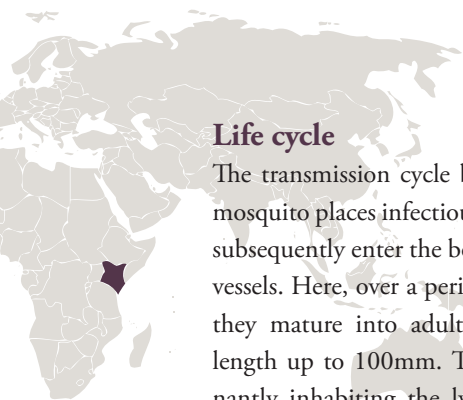
### Epidemiology

Lymphatic filariasis is endemic in tropical regions of South-east Asia, sub-Saharan Africa, Central and South America,

and many Pacific islands, where 90% of the infections are caused by the *Wuchereria Bancrofti* parasite. Estimations suggest that of the more than 120 million people currently infected, over 30% live in Africa and 60% in Asia. India alone accounts for 40% of the global infection prevalence. Worldwide, more than 40 million people are disfigured and severely incapacitated by the disease, many of them living with social stigmatization. This causes a high burden of disease, both on the individual as on the community. Approximately 15 million people live with the characteristic severe lymphedema also known as elephantiasis.

In endemic areas, the occurrence of microfilaremia increases with the age of individuals, as nearly everyone has been exposed by their forties. The adult worms however, only subsist when somebody stays in an endemic area, as these worms do not replicate inside the human host, and demand exposure to new infective larvae to increase the worm burden. The mosquitoes are relatively ineffective transmission vectors, hence the acquired prolonged stay before symptomatic infection occurs.





### Life cycle

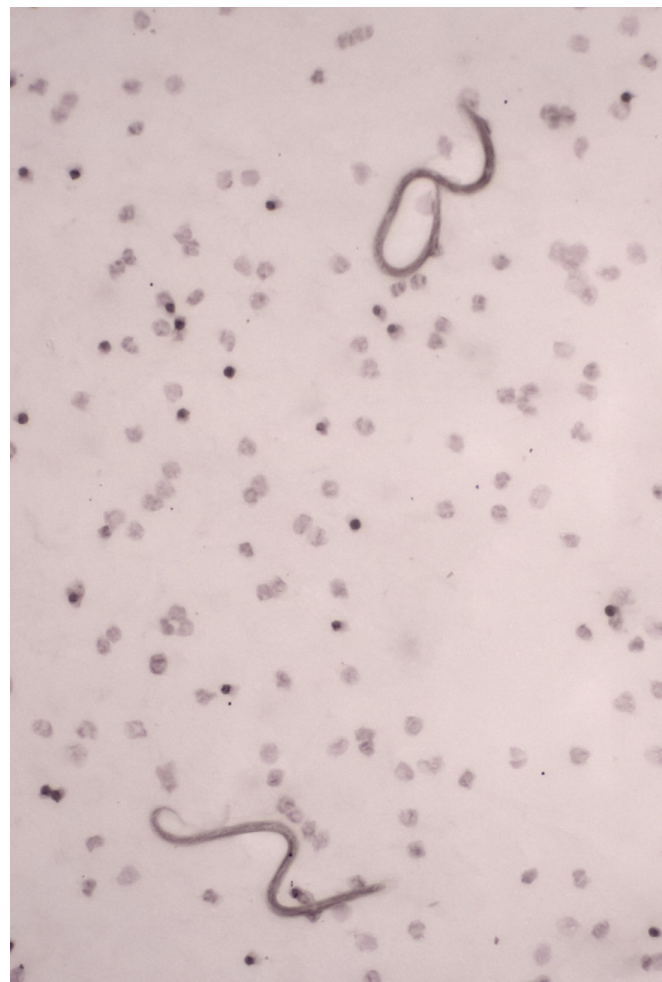
The transmission cycle begins when a bite of an infected mosquito places infectious larvae on the human skin, which subsequently enter the body and migrate to local lymphatic vessels. Here, over a period of approximately nine months, they mature into adult threadlike worms, some with a length up to 100mm. These full-grown worms, predominantly inhabiting the lymphatic vessels of the lower extremities or scrotum, remain in the human body for 5 to 10 years. Male and female worms mate and produce thousands of so-called microfilariae daily. The microfilariae circulate in the bloodstream and generally have a lifespan of one year. Subsequently, a vector bites an infected person once again, engorging the microfilariae. Inside the mosquito they develop into 'third stage' larvae within two weeks and the cycle starts all over again.

### Clinical features

Most people in endemic areas are infected early in life, but the disease onset usually starts from the adolescence onwards once worms have accumulated in the lymphatic ducts. About one third of the patients go through periods of acute adenolymphangitis with self-limiting fever and pulmonary eosinophilia provoking nocturnal wheezing and shortness of breath.

Most infected people stay asymptomatic but do develop subclinical lymphatic dilation and dysfunction. In 30% of all patients the affected limbs, predominantly the lower extremities, eventually start to swell, over time transforming from pitting to irreversible non-pitting lymphedema. Hyperpigmentation and hyperkeratosis finally create the image of an elephant skin, hence the name elephantiasis. In males there might be scrotal involvement where serous fluid accumulates and a hydrocele forms. Regularly, the skin

cracks and secondary infections occur in the affected limb causing severe pain, fever and chills. Additional nutritional deficiencies and anaemia, mainly caused by chyluria due to renal involvement, weakens the patients severely. Elephantiasis is seen as the leading cause of permanent disability in the world.



## Diagnosis

There are several tools to diagnose lymphatic filariasis. In the clinical setting, the disease is usually diagnosed based on clinical findings and detection of microfilaria in the peripheral blood. The parasites are detectable after a latent period of twelve months after infection. Blood is drawn around midnight, in the nocturnal periodicity, when the number of microfilariae in the bloodstream is greatest. This corresponds to the peak biting period of the mosquito vector. A Giemsa stained blood smear is then examined under the microscope. Serologic techniques, such as enzyme immune assay tests have very high sensitivity and specificity results but cannot be used for follow up, as the antigens stay present after the parasites have perished. Furthermore, filarial specific antibodies and PCR based assays are available. Ultimately, the ultrasound can show the filarial dance sign, their distinctive pattern of movement, detecting where in lymphatic duct the adult worm has its residence. This non-invasive technique is particularly used in the scrotal area where the worms in 80% of the infected men abide in the lymphatic vessels of the spermatic cord.

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## Treatment and prevention

There are two main treatment goals, namely bringing the disease to a halt by trying to reverse the progress of the parasite, and interrupting its transmission. Until recently, all infected people living in endemic areas received intense Diethylcarbamazine (DEC, an antiparasitic chemotherapeutic) courses as this has a profound micro- and macro-filaricidal working.

Unfortunately, DEC has a lot of side effects most probably triggered by the dying parasites sourcing local and systemic adverse effects such as fever, malaise, abdominal pain, arthralgia, diarrhea, dizziness, nausea, vomiting and chest pain. Another drug available is albendazole. Different studies showed that albendazole is as effective as DEC (alone or combined with albendazole) and has proven to have the same amount of adverse effects. In addition, ivermectin is used, mainly to reduce the microfilariae intensity.

A global program to eliminate lymphatic filariasis was launched in 1997 by the WHO. A mass drug administration was initiated, providing the endemic population with yearly doses of DEC, co-administrating albendazole for 5 to 6 years, and mass distribution of diethylcarbamazine-fortified salt. The outcome of the ongoing mass administration strongly depends on three main factors, namely (A) the pre-treatment endemicity microfilariae level, (B) the proportion of the population treated per round and (C) the efficiency of the applied drugs regimen. Besides killing the adult worms, the administered drugs reduces the blood borne reservoir of microfilariae, making it less likely the vector will ingest a parasite during a blood meal, diminishing the overall infection risk.

The eradication-program of the *Wuchereria Bancrofti* is showing positive progression towards elimination of the disease. Hopefully it will become a successful objective in the future.

Most affected countries completed mapping the endemic foci and 80% of these have started mass drug administration covering over 500 million endemic individuals. So far only China and South Korea have managed to complete elimination, but it is expected that soon more countries will follow.

### Conclusion

Although neglected by the western world, the *Wuchereria Bancroft* parasite causes a high burden of disease amongst people living in the endemic areas. Global eradication of lymphatic filariasis is possible but will require much effort from policy makers worldwide.

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### About the author

Sanne Jongma is a fifth year medical student at the VUmc in Amsterdam and editor at Global Medicine.

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### Further reading

- Lymphatic Filariasis: Transmission, Treatment and Elimination – Thesis by W.A. Stolk; Erasmus MC; 2005

