Helminths (Parasitic worms)

- Kingdom Animalia
  - Phylum Platyhelminths
    - Trichurida
    - Ascarida
    - Rhabditita
  - Phylum Nematoda
    - Strongylida
    - Spirurida

Hookworms

- *Ancylostoma* was found throughout mines in Europe (at the turn of the last century, severe hookworm disease was an official occupational hazard in German coal mines eligible for workman’s compensation)
- Hookworms were widespread in the Southern USA (read Jimmy Carter’s biography for detail on hookworm and other infectious diseases in rural Georgia)
- 1972 12% of school children from rural coastal Georgia tested positive for hookworm infection
History of Disease

Antonie Dubini* and the Saint Gotthard Tunnel
Hookworm Epidemic of 1880

Length - 15 kilometers
Depth - 1,700 meters


Circa 1920
Unsanitary defecation habits
Lack of shoes, or not wearing shoes
Southern US developed an undeserved reputation for apathetic, lazy people
The Rockefeller Commission

- Rockefeller foundation - Sanitary Commission 1909
  - Inspected ~190,000 households
  - Only 412 had sanitary latrines
- Hookworm is basically responsible for development of our USPHS

JDR established a sanitary commission (1909-1915) headed by Charles Wardell Stiles to look into the matter of "southern laziness".

Economic recovery was slow following the Civil War, and J. D. Rockefeller wanted to know why!
The Pit Privy

Distribution and installation began in the 1920’s following The Rockefeller Sanitary Commission Report to Congress.

Height to which hookworm larvae can crawl = 4 feet.

Prevention and Control

“To prevent this (hookworm) it is only necessary to prevent soil pollution with the feces of infested individuals”

Hookworm Disease

Asa Chandler, 1929

Greatest single invention of the 20th century!
May explain the lower economic status in many developing countries.
- Lethargic population (anemic) can't produce as many goods as healthy population
- Proper sanitation has eliminated it from most of U.S., Caribbean, and many other areas.
  - Latrines and treatment was provided by J.D. Rockefeller and lead to formation of Rockefeller Foundation
- However, incidence worldwide has increased in last 50 years
  - 25% of world population still infected.
Hookworm mouths

- Head is slightly bent (Hookworm)
- Well developed buccal cavity with teeth or plates.

Bursate rhabditians

- Nearly all male members of this family have broad copulatory bursa at posterior end
- Used as taxonomic identification
Hookworm infections

- Four Larval stages.
  - J1 and J2 are free-living
  - J3 burrows into definitive host skin and migrates to intestine
- Require warm, wet climate and shady areas
  - J1 and J2 can't tolerate drying, freezing, or exposure to sun.
- Adults actively graze on intestinal mucosa

Hookworm Life Cycle
Ancylostoma duodenale

- **Definitive Host**: Humans
- **Intermediate Host**: None
- **Geographic Distribution**:
  - southern Europe, northern Africa, India, southeast Asia, China.
  - Scattered locations in US, Caribbean Islands, and South America.
  - Found in 1000 yr mummy in Peru
    - May not have been brought over with slave trade.
  - Frequently found in mines well north of freeze line
    - Provides stable climate, no freezing, no sun.
- **Transmission**: J3 burrows into skin.

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**Ancylostoma duodenale**

- **Pathology**: Due to damage of tissue during migration of J3 larvae and ingestion of intestinal mucosa by J4 larvae and adults
- **Symptoms**: Usually asymptomatic. May cause hookworm disease.
  - We will discuss Hookworm disease later.
- **Diagnosis**: Eggs in feces
- **Treatment**: Mebendazole
**Ancylostoma duodenale**

- **Notes:** First hookworm for which the life cycle was determined
  - In 1896 Arthur Looss was dropping cultures of worm into mouth of guinea pigs
  - He accidentally dropped a drop on his hand.
    - The area began to itch and turned red.
    - He wondered if the worm could have penetrated skin
  - He then started sampling his own feces
    - Found hookworm eggs in feces a few weeks

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**Necator americanus**

- **Definitive Host:** Humans
  - Most common human hookworm
- **Intermediate Host:** None
- **Geographic Distribution:** Indigenous to Africa, India, southeast Asia, China, islands of sw Pacific.
  - First found in Brazil and Texas
  - Probably brought to New World with slave trade
- **Transmission:** J3 burrows into skin.
**Necator americanus**

- **Pathology:** Due to damage of tissue during migration of J3 larvae and ingestion of intestinal mucosa by J4 larvae and adults
- **Symptoms:** Usually asymptomatic. May cause hookworm disease.
  - We will discuss Hookworm disease later.
- **Diagnosis:** Eggs in feces
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**Hookworms**

- Symptoms of hookworm infection vary by species and number of worms.
  - Most infections are asymptomatic.
  - *A. duodenale* causes more damage than *N. americana*
  - Nutrition of host also important in determining the degree of symptoms
  - Race also affects symptoms
    - Blacks are more resistant to infection than whites
Hookworm Disease

- Hookworm infection does not always lead to hookworm disease.
  - Most infections are asymptomatic
- Development and severity of Hookworm disease depends on three factors.
  - Number of worms present
  - Species of hookworm
  - Nutritional status of the host.

Hookworm infections

- Number of worms
  - Less than 25 *N. americanus* are asymptomatic
  - 25-100 light symptoms
  - 100-500 moderate symptoms
  - 500-1000 severe symptoms
  - >1000 are frequently fatal.
- Species of worm
  - *A. duodenale* sucks more blood so fewer worms required to cause symptoms
- Nutritional status of Host
  - Poor nutrition leads to worse symptoms.
  - Suppresses immune system
  - Fewer nutrients to repair damage
Incidence of Hookworm disease

- Unsanitary conditions: feces released into soil
  - Repeated contamination of soil
  - Repeated visit to same area to defecate increases transmission
- Environmental conditions: Warm, humid, climate without freezing, proper soil
  - Must have loose, aerated soil, with lots of humus.
  - Warm, humid climate necessary for the worm to develop in soil in shady areas
- Exposure of skin to soil
  - Must have access to skin so it can burrow into the skin.
- Race
  - In general, white americans were 10 times more susceptible to hookworm disease than black americans.
    - Exact mechanism isn’t clear
  - Gave rise to image of “poor white trash” in southern U.S.
    - Whites were frequently victims of high hookworm loads
      - Made them weak, apathetic, and lethargic
    - Black americans of the same socioeconomic situation were resistant to hookworm disease
      - They were industrious and hard-working

Phases of Hookworm Disease

- Cutaneous Phase
  - Occurs when larvae burrow into skin and enter vessels
  - Localized allergic reaction
- Pulmonary Phase
  - Caused by larval migration through lungs and up trachea
  - Usually asymptomatic but can cause dry coughing and sore throat
  - May allow for secondary bacteria infections
  - Pneumonia can occur in very large infections
- Intestinal Phase
  - Larvae and adults suck blood from intestinal lining
    - 0.03 ml/day for *N. americanus*
    - 0.26 ml/day for *A. duodenale*
  - Bleeding into intestines can occur
    - Most iron is reabsorbed in intestines
  - Iron deficiency anemia can result if dietary intake isn’t sufficient to replace the lost iron
    - Severity depends on worm load and dietary intake.
Hookworm disease

- Chronic Heavy Infections
  - Patient suffers from severe protein deficiency
    - Can cause dry skin and hair, spoon nail, edema, potbelly, delayed puberty, metal dullness, heart failure and death.
  - Hookworms don’t block absorption of nutrients
    - Disease complicated by malnutrition
    - Loss of protein and iron to worm is catastrophic to those subsisting on minimal diet
  - Prolonged exposure during childhood can lead to growth retardation, intelligence and cognitive impairments: “laziness”

Hookworm and Malaria

Geographic Overlap

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<thead>
<tr>
<th>Geographic Overlap</th>
<th>Anemia Co-Morbidity</th>
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Brooker S et al.
Feasibility of a Hookworm Vaccine

Lines of Evidence with L3 (third-stage infective larvae)

- Success vaccinating dogs against canine hookworm infections (*Ancylostoma caninum*) with L3
- Trickle doses of live L3 or live L3 attenuated by ionizing radiation (X-rays, gamma-rays, Ultraviolet irradiation)
- Vaccine protection mediated by L3 secreted antigens

Hotez et al. *Int J Parasitol* 2003; 33: 1245-58

Cutaneous Larval Migrans

- A.K.A. Creeping eruption
- Human occasionally get infected with hookworm larvae from dogs and cats
- L3 larvae penetrate skin of the wrong host
- The larvae can not establish a productive infection
- Wander about in the subcutaneous tissue, causing significant inflammation and painful swelling
Cutaneous Larval Migrans

- Larvae die during migration
  - Body reacts to worm and creates nasty skin irritation where ever the worm migrated.

- Treat with closantel
  - Anthelmintic which associates with plasma albumin and is useful for the control of sheep parasites, such as *Haemonchus contortus*, that ingest blood.

- *A. braziliense* L3 are the most common cause
  - *A. caninum* as well.
  - Many other hookworms can cause it.