Filariasis

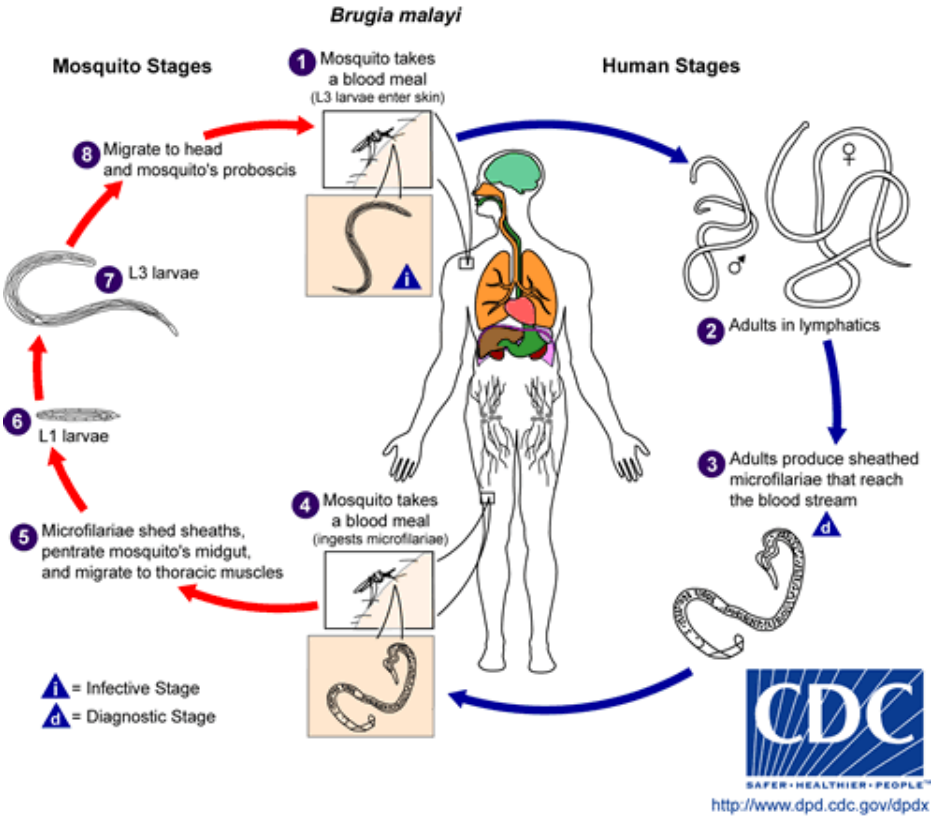
Causal Agents:

Filariasis is caused by nematodes (roundworms) that inhabit the lymphatics and subcutaneous tissues. Eight main species infect humans. Three of these are responsible for most of the morbidity due to filariasis: *Wuchereria bancrofti* and *Brugia malayi* cause lymphatic filariasis, and *Onchocerca volvulus* causes onchocerciasis (river blindness). The other five species are *Loa loa*, *Mansonella perstans*, *M. streptocerca*, *M. ozzardi*, and *Brugia timori*. (The last species also causes lymphatic filariasis.)

Life Cycles:

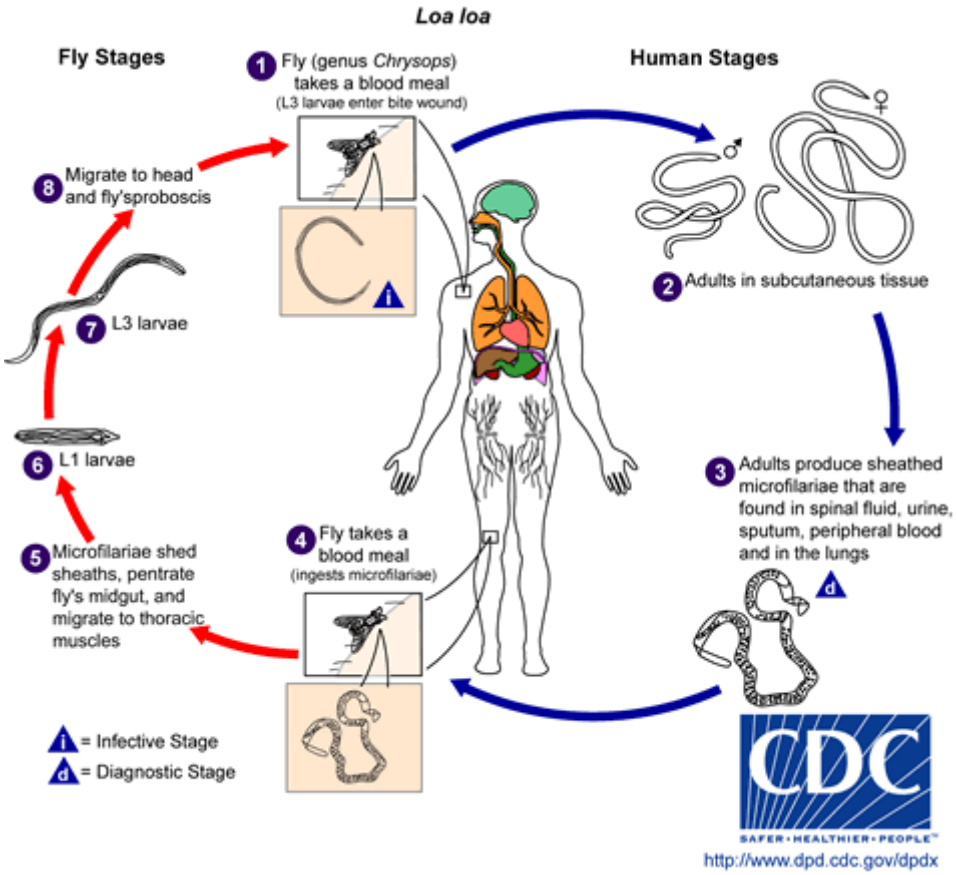
Infective larvae are transmitted by infected biting arthropods during a blood meal. The larvae migrate to the appropriate site of the host's body, where they develop into microfilariae-producing adults. The adults dwell in various human tissues where they can live for several years. The agents of lymphatic filariasis reside in lymphatic vessels and lymph nodes; *Onchocerca volvulus* in nodules in subcutaneous tissues; *Loa loa* in subcutaneous tissues, where it migrates actively; *Brugia malayi* in lymphatics, as with *Wuchereria bancrofti*; *Mansonella streptocerca* in the dermis and subcutaneous tissue; *Mansonella ozzardi* apparently in the subcutaneous tissues; and *M. perstans* in body cavities and the surrounding tissues. The female worms produce microfilariae which circulate in the blood, except for those of *Onchocerca volvulus* and *Mansonella streptocerca*, which are found in the skin, and *O. volvulus* which invade the eye. The microfilariae infect biting arthropods (mosquitoes for the agents of lymphatic filariasis; blackflies [*Simulium*] for *Onchocerca volvulus*; midges for *Mansonella perstans* and *M. streptocerca*; and both midges and blackflies for *Mansonella ozzardi*; and deerflies [*Chrysops*] for *Loa loa*). Inside the arthropod, the microfilariae develop in 1 to 2 weeks into infective filariform (third-stage) larvae. During a subsequent blood meal by the insect, the larvae infect the vertebrate host. They migrate to the appropriate site of the host's body, where they develop into adults, a slow process than can require up to 18 months in the case of *Onchocerca*.

Life Cycle of *Brugia malayi*:



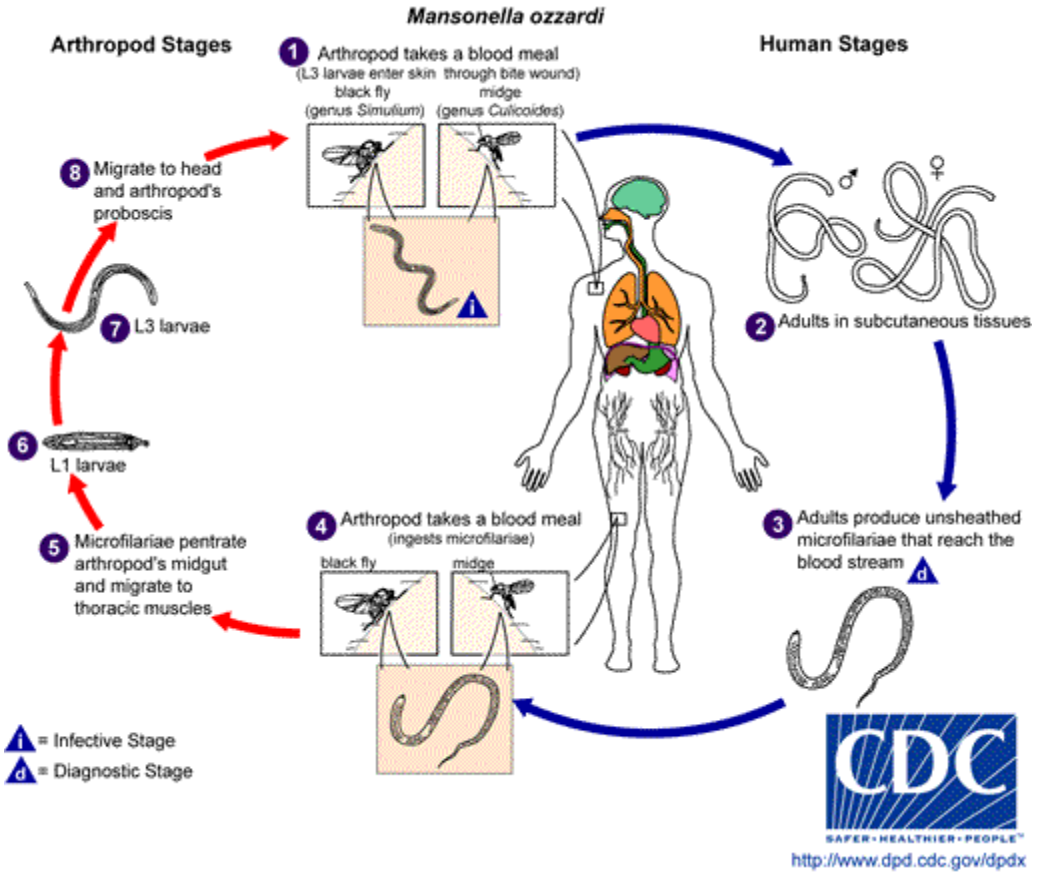
The typical vector for *Brugia malayi* filariasis are mosquito species from the genera *Mansonia* and *Aedes*. During a blood meal, an infected mosquito introduces third-stage filarial larvae onto the skin of the human host, where they penetrate into the bite wound ❶. They develop into adults that commonly reside in the lymphatics ❷. The adult worms resemble those of *Wuchereria bancrofti* but are smaller. Female worms measure 43 to 55 mm in length by 130 to 170 µm in width, and males measure 13 to 23 mm in length by 70 to 80 µm in width. Adults produce microfilariae, measuring 177 to 230 µm in length and 5 to 7 µm in width, which are sheathed and have nocturnal periodicity. The microfilariae migrate into lymph and enter the blood stream reaching the peripheral blood ❸. A mosquito ingests the microfilariae during a blood meal ❹. After ingestion, the microfilariae lose their sheaths and work their way through the wall of the proventriculus and cardiac portion of the midgut to reach the thoracic muscles ❺. There the microfilariae develop into first-stage larvae ❻and subsequently into third-stage larvae ❼. The third-stage larvae migrate through the hemocoel to the mosquito's prosbocis ❽and can infect another human when the mosquito takes a blood meal ❶.

Life Cycle of *Loa loa*:



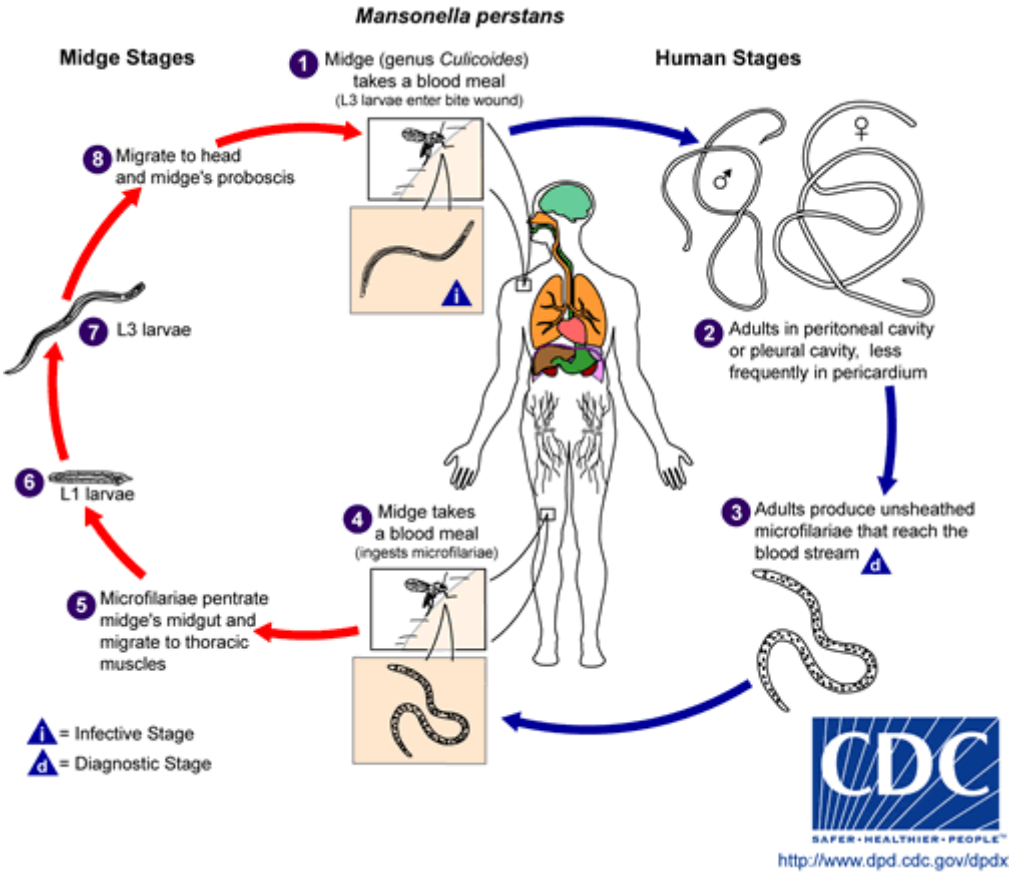
The vector for *Loa loa* filariasis are flies from two species of the genus *Chrysops*, *C. silacea* and *C. dimidiata*. During a blood meal, an infected fly (genus *Chrysops*, day-biting flies) introduces third-stage filarial larvae onto the skin of the human host, where they penetrate into the bite wound ❶. The larvae develop into adults that commonly reside in subcutaneous tissue ❷. The female worms measure 40 to 70 mm in length and 0.5 mm in diameter, while the males measure 30 to 34 mm in length and 0.35 to 0.43 mm in diameter. Adults produce microfilariae measuring 250 to 300 µm by 6 to 8 µm, which are sheathed and have diurnal periodicity. Microfilariae have been recovered from spinal fluids, urine, and sputum. During the day they are found in peripheral blood, but during the noncirculation phase, they are found in the lungs ❸. The fly ingests microfilariae during a blood meal ❹. After ingestion, the microfilariae lose their sheaths and migrate from the fly's midgut through the hemocoel to the thoracic muscles of the arthropod ❺. There the microfilariae develop into first-stage larvae ❻ and subsequently into third-stage infective larvae ❼. The third-stage infective larvae migrate to the fly's proboscis ❽and can infect another human when the fly takes a blood meal ❶.

Life Cycle of *Mansonella ozzardi*:



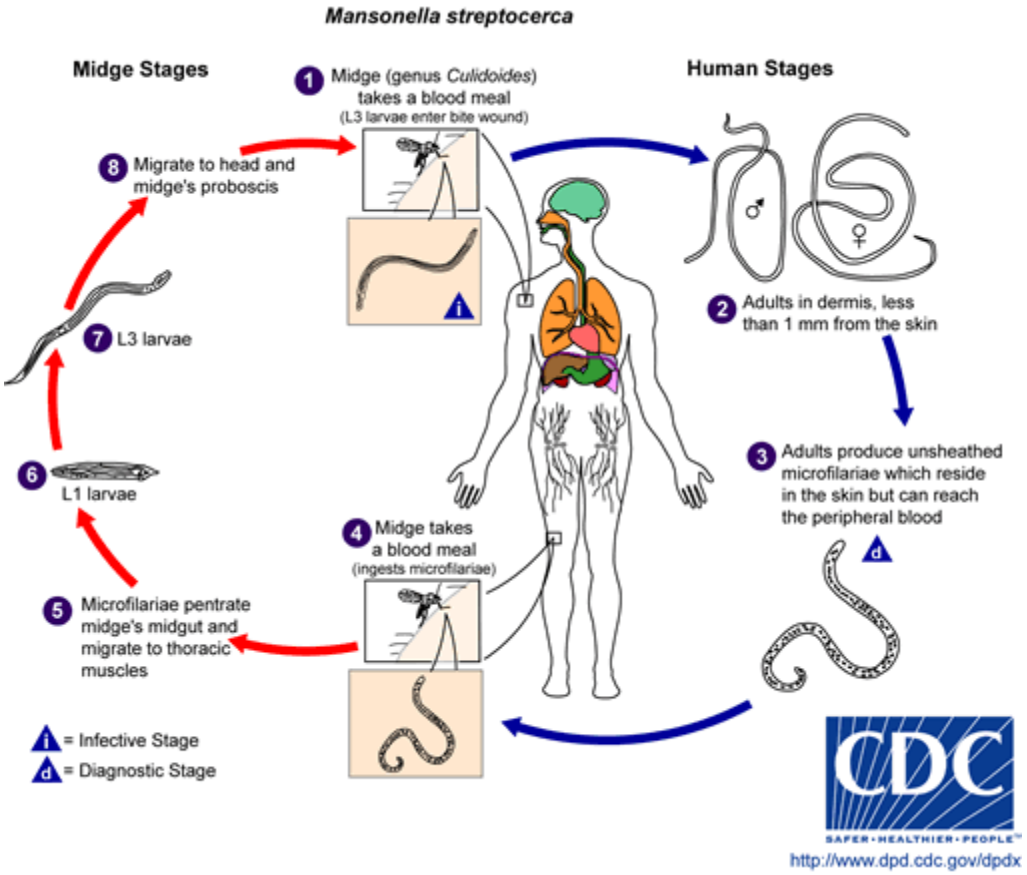
During a blood meal, an infected arthropod (midges, genus *Culicoides*, or blackflies, genus *Simulium*) introduces third-stage filarial larvae onto the skin of the human host, where they penetrate into the bite wound ❶. They develop into adults that commonly reside in subcutaneous tissues ❷. Adult worms are rarely found in humans. The size range for females worms is 65 to 81 mm in length and 0.21 to 0.25 mm in diameter but unknown for males. Adults worms recovered from experimentally infected Patas monkeys measured 24 to 28 mm in length and 70 to 80 µm in diameter (males) and 32 to 62 mm in length and .130 to .160 mm in diameter (females). Adults produce unsheathed and non-periodic microfilariae that reach the blood stream ❸. The arthropod ingests microfilariae during a blood meal ❹. After ingestion, the microfilariae migrate from the arthropod's midgut through the hemocoel to the thoracic muscles ❺. There the microfilariae develop into first-stage larvae ❻and subsequently into third-stage infective larvae ❼. The third-stage infective larvae migrate to arthropod's proboscis ❽and can infect another human when the arthropod takes a blood meal ❶.

Life Cycle of *Mansonella perstans*:



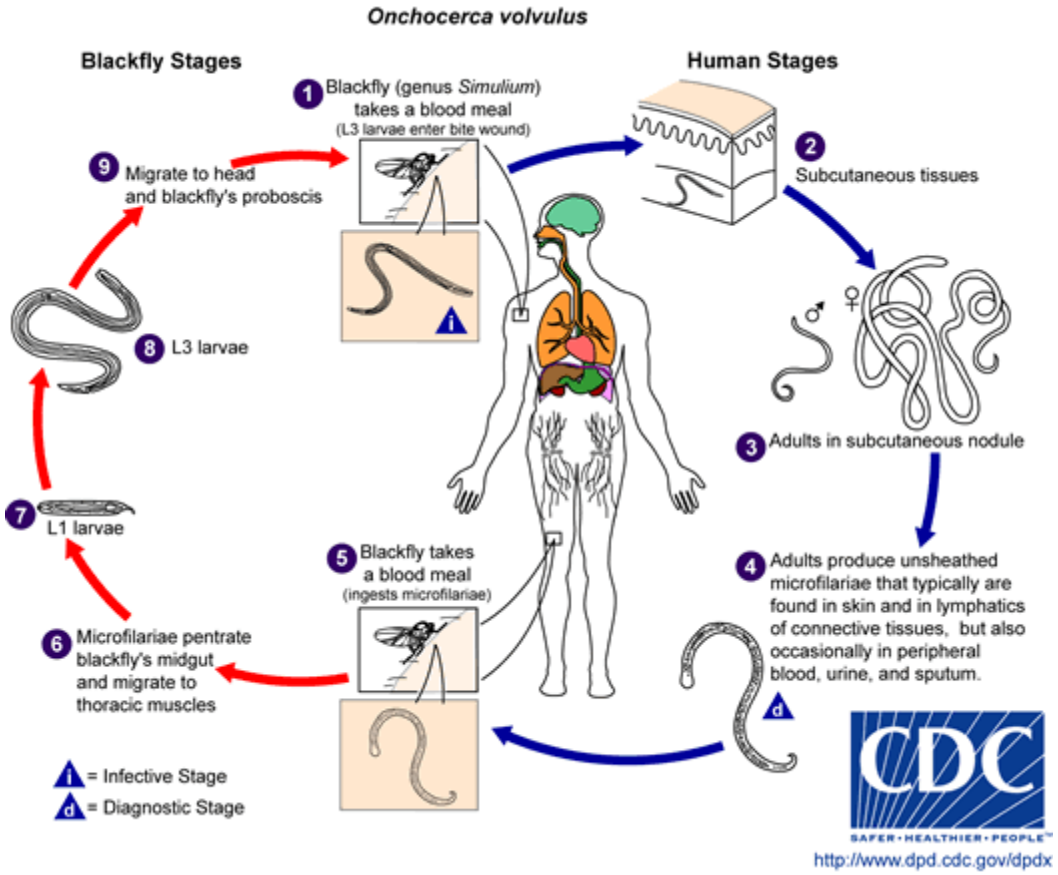
During a blood meal, an infected midge (genus *Culicoides*) introduces third-stage filarial larvae onto the skin of the human host, where they penetrate into the bite wound 1. They develop into adults that reside in body cavities, most commonly the peritoneal cavity or pleural cavity, but less frequently in the pericardium 2. The size range for female worms is 70 to 80 mm in length and 120 µm in diameter, and the males measure approximately 45 mm by 60 µm. Adults produce unsheathed and subperiodic microfilariae, measuring 200 by 4.5 µm that reach the blood stream 3. A midge ingests microfilariae during a blood meal 4. After ingestion, the microfilariae migrate from the midge's midgut through the hemocoel to the thoracic muscles of the arthropod 5. There the microfilariae develop into first-stage larvae 6 and subsequently into third-stage infective larvae 7. The third-stage infective larvae migrate to the midge's proboscis 8 and can infect another human when the midge takes a blood meal 1.

Life Cycle of *Mansonella streptocerca*:



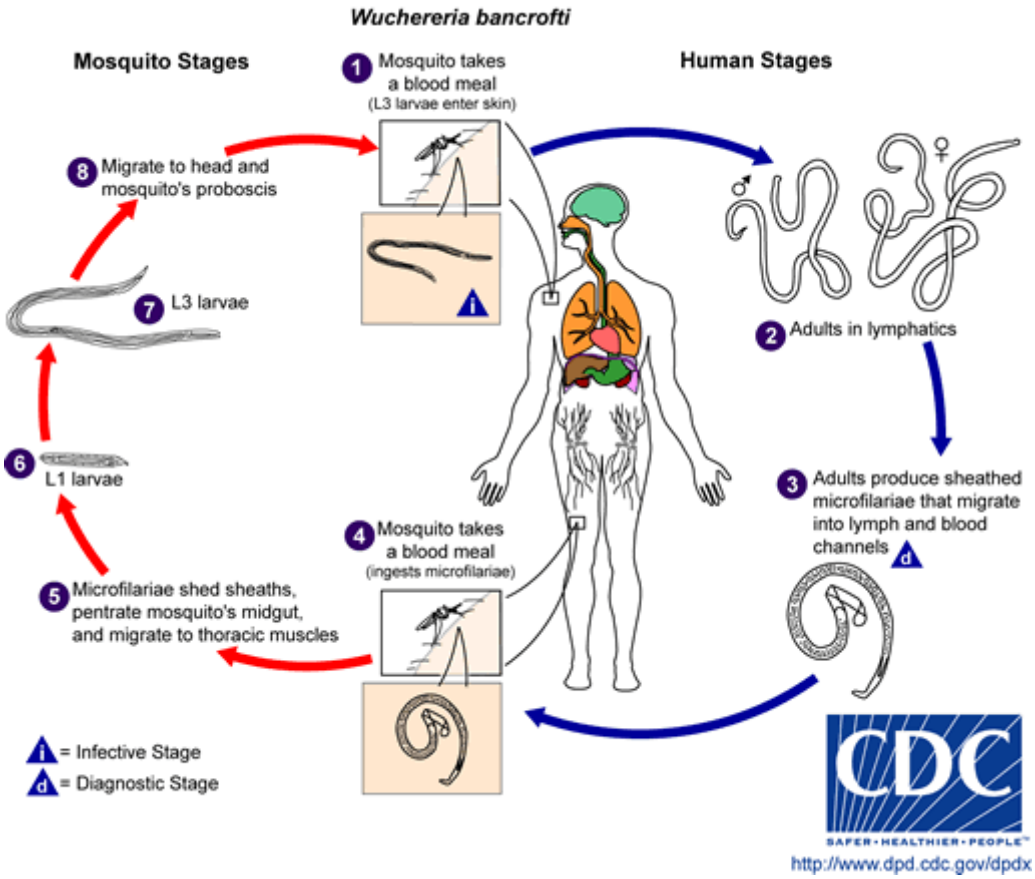
During a blood meal, an infected midge (genus *Culicoides*) introduces third-stage filarial larvae onto the skin of the human host, where they penetrate into the bite wound ❶. They develop into adults that reside in the dermis, most commonly less than 1 mm from the skin surface ❷. The females measure approximately 27 mm in length. Their diameter is 50 µm at the level of the vulva (anteriorly) and ovaries (near the posterior end), and up to 85 µm at the mid-body. Males measure 50 µm in diameter. Adults produce unsheathed and non-periodic microfilariae, measuring 180 to 240 µm by 3 to 5 µm, which reside in the skin but can also reach the peripheral blood ❸. A midge ingests the microfilariae during a blood meal ❹. After ingestion, the microfilariae migrate from the midge's midgut through the hemocoel to the thoracic muscles ❺. There the microfilariae develop into first-stage larvae ❻and subsequently into third-stage larvae ❼. The third-stage larvae migrate to the midge's proboscis ❽and can infect another human when the midge takes another blood meal ❶.

Life Cycle of *Onchocerca volvulus*:



During a blood meal, an infected blackfly (genus *Simulium*) introduces third-stage filarial larvae onto the skin of the human host, where they penetrate into the bite wound 1. In subcutaneous tissues the larvae 2 develop into adult filariae, which commonly reside in nodules in subcutaneous connective tissues 3. Adults can live in the nodules for approximately 15 years. Some nodules may contain numerous male and female worms. Females measure 33 to 50 cm in length and 270 to 400 µm in diameter, while males measure 19 to 42 mm by 130 to 210 µm. In the subcutaneous nodules, the female worms are capable of producing microfilariae for approximately 9 years. The microfilariae, measuring 220 to 360 µm by 5 to 9 µm and unsheathed, have a life span that may reach 2 years. They are occasionally found in peripheral blood, urine, and sputum but are typically found in the skin and in the lymphatics of connective tissues 4. A blackfly ingests the microfilariae during a blood meal 5. After ingestion, the microfilariae migrate from the blackfly's midgut through the hemocoel to the thoracic muscles 6. There the microfilariae develop into first-stage larvae 7 and subsequently into third-stage infective larvae 8. The third-stage infective larvae migrate to the blackfly's proboscis 9 and can infect another human when the fly takes a blood meal 1.

Life Cycle of *Wuchereria bancrofti*:



Different species of the following genera of mosquitoes are vectors of *W. bancrofti* filariasis depending on geographical distribution. Among them are: *Culex* (*C. annulirostris*, *C. bitaeniorhynchus*, *C. quinquefasciatus*, and *C. pipiens*); *Anopheles* (*A. arabinensis*, *A. bancroftii*, *A. farauti*, *A. funestus*, *A. gambiae*, *A. koliensis*, *A. melas*, *A. merus*, *A. punctulatus* and *A. wellcomei*); *Aedes* (*A. aegypti*, *A. aquasalis*, *A. bellator*, *A. cooki*, *A. darlingi*, *A. kochi*, *A. polynesiensis*, *A. pseudoscutellaris*, *A. rotumae*, *A. scapularis*, and *A. vigilax*); *Mansonia* (*M. pseudotitillans*, *M. uniformis*); *Coquillettidia* (*C. juxtamansonia*). During a blood meal, an infected mosquito introduces third-stage filarial larvae onto the skin of the human host, where they penetrate into the bite wound ❶. They develop in adults that commonly reside in the lymphatics ❷. The female worms measure 80 to 100 mm in length and 0.24 to 0.30 mm in diameter, while the males measure about 40 mm by .1 mm. Adults produce microfilariae measuring 244 to 296 µm by 7.5 to 10 µm, which are sheathed and have nocturnal periodicity, except the South Pacific microfilariae which have the absence of marked periodicity. The microfilariae migrate into lymph and blood channels moving actively through lymph and blood ❸. A mosquito ingests the microfilariae during a blood meal ❹. After ingestion, the microfilariae lose their sheaths and some of them work their way through the wall of the proventriculus and cardiac portion of the mosquito's midgut and reach the thoracic muscles ❺. There the microfilariae develop into first-stage larvae ❻ and subsequently into third-stage infective larvae ❼. The third-stage infective larvae migrate through the hemocoel to the mosquito's prosbocis ❽and can infect another human when the mosquito takes a blood meal ❶.

Geographic Distribution:

Among the agents of lymphatic filariasis, *Wuchereria bancrofti* is encountered in tropical areas worldwide; *Brugia malayi* is limited to Asia; and *Brugia timori* is restricted to some islands of

Indonesia. The agent of river blindness, *Onchocerca volvulus*, occurs mainly in Africa, with additional foci in Latin America and the Middle East. Among the other species, *Loa loa* and *Mansonella streptocerca* are found in Africa; *Mansonella perstans* occurs in both Africa and South America; and *Mansonella ozzardi* occurs only in the American continent.

Clinical Features:

Lymphatic filariasis most often consists of asymptomatic microfilaremia. Some patients develop lymphatic dysfunction causing lymphedema and elephantiasis (frequently in the lower extremities) and, with *Wuchereria bancrofti*, hydrocele and scrotal elephantiasis. Episodes of febrile lymphangitis and lymphadenitis may occur. Persons who have newly arrived in disease-endemic areas can develop afebrile episodes of lymphangitis and lymphadenitis. An additional manifestation of filarial infection, mostly in Asia, is pulmonary tropical eosinophilia syndrome, with nocturnal cough and wheezing, fever, and eosinophilia. Onchocerciasis can cause pruritus, dermatitis, onchocercomata (subcutaneous nodules), and lymphadenopathies. The most serious manifestation consists of ocular lesions that can progress to blindness. Loiasis (*Loa loa*) is often asymptomatic. Episodic angioedema (Calabar swellings) and subconjunctival migration of an adult worm can occur. Infections by *Mansonella perstans*, while often asymptomatic, can be associated with angioedema, pruritus, fever, headaches, arthralgias, and neurologic manifestations. *Mansonella streptocerca* can cause skin manifestations including pruritus, papular eruptions and pigmentation changes. Eosinophilia is often prominent in filarial infections. *Mansonella ozzardi* can cause symptoms that include arthralgias, headaches, fever, pulmonary symptoms, adenopathy, hepatomegaly, and pruritus.

Laboratory Diagnosis:

Identification of microfilariae by microscopic examination is the most practical diagnostic procedure.

Examination of blood samples will allow identification of microfilariae of *Wuchereria bancrofti*, *Brugia malayi*, *Brugia timori*, *Loa loa*, *Mansonella perstans*, and *M. ozzardi*. It is important to time the blood collection with the known periodicity of the microfilariae. The blood sample can be a thick smear, stained with Giemsa or hematoxylin and eosin. For increased sensitivity, concentration techniques can be used. These include centrifugation of the blood sample lyzed in 2% formalin (Knott's technique), or filtration through a Nucleopore® membrane. Examination of skin snips will identify microfilariae of *Onchocerca volvulus* and *Mansonella streptocerca*. Skin snips can be obtained using a corneal-scleral punch, or more simply a scalpel and needle. The sample must be allowed to incubate for 30 minutes to 2 hours in saline or culture medium, and then examined for microfilariae that would have migrated from the tissue to the liquid phase of the specimen.

Diagnostic findings

- Microscopy
- **Antigen detection** using an immunoassay for circulating filarial antigens constitutes a useful diagnostic approach, because microfilaremia can be low and variable. A rapid-format immunochromatographic test, applicable to *Wuchereria bancrofti* antigens, has been recently evaluated in the field.
- **Molecular diagnosis** using polymerase chain reaction is available for *W. bancrofti* and *B. malayi*.
- **Identification of adult worms** is possible from tissue samples collected during nodulectomies (onchocerciasis), or during subcutaneous biopsies or worm removal from the eye (loiasis).
- **Antibody detection** is of limited value. Substantial antigenic cross reactivity exists between filaria and other helminths, and a positive serologic test does not distinguish between past and current infection.
- **Special Procedures for Detecting Microfilariae**

Treatment:

Different drugs are recommended for the treatment of filariasis depending on the specific causal agent.