Bancroftian Filariasis

Lymphatic Filariasis (LF)

'There is the elephant disease which is generated beside the streams of the Nile in the midst of Egypt and nowhere else. In Attica the feet are attacked and the eyes in Achean lands. And so different places are hurtful to different parts and members: the variations of air occasion that…this…destroying power and pestilence therefore all at once either fall upon the waters or else sink deep into the corn-crops or the food of man…or else their force remains suspended in the atmosphere, and when we inhale from it mixed airs, we must absorb at the same time into our body those things as well.'

--Lucretius (99-55 B.C.)

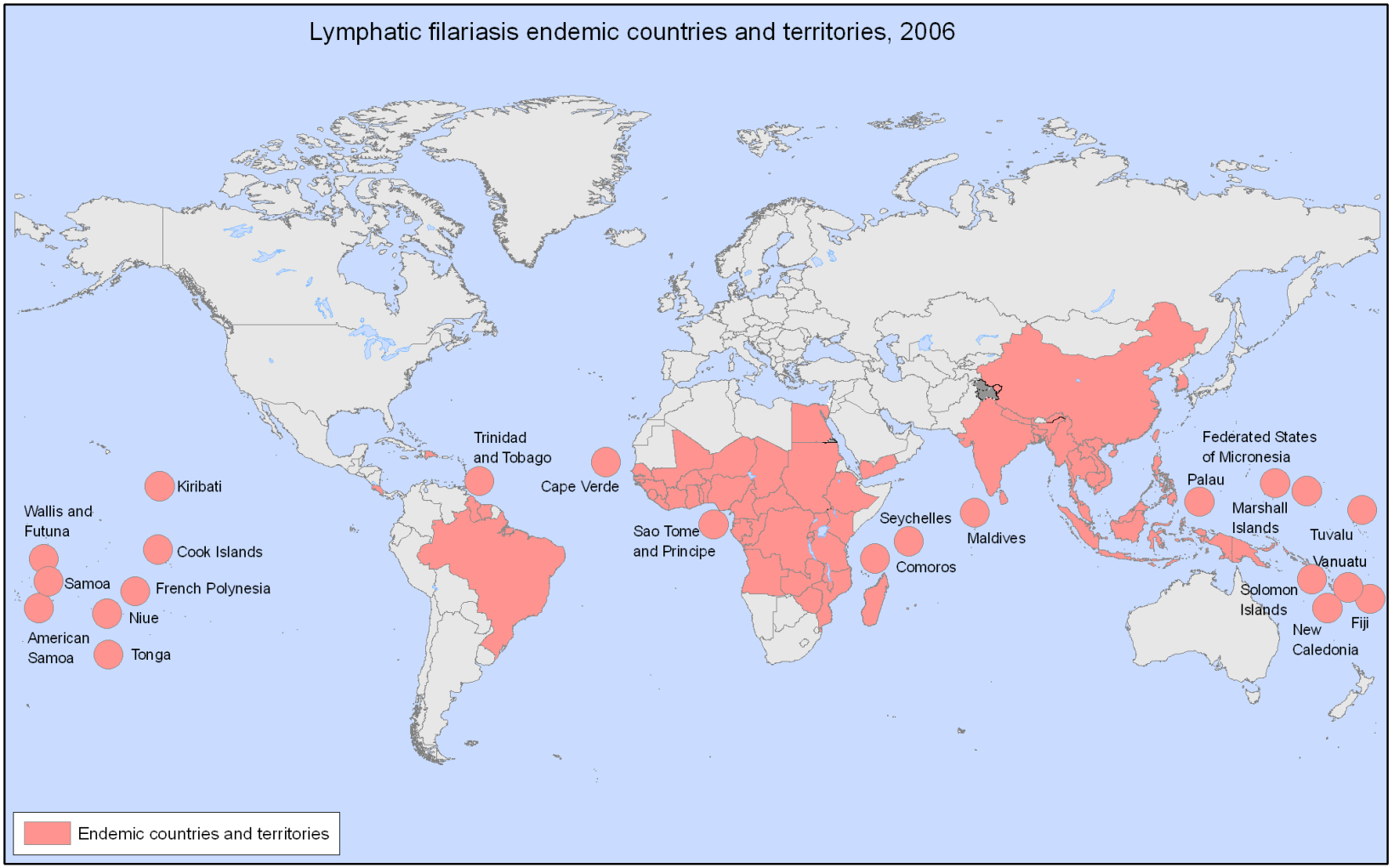
Introduction

- **Bancroftian filariasis is infection by any one of the three lymphatic-dwelling parasitic nematodes:**
  - ***Wuchereria bancrofti***
  - ***Brugia malayi***
  - ***Brugia timori***
- **Estimated 100-120 million persons affected worldwide.**

Introduction

- **For *W. bancrofti*, humans are the exclusive host.**
  - **With the exception of some strains in the South Pacific, most *W. bancrofti* strains are nocturnal, referring to the periodicity with which the microfilariae appear in the peripheral circulation.**
- ***B. malayi* infection is a zoonosis, with both feline and monkey reservoirs.**
- **May be water-borne.**

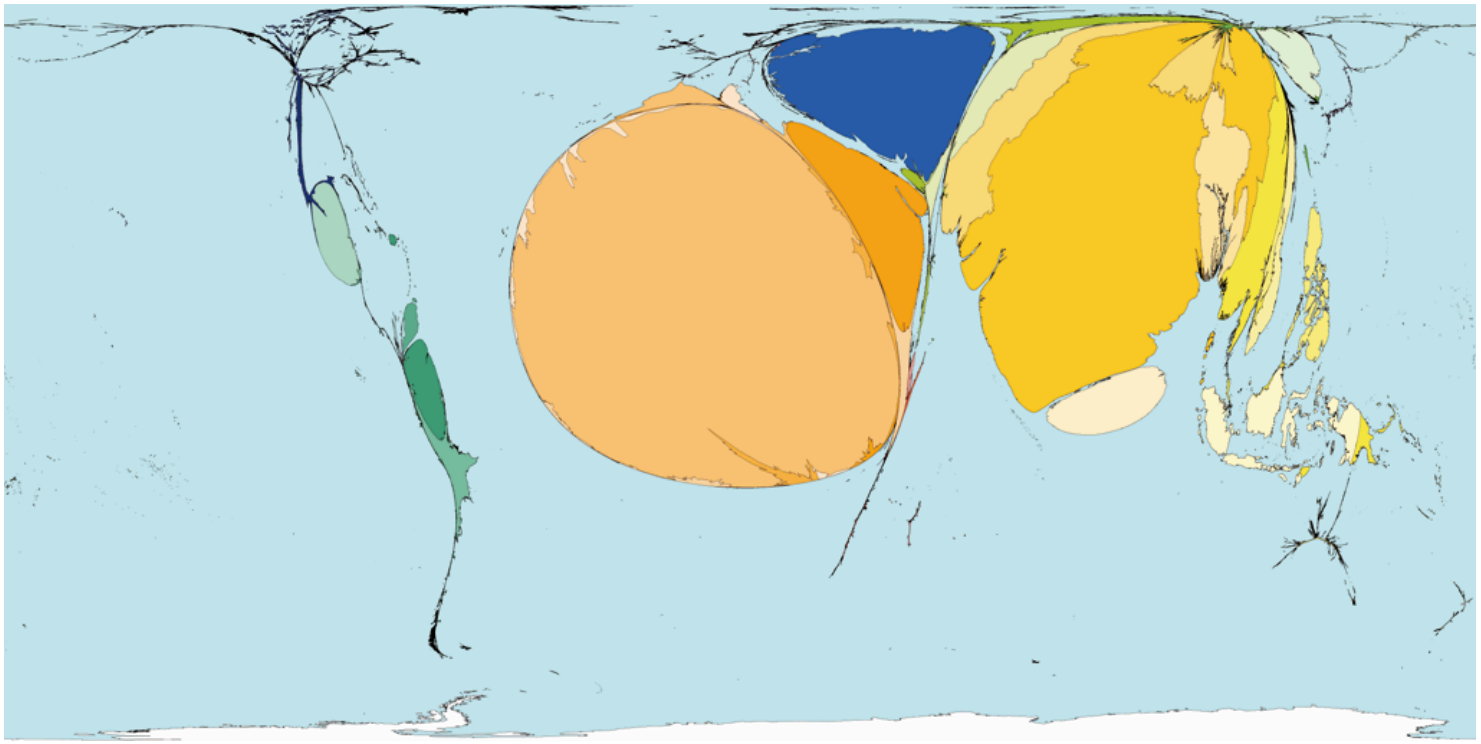
Introduction: Distribution



Data Source: Lymphatic Filariasis Elimination Programme Map
Production: Public Health Mapping and GIS
Communicable Diseases (CDS) World Health Organization

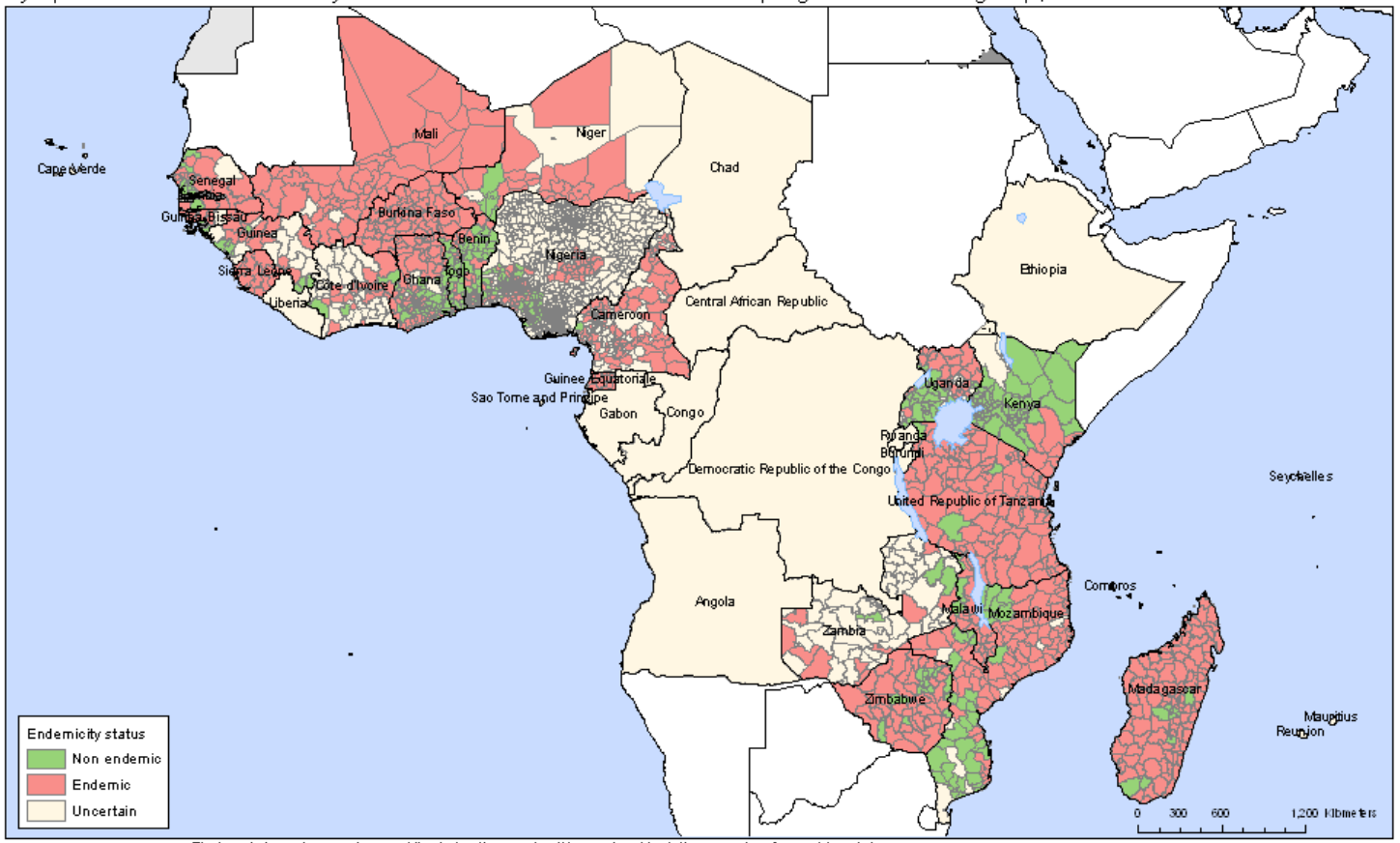
Introduction: Distribution

Territories are sized in proportion to the absolute number of people who died from lymphatic filariasis (elephantiasis) in one year.



Introduction: Distribution

Lymphatic filariasis endemicity status in the countries of the African programme review group, latest available

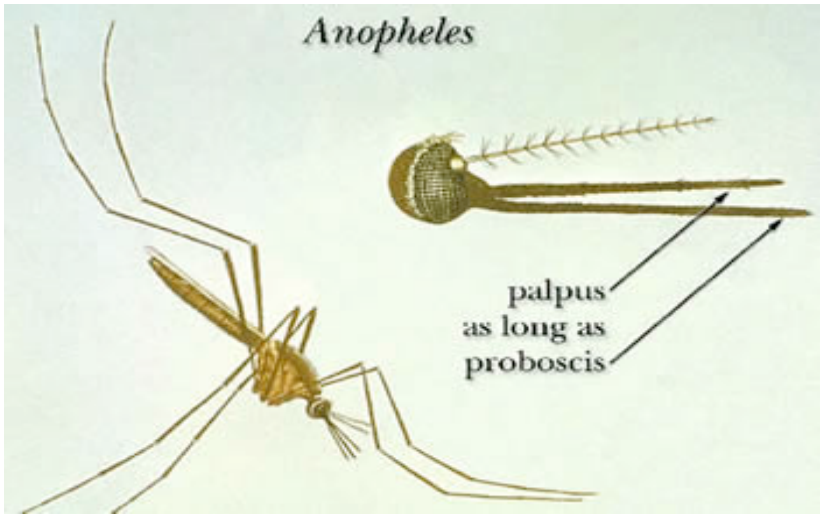


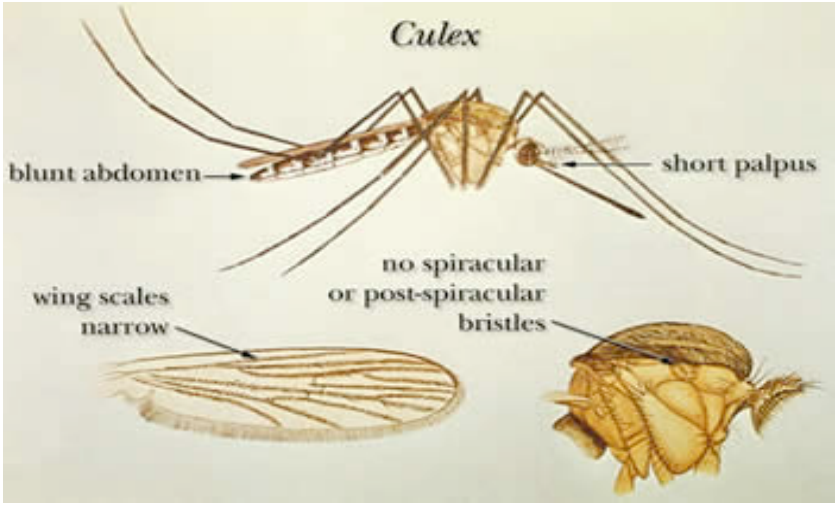
World Health Organization

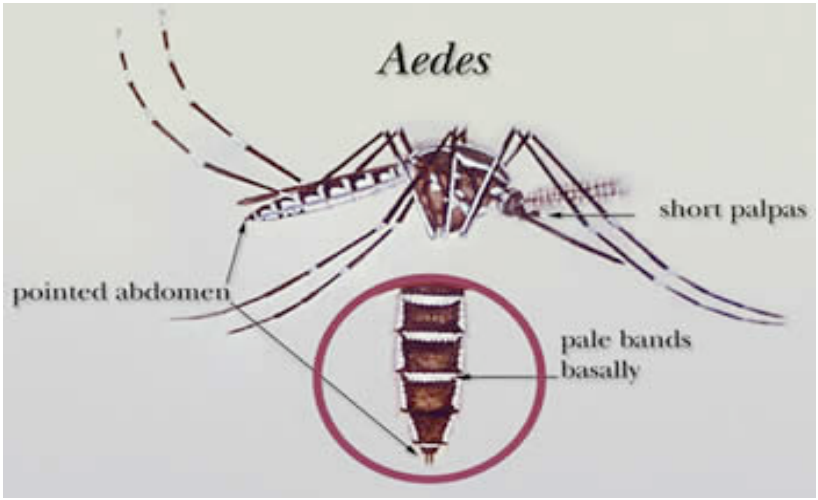
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: Lymphatic Filariasis Elimination Programme
Map Production: Public Health Mapping and GIS
Communicable Diseases (CDS), World Health Organization

Bancroftian Filariasis: Vectors





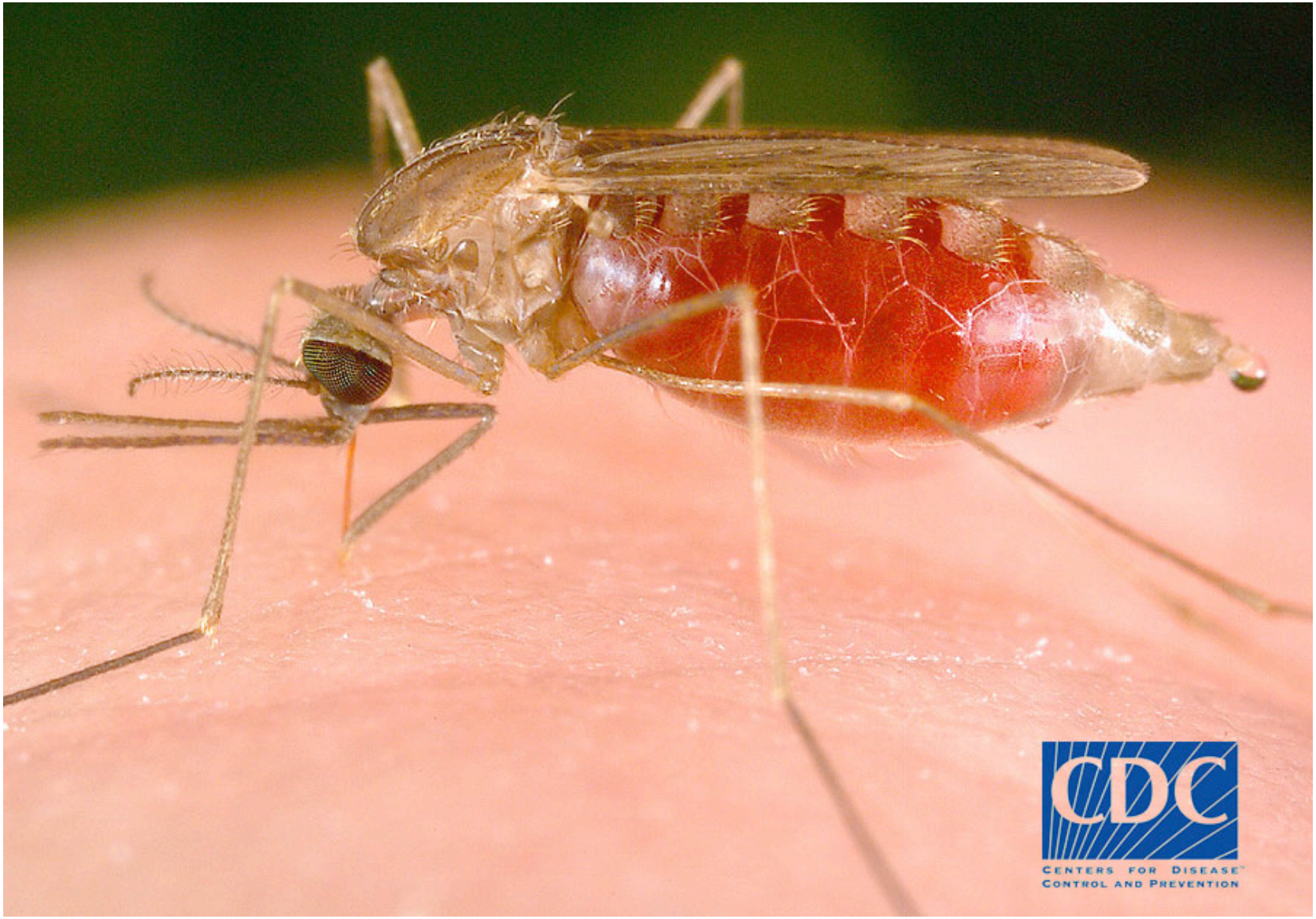


***Anopheles*-Dusk, Dawn, Nocturnal**

***Culex*-Dusk & Dawn**

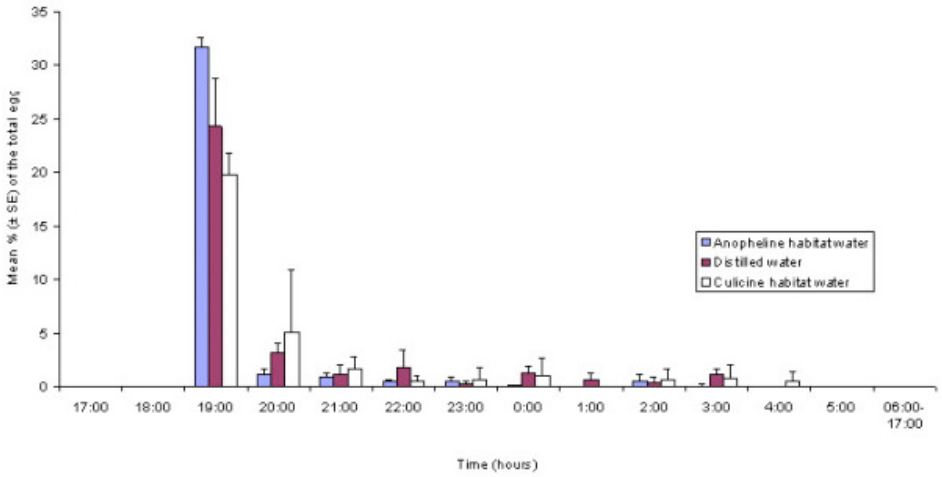
***Aedes*-Aggressive day feeders**

***Mansonia spp*.-Nocturnal**


CDC
CENTERS FOR DISEASE
CONTROL AND PREVENTION

Daily oviposition patterns of the African malaria mosquito *Anopheles gambiae* Giles (Diptera: Culicidae) on different types of aqueous substrates
J Circadian Rhythms. 2004; 2: 6. Sumba et al.

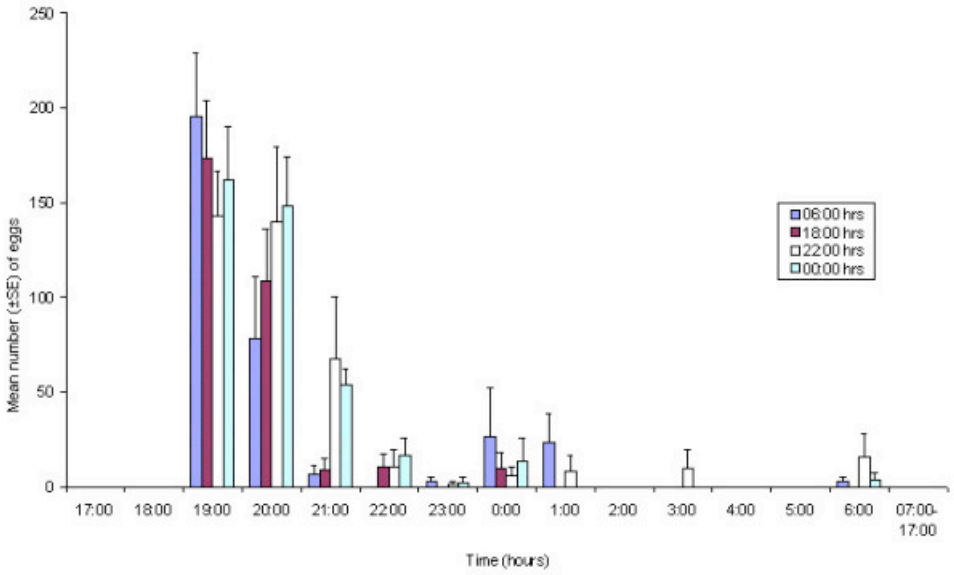
- **Daily oviposition patterns of *Anopheles gambiae* s.s. on different oviposition substrates in a no-choice bioassay.** Mean percentage (± SE) of the total eggs laid on each of three different oviposition substrates during 1-h time intervals. n = 24 cages containing five females each. Mosquitoes in each cage were exposed to one type of substrate under a natural LD cycle (sunset at 18:00).



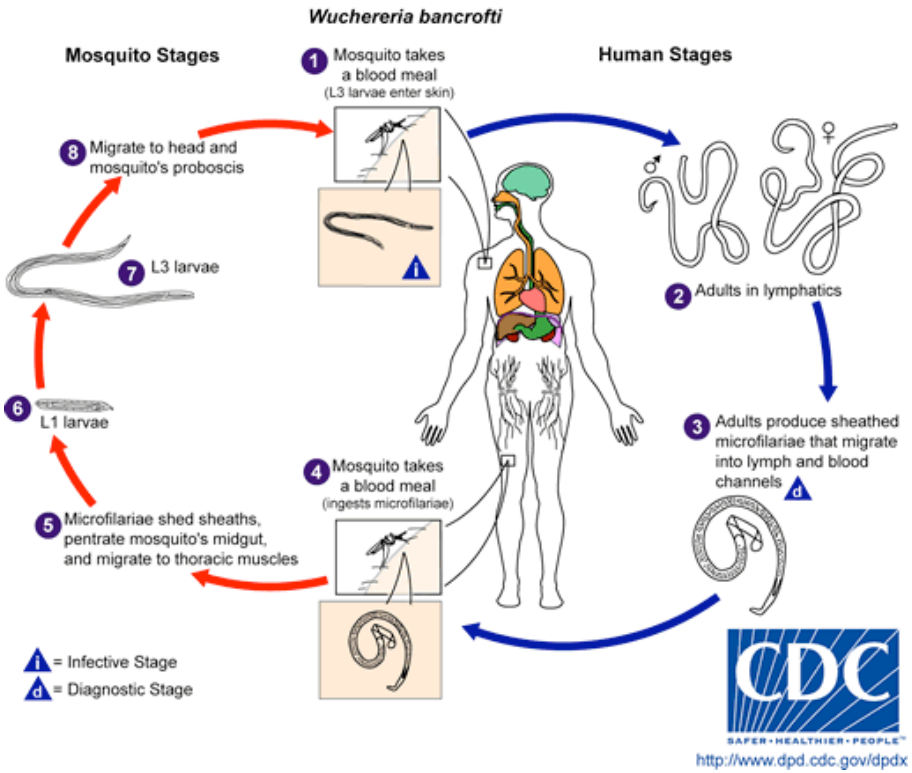
Daily oviposition patterns of the African malaria mosquito *Anopheles gambiae* Giles (Diptera: Culicidae) on different types of aqueous substrates

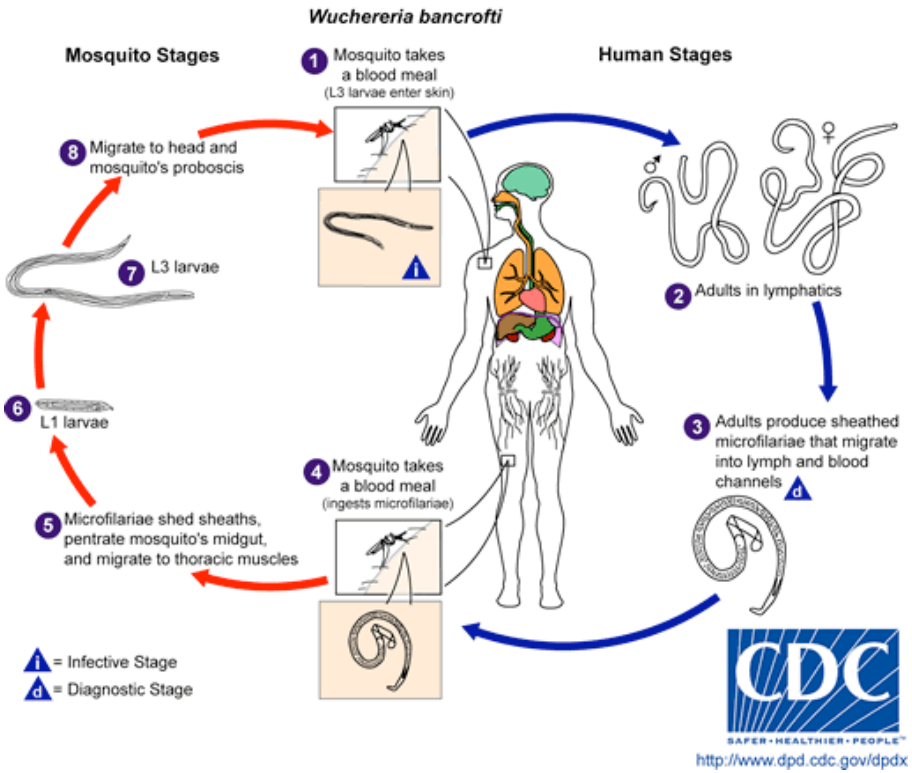
J Circadian Rhythms. 2004; 2: 6. Sumba et al.

- **Daily oviposition patterns of *Anopheles gambiae* s.s. fed at different times**. Mean number (± SE) of eggs oviposited during 1-h time intervals. n = 8 cages containing five females each. Mosquitoes were kept under a natural LD cycle (sunset at 18:00).



W. bancrofti & B. malayi Lifecycles



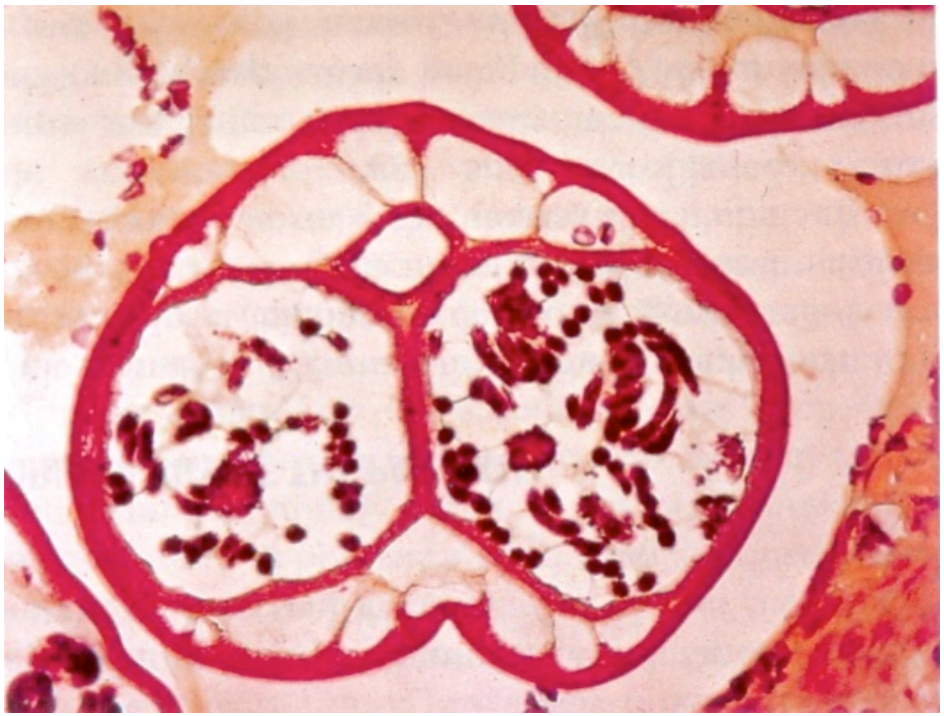


Bancroftian Filariasis: Adult Worms

- **Adult worms occupy the lumen of the lymphatic vessels.**
- **Female typically measures 4-10 cm.**
- **Male typically measures 2-4 cm.**

Bancroftian Filariasis: Adult Worms

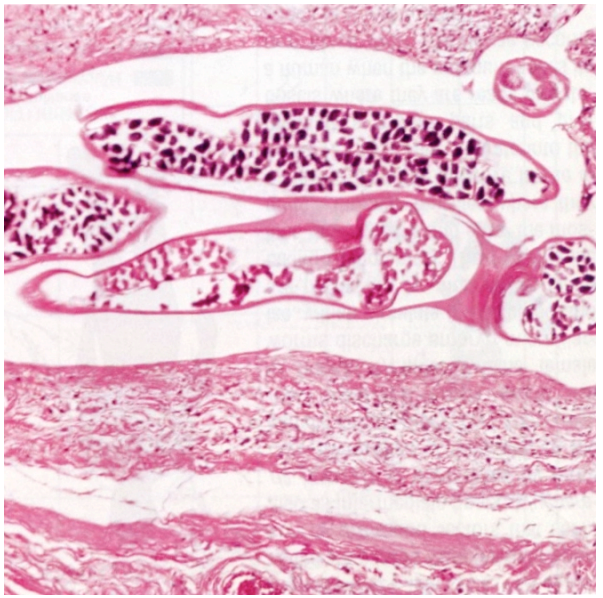
- **Have been found in all sites within the lymphatic circulation.**
- **May also occupy the adjacent subcutaneous tissue.**
- **Most commonly live in the lymphatics of the lower and upper extremities of the male genitalia.**

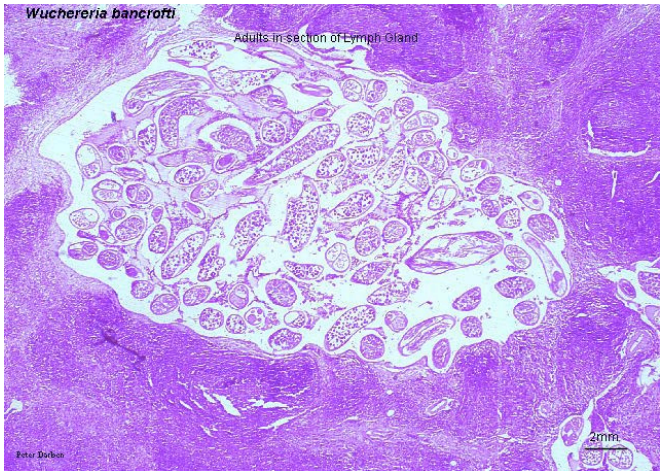


Cross-section of a gravid femal *W. bancrofti* in the epididymis .

Bancroftian Filariasis: Adult Worms

- **After mating, the female worm can release 10,000 or more microfilariae per day (L1).**
- **270 *μ*m-10 *μ*m.**
- **Encased in a sheath comprised of chitin.**
  - **Possibly an eggshell remnant.**

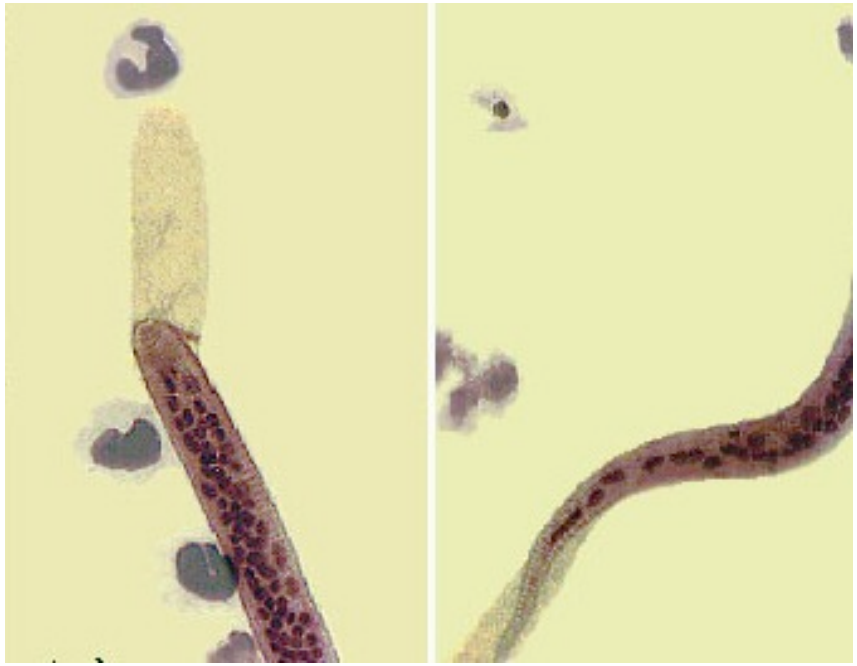




Bancroftian Filariasis: Microfilaria

- **Microfilaria contain nuclei that cover the majority of the body.**
- **Unlike, *Brugia* sp., W*. bancrofti* does not have tail nuclei.**

Bancroftian Filariasis: Microfilaria Who's who?



Bancroftian Filariasis: Microfilaria

- Microfilariae migrate from the lymphatic circulation into the bloodstream.
- Typically present in large numbers in the peripheral blood only at night in most endemic areas of the world.
- During the day, the microfilariae aggregate in the capillaries of the lungs when the activity of the host is increased.
- The diurnal periodicity pattern characteristic of the South Pacific strain has not been explained.
  - Periodicity defined as a circadian rhythm.

Bancroftian Filariasis: Microfilaria

- Once taken up by the mosquito vector, larvae molt 3 times and by 10-20 days become infective L3 larvae.
- After a blood meal, the mosquito removes the mouthparts form the skin, larvae crawl into the open wound.
- Development to adulthood takes approximately 1 year.
  - Adult longevity 5-8 years but a 40-year life spans has been reported.

Bancroftian Filariasis: Pathogenesis

- Pathogenesis may result from a sequence of host-mediated immunopathologic events that occur in response to dead and dying adults within the lymphatics.
- In contrast, adult living worms and microfilariae suppress these responses.
  - Prostaglandin E2
- The processes of associated with lymphangitis can take years to develop and therefore not commonly seen in children.
  - Individuals visiting endemic regions for short periods usually do not develop lymphedema, even though they may have microfilaremia.

Bancroftian Filariasis: Pathogenesis

- In the absence of worm-mediated immune suppression, a series of inflammatory reactions causing alterations of the lymphatic walls takes place.
- After intense lymphocytic infiltration, the lumen of the vessel eventually closes and worm remnants calcify.
- The blockage of lymphatic circulation continues in heavily infected individuals until most major lymph channels are occluded, causing lymphedema in the affected region.
- Smooth muscle hypertrophy also occurs in the immediate region.

Bancroftian Filariasis: Pathogenesis

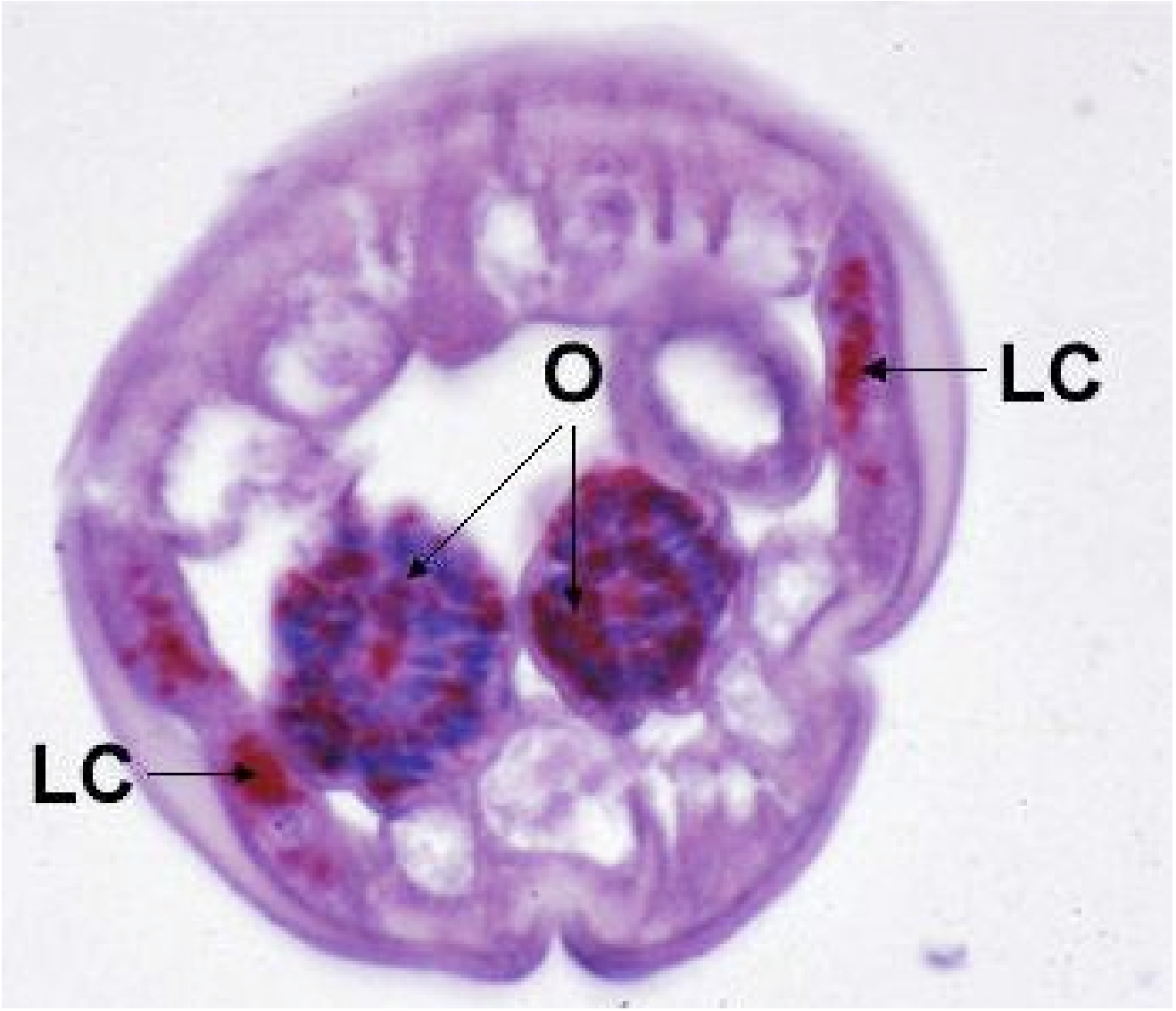
- **Not all patients with chronic exposure of infective *W. bancrofti* develop overt clinical disease.**
  - **Suggested that different populations are prone to Th1 or Th2 biases in their cellular inflammatory responses.**
    - **Asymptomatic-Th2**

Bancroftian Filariasis: Pathogenesis

- **Two major 0bservations within the last lymphangitis, lymphedema and elephantiasis occurs.**
  - **Ultrasound studies conducted in LF-endemic regions showed that the living adult worms elicit lymphatic dilatation which may lead to chronic changes.**
  - **Secondary bacterial and fungal infections contribute significantly to the chronic pathology of elephantiasis.**
    - **Wolbachia**
      - **Endotoxin-like molecules several years have challenged the conventional thinking about how the pathologic sequence of events leading to**

Wolbachia staining

Positive staining of *Wolbachia* in the lateral cords (LC) and oocytes (O) (magnification x 160).



Bancroftian Filariasis: Clinical Disease

- **Asymptomatic infection.**
  - **Majority of residents living in an endemic area are 'asymptomatic.'**
    - **Harbor circulating microfilariae.**
  - **These so-called asymptomatic patients have been observed to exhibit subtle pathology when examined more closely by ultrasound.**
    - **More advanced disease begins at this stage.**
    - **This dilatation initiates a subsequent series of events that results in the chronic clinical manifestation of LF.**
    - **In some cases, the dilated vessels rupture to produce chyluria (presence of lymph in the urine) and chylocele (cyst-like lesion resulting from the effusion of chyle).**

Bancroftian Filariasis: Clinical Disease

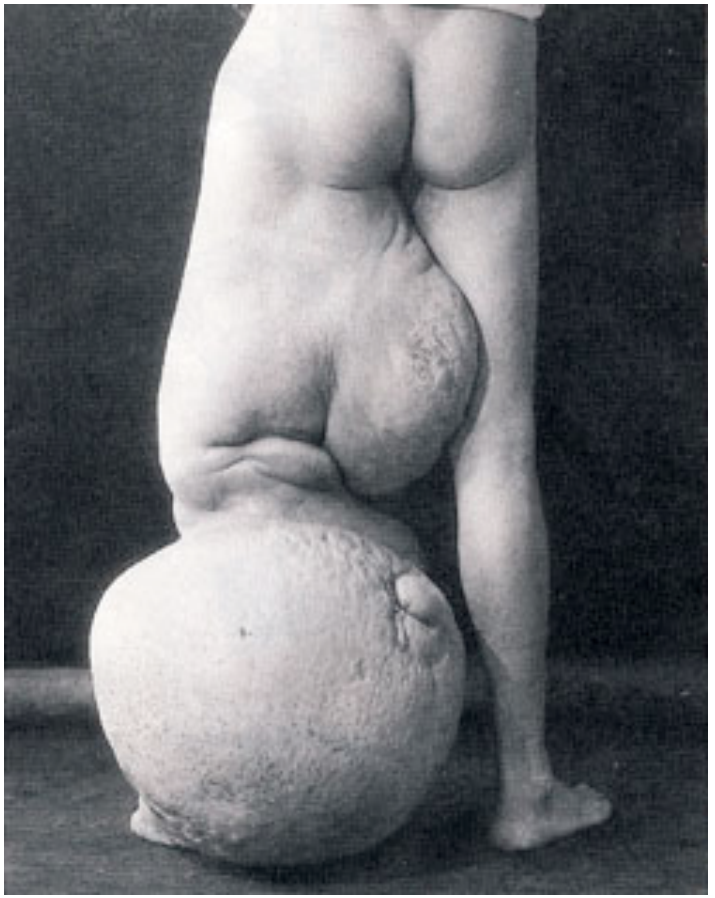
- **Acute Lymphadenitis and Filarial Fevers**
  - **Death of the adult worm causes the next step in the progression of disease by producing an acute inflammatory response that manifests as acute lymphadenitis (lymph node inflammation).**
    - **In endemic area this occurs typically during the teen years.**
    - **Episodes of painful swellings can last up to a week and commonly recur.**
    - **Secondary bacterial infections may also result.**

Bancroftian Filariasis: Clinical Disease

- **Tropical Pulmonary Eosinophilia**
  - **Occurs frequently in southern India.**
  - **More common in young adult men.**
  - **Characterized by high IgE levels.**
  - **Nocturnal asthma.**
    - **Pathogenesis is related to local immune response to microfilariae in the pulmonary vasculature.**
      - **Eosinophils**

Bancroftian Filariasis: Clinical Disease

- **Elephantiasis**
  - Skin becomes doughy and exhibits some degree of pitting, though it is rather firm.
  - *W. bancrofti* infection can be distinguished from lyphedema caused by *B. malayi* in that infection by the former produces swelling of the entire limb, whereas the latter involves only the area below the knee.



Bancroftian Filariasis: Clinical Disease

- **Disease of the male genitalia is an important clinical feature associated with *W. bancrofti* infection.**
- **Inflamed scrotums may weigh up to 10 kg.**

Bancroftian Filariasis: Diagnosis

- **LF suspected in an individual living in an endemic region.**
- **Microscopic observation of microfilariae in the blood.**
  - **If a heavy enough infection occurs, visualization can be done using a thin blood smear.**
  - **Filter blood through 0.45 *μ*m filter to collect microfilaria.**
  - **Monoclonal assay tests.**
    - **Rapid format card test.**

Bancroftian Filariasis: Treatment

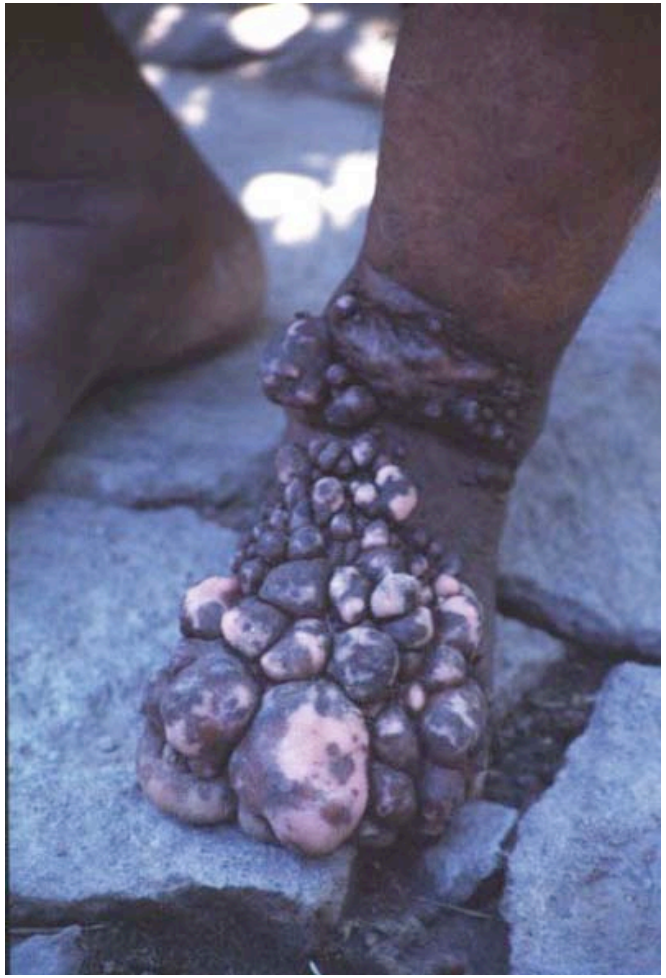
- **All patients should be treated.**
  - **'Asymptomatic' patients have abnormal lymphatics.**
  - **Treatment may prevent subsequent lymphatic damage.**
- **Diethylcarbamazine (DEC).**
- **For *W. bancrofti* infections, DEC treatment can reduce microfilariae loads by 90% in one month.**
- **Affects microfilariae primarily.**
  - **DEC only partially effective against the adult worm, therefore multiple treatments needed.**

Bancroftian Filariasis: Treatment

- **DEC treatment is associated with fever.**
  - **Linked to parasite disintegration.**
- **Ivermectin also kills microfilariae of *W. bancrofti* but appears to have no macrofilaricidal properties.**
- **DEC + Albendazole**

Bancroftian Filariasis: Treatment

- **Aside from the use of DEC, treatment modalities that may help to improve the chronic sequelae of LF include hygienic regimens that help prevent bacterial infections .**
- **Antibiotic treatment.**
- **Antifungals.**

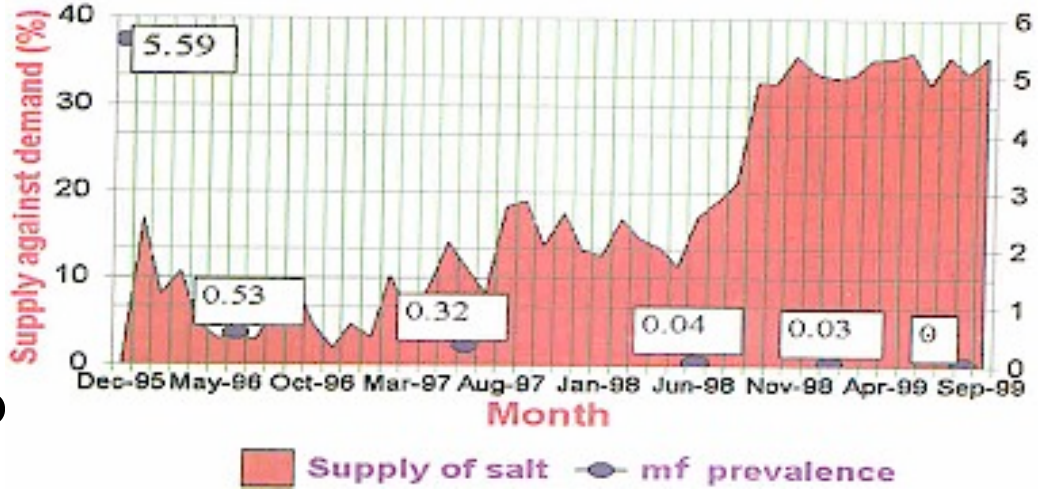


Prevention and Control

- **The Global Alliance to Eliminate Lymphatic Filariasis.**
  - **Created in 2000**
  - **Private/Public alliance**
  - **Annual treatments have jumped up from 25 million in 12 countries in 2000 to 122 million in 26 countries in 2003 to 250 million in 39 countries in 2004.**
  - **In 2005, 381 million people received the necessary drugs.**

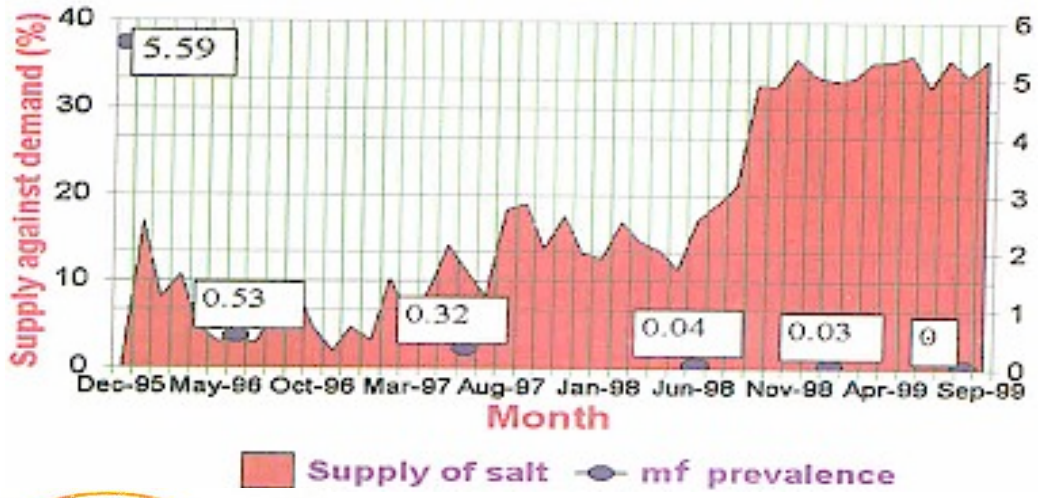
Prevention and Control

- The mass DEC fortified salt program to control filariasis was launched in 1996 to cover the Kanyakumari district of Tamil Nadu.
- 1886 villages.
- Fortification of salt with DEC (0.2% w/w) was done by the Tamil Nadu Salt Corporation and supplied to the district civil supply department. Distribution of salt to the community was carried out through Fair Price Shops under the Public Distribution System (PDS).



Prevention and Control

- **Microfilaria prevalence reduced to zero after 44 months of DEC salt introduction (August 1999).**



Prevention and Control

- **The reason that the DEC + Albendazole combination was changed to the Albendazole + Ivermectin combination is that in many regions co-infections with *Onchocerca volvulus*, the toxicities caused by DEC were too great.**

- http://www.filariasis.net/films_videos/kill_or_cure.mp4