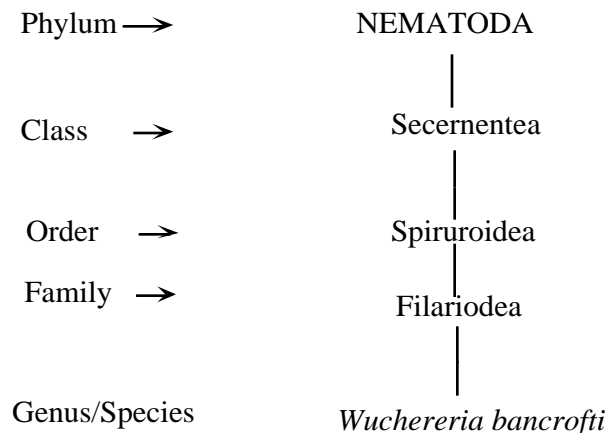


FILARIASIS: HANDOUT I

BACKGROUND

Filarial nematodes are long slender multicellular worms that cause disease in humans. Insect vectors commonly transmit the disease. Filaria belong to the phylum **Nematoda** which includes an unusually large number of worms. Nematodes are both free living in water and soil and many are parasitic to plants and animals. **Nematodes** are **roundworms**. Some species are distributed worldwide while others are restricted to tropical areas. Most are unsegmented worms with separate sexes and do not multiply their numbers in their intermediate hosts.

Filaria nematodes belong to the class **Secernentea** (or **Phasmidia**). This class is defined by the presence of sense organs known as phasmids which are structures comprising parts of a coordinated sensitive nervous system. Complex nervous systems are characteristic of nematodes. The family to which Filaria belongs, Filariodea, is generally one in which the bodies of the worms are tapered.



Wuchereria bancrofti, ***Brugia malaya*** and ***Loa Loa*** are the three major nematode species of significance. ***W. bancrofti*** is the best known of these parasites. ***W. bancrofti*** is a strict parasite of vertebrates and is transmitted by mosquitoes. Approximately 600 million individuals are exposed to ***W. bancrofti*** and 80 million are currently infected. They cause diseases throughout the tropics especially in South America, Central America, India and South China. The disease is also found in Spain, Egypt and Australia. The disease they cause is often referred to as Bancroftian filariasis. ***Brugia malaya*** is a less widely distributed nematode being limited to South Asia up to China and Korea. In these areas 8.6 million infections have been recorded.

TRANSMISSION, LIFE CYCLE AND DISEASE

Filarial nematodes generally survive and complete their life cycles in the lymphatic systems of their vertebrate hosts. ***Wuchereria bancrofti*** and ***Brugia malaya*** are therefore referred to as organisms causing lymphatic filariasis. The adult forms of these organisms generally release embryos into the blood or lymph of their human hosts and these larvae are then taken up by insects (e.g. mosquitoes) where they undergo development. In addition to insect transmission, filarial infections can be acquired congenitally and by oral transmission. Although less common, filarial nematodes and thus filariasis can also be carried by cats.

LIFE CYCLE

There are two major filarial life cycle stages:

1. MICROFILARIAE
2. ADULT WORM

Microfilariae are the larval forms of both *Wuchereria bancrofti* and *Brugia malaya*. Microfilariae are extremely small in comparison to their adult state. Their average size is approximately 2/10th of a mm in their largest dimension. Microfilariae are produced by actively mating sexual adult pairs. The progeny larval forms produced by mating can survive in the host for as long as one year prior to further development, which itself requires transmission to an insect vector. Microfilariae are nocturnally periodic.

Adult Filariae (*Wuchereria bancrofti* and *Brugia malaya*) mature from larvae. Developed larvae from insects enter the lymphatic system including the lymph nodes of the vertebrate host where they mature. Here, mating occurs and early larval microfilarial forms work their way from the lymphatics to the blood. Mated adults continue to shed microfilariae for 4 - 40 years. In the blood, microfilariae are picked up in the bloodmeal of feeding insects and are transmitted to another host after having undergone further development in these intermediate hosts.

TRANSMISSION OF *W. BANCROFTI* AND *BRUGIA MALAYA*

Transmission *via* the nocturnal cycle of microfilariae occurs by the bites of night feeding mosquitoes. Biting mosquitoes take bloodmeals late at nights. This results in uptake of microfilariae. Microfilariae begin development in the stomach of the insect. During their development, a process that takes approximately two weeks, molting larvae become lodged in thoracic muscle of the insect and eventually migrate to the proboscis. In the proboscis, these matured larval stages wait to penetrate host skin when the mosquito takes another bloodmeal. Light microfilariae infection loads on mosquitoes do not kill mosquitoes, heavy infection load however do. When transferred to the human host, microfilariae develop into mature adults.

In the vertebrate host, blood **microfilariae** possess a remarkable property of appearance periodicity. That is, their numbers in the blood of humans at nights is high and low during the day. Specifically, *Wuchereria bancrofti* microfilariae gradually begin to appear in the blood in the evening (approximately twilight) and reach maximal numbers around midnight. These numbers then diminish in the blood by early morning. The basis for this periodicity remains unclear. It is believed to be related to oxygen tension of the peripheral blood and/or host and parasite circadian rhythm. The periodicity of microfilariae in the blood is important to transmission. Since insect vectors feed on hosts in the evening, optimal parasite acquisition occurs when microfilariae peak numbers coincide with female mosquito nocturnal feeding patterns.

RELATIONSHIP OF FILARIAL INFECTION TO LYMPHATIC DISEASE

Both *Wuchereria bancrofti* and *Brugia malaya* are often indistinguishable to the naked eye and appear as white thread-like worms. The females in both species are 8-10cm (approx. 4 inches) in length and the male one half the length of the female. Disease is caused by the presence of **worms** in lymphatic vessels. Hence the term lymphatic filariasis. The adult filaria spend their entire lives in the lymphatic system (vessels and nodes) of their hosts. Their presence causes dilation of lymph ducts, obstructed lymph flow, and lymph backpressure. Additionally, the presence of dead and dying worms elicits very strong immune responses that causes just as much damage as the presence of live worms. Individuals living in endemic areas develop strong immune responses eventually develop disfiguring abnormalities such as elephantitis (enlargement of affected organs) of the lower limbs and the genitalia. This is a disease in which fluids accumulates in the host lymphatic system and causes serious disfiguring. The basis of disease is poorly understood. It is likely that dying adult worms stimulate

local immune functions, and cause tissue swelling and blockage in the lymphatic system. Dying worms stimulate disease symptoms by releasing antigens that stimulate immune function. These worms exacerbate immune responses that eventually lead to host immune infiltration followed by lymphatic vessel closure. Microfilarial forms do not appear to be very immunostimulatory and thus are not believed to be responsible for much of the host immune response. Live worms generally cause less inflammation because they are capable of producing immunomodulators that suppress host immune responses to their presence.