Disease: Lymphatic Filarasis

856 million people exposed to this disease in 56 countries
120 million infections worldwide (underestimate)
40 million of these people are disfigured
Introduction to Lymphatic Filariasis in Nigeria
Disease: Lymphatic Filariasis
Filarial nematode
Next week & Final Exam

1. Graduate Student Presentations
   3 on Tuesday, 3 on Thursday
   Attendance will be taken and figure into your participation grade

2. Student presentations will be posted on website (so no need to take notes)

3. For the final exam (May 7: 8 am in here) - you will select any two student topics to answer questions
   Details will be provided on study guide (posted next week)
Disease: Lymphatic Filariasis (aka Elephantiasis)

Filarial Nematode: *Wuchereria bancrofti*

Characteristics

- Lives in Lymphatic System (feeds on lymph and WBCs)
- Transmitted by mosquito vector
- Sexual size dimorphism
  - Male (1-2 in) & Female (3-4 in)
  - Females are ovoviviparous
- Lives for 6-8 years
- Humans are the only definitive host
  - No animal reservoirs
W. bancrofti - Vector = Mosquito
Mosquito takes a blood meal

L3s drop from proboscis to open wound

L3 move from integument to afferent vessel of lymph nodes

L3s eat and molt twice to adult stage (6-12 months)
Mate and live for 6-8 years
Females can be reproductive their entire lives

L1s circulate mostly at night (10 pm – 2am) - L1s are sucked up on next bite

L1s migrate to the thoracic duct ➔ blood circulation

Females release L1s

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Where the filarial nematodes live

- Mosquito – Vector & Intermediate Host
- Human – Definitive Host
Filarial Infection of Mosquitoes
1. L1s enter & penetrate gut
2. Leave gut and migrate to **thoracic muscles** (wings)
3. Consume glycogen (can affect flight)
4. Molt twice to L3 (7-14 days)
5. L3 migrate to the proboscis
6. “Drill” out of the proboscis
Lymphatic Filariasis – *Wuchereria bancrofti*

Lives in the lymphatic system
Humans – Lymphatic System

1. Lymph vessels, lymph organs, and lymph nodes that parallel our blood vascular system
2. Recollect fluids that leak from blood vessels
3. Lymph consists of water, sugars, proteins, lipids, WBCs
Lymph Nodes
Wuchereria bancrofti
Disease: Lymphatic Filariasis

3 Pathological Phases of the disease

1. **Asymptomatic Phase**
   A. 1\textsuperscript{st} infection onward (last months to years) – L3, L4, Adults
   B. No symptoms
   C. Some pathologies are occurring
      - Females are releasing CFAs (circulating filarial antigens)
      - **Microfilaremia** may be occurring (microfilarial antigens)
      - Female E-S system secretes chemicals that downregulate immune system:
        - **Depresses** APCs
        - **Hyporesponsiveness of the immune system**
          - This doesn’t mean no response, only that it is a very weak one
Disease: Lymphatic Filariasis

2. Inflammatory Phase
   - Begins months or years after initial infection
   - Immune system “wakes up”

**Question: Why?**

**Answer: Change in the types of E-S secretions**

Two new CFAs secreted:

1. Wb123 (male & female)
2. Og4C3 (female only)

**Results**

- Antibody production
- **Eosinophilia** (pathology)
  - Eosinophil secretions toxic to nematodes
  - Some nematodes die -> Release antigens
  - Host tissue damage by eosinophils
    - Inflammation of afferent lymph node vessels
Disease: Lymphatic Filariasis

2. Inflammatory Phase Symptoms

**Pathology:** Temporary Lymphodema (both host sexes)
- swollen lymph nodes (symptom due to blockage)
- painful lymph nodes (symptom – due to eosinophils)

**Other symptoms:** chills, fever

All cases of lymphodeam during this phase are temporary = 1-2 weeks for each episode, but can reoccur over months or years.
Disease: Lymphatic Filariasis

3. Obstructive Phase

Pathology = Persistent Lymphoedema

1. Worm blocks flow of afferent vessels
   A. Lymph leaks from afferents
2. Constant CFAs cause efferents to permanently close
   A. Leakage from lymph nodes
   B. Lymph leaks from efferents
3. Fibroblasts migrate to lymph areas and begin secreting collagen (for structural support)
4. Sex specific pathologies
Sex- specific pathology - Men Only

Males: **Scrotal Hydrocele** – increase of lymph in scrotum

**Symptoms:** scrotal and penial swelling, hypoelastic skin, pain

**Treatment:** Surgical
Male Specific

**Inguinal hydrocele** – accumulation of lymph in the inguinal lymph nodes

**Symptoms** – swelling above the genital area, bulging skin, pain

**Treatment:** Surgical
Specific Pathology – Obstructive (women & men)

Persistent Lymphoedema of the legs – accumulation of lymph in the legs

Symptoms – swollen legs (permanent), bulging hypoelastic skin, pain

Treatment: Surgical (drainage is possible but not complete)
Specific Pathology - Females

**Persistent Lymphoedema of the breast** – unilateral enlargement of the breasts

**Symptoms**: swelling of the breast, hypoelastic skin, pain

**Treatment**: surgical (drainage is possible but not complete)
Obstructive Phase: Sex specific persistent lymphodema

**Secondary Disease = Elephantiasis**

A. Extreme hypoelasticity of the skin (saggy skin)
B. Inflammatory reaction
   
   **Keratinocytes** – secrete keratin (protein) into the epidermis and dermis
C. Leads to a thickening and wart–like appearance of the skin
Bilateral persistent lymphoedema of the legs

Unilateral elephantiasis
DIAGNOSIS

Want to detect prior to showing symptoms
Want to stop disease before it spreads to others

1. **Finger Prick Test** = Blood sample to look for microfilaria

**BENEFITS:**
- Inexpensive ~ $0.05 per sample
- Easy to perform

**DRAWBACKS:**
- Low sensitivity (difficult to find microfilariae)
- False negatives: no worms = no infection
- How can there be no worms in an infected person?
  - Females are not reproducing
- Test was performed during the day
- Microfilaremia: 10pm to 2 am
DETECTION of LF

2. ELISA
   Detects antibody to CFA: **Og4C3** (CFA)

**Benefits:** Extremely sensitive (detect low levels of antibodies)
   - Can be done in Phase 1 (Asymptomatic phase)
   - Females are suppressing antibody respond but not eliminating it

**Drawbacks:** Expensive
   - Technical expertise
   - Laboratory (not field work)
DETECTION of LF

3. ICT card – Immunochromatographic Card Test

Drop of patient’s blood

Detect Wb123 antigen
Detection of Lymphatic Filariasis

3. ICT card – immunochromatographic card test

Benefits –
- High sensitivity
- Easy to use
- Instant (10 mins until reaction)
- Can be performed anytime

Drawbacks –
- Only indicates adult females
- Low or no sensitivity to males or L1s
- Relatively expensive ($1/sample)
Treatment

Treatment is mainly prophylactic (stops transmission)

Treatment is done through MDA: Mass Drug Administration
Single Dose:
Albendazole (stops embryonic development) + Ivermectin (kills microfilariae, shortens lifespan of adults)
Dosage has to continue for 5-8 years (lifespan of the adults)
- blood is monitored for L1s
- ELISA and ICTs may also be done for monitoring infection

Surgery is the only treatment for obstructive phase symptoms
Epidemiology of Lymphatic Filariasis
Mostly equatorial - mosquitoes are tropical species
Main Vector: *Anopheles gambiae*
Comes from sub-saharan Africa
Control Strategies for LF

1. MDA
   - ELISA and ICT cards may be used during MDA to monitor select populations during treatment
2. Bed netting (least expensive) to stop mosquitoes
3. Spray insecticides for mosquitoes

PROBLEM
Like many diseases, medications only treat for a limited time and during their use. They do not prevent reinfections.