Lecture 4: Emerging Parasitic Helminths part 2: Intestinal Nematodes

Presented by Matt Tucker, M.S, MSPH
mtucker@health.usf.edu

Learning Objectives

- Be familiar with general prevalence of nematodes and life stages
- Know most important soil-borne transmitted nematodes
- Know basic attributes of intestinal nematodes and be able to distinguish these nematodes from each other and also from other types of nematodes
- Understand life cycles of nematodes, noting similarities and significant differences
  - Know infective stages, various hosts involved in a particular cycle
  - Be familiar with diagnostic criteria, epidemiology, pathogenicity, & treatment
- Identify locations in world where certain parasites exist
- Note common drugs that are used to treat parasites
- Describe factors of intestinal nematodes that can make them emerging infectious diseases

Readings-Nematodes

- Ch. 11 (pp. 288-289, 289-90, 295 [box 11.1], 298-99, 299-301, 304 [box 11.2])
- Ch. 14 (p. 365, 367 [table 14.1])

Monsters Inside Me

- Just for fun:
  - Baylisascaris procyonis (Baylisascaris procyonis, raccoon zoonosis):
    Background: http://animal.discovery.com/invertebrates/monsters-inside-me/baylisascaris-raccoon-zoonosis
  - Strongyloides stercoralis (Strongyloides stercoralis, the threadworm):
    Background: http://animal.discovery.com/invertebrates/monsters-inside-me/strongyloides-stercoralis-threadworm/
  - Angiostrongylus cantonensis (Angiostrongylus cantonensis, the rat lungworm):

On the Menu

Intestinal Nematodes

- Ascaris lumbricoides
- Baylisascaris procyonis
- Hookworms
- Trichuris trichiura
- Capillaria spp.
- Strongyloides stercoralis
- Angiostrongylus spp.
- Anisakis simplex

Nematodes (Roundworms):

- Mostly free living (500,000 species)
- ~15,000 are parasitic
- Most nematodes are dioecious (either male or female), with males commonly being smaller than females
- Eggs, larvae (molts), and adults
- Moderately long-lived worms
  - Ascaris (1 yr)
  - Trichuris (8-16 yr)
- Autoinfection may enhance persistence (Strongyloides)
Nematodes impact human life in many important ways

- Nematodes cause numerous human diseases
- Nematodes are abundant pathogens in life-stock and pets
- Nematode are important pests of many crops
- Nematodes provide powerful genetic models to study the basis of development, aging and many diseases including cancer

Nematodes Stages

- In the vast majority of nematode life cycles, the stage that passes from the definitive host is not the same stage that is infective for another definitive host.
- The nematode stage (usually an egg or L1) that passes from a definitive host must develop through to a stage (usually the L3) that can then infect another host.

Nematode Stages

<table>
<thead>
<tr>
<th>Nematode Stages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-parasitic</td>
</tr>
<tr>
<td>Parasitic</td>
</tr>
<tr>
<td>Post-parasitic</td>
</tr>
</tbody>
</table>

Nematodes of medical importance

- ‘Unholy trinity’: *Ascaris lumbricoides*, *Trichuris trichiura*, and the hookworms
  - The global burden of disease is an estimated 22.1 DALYs to hookworm, 10.5 million to *A. lumbricoides*, 6.4 million to *T. trichiura* = total of 39 million life years (Kirwan et al. 2009)
- Major problem for children 5-14 years old
- Cause morbidity by affecting nutritional equilibrium inducing intestinal bleeding, competing for absorption of micronutrients, reducing growth and food intake
- Fecal-oral route

Soil-transmitted nematodes

- ‘Unholy trinity’: *Ascaris lumbricoides*, *Trichuris trichiura*, and the hookworms
- The global burden of disease is an estimated 22.1 DALYs to hookworm, 10.5 million to *A. lumbricoides*, 6.4 million to *T. trichiura* = total of 39 million life years (Kirwan et al. 2009)
- Major problem for children 5-14 years old
- Cause morbidity by affecting nutritional equilibrium inducing intestinal bleeding, competing for absorption of micronutrients, reducing growth and food intake
- Fecal-oral route
Common characteristics of *Ascaris* spp.

- Cause the most common helminth infections
  - An estimated 1.5 billion persons are infected (1/4 world’s population?)
- Two main populations
  - *A. lumbricoides*
  - *A. suum*
- Adult worms can lay up to 200,000 eggs per day

*Ascaris* life cycle

- Worldwide distribution
- High prevalence in tropical and subtropical regions, and areas with inadequate sanitation.
  - In the U.S., approximately 4 million people are infected.
    - High-risk groups: international travelers, recent immigrants (especially from Latin America and Asia), refugees, and international adoptees.
    - Indigenous to the rural southeast, where cross-infection by pigs with the nematode *Ascaris suum* is thought to occur.
- Transmission enhanced by asymptomatic carriers that continue to shed eggs for years

*Ascaris*: Epidemiology

- Adult worms usually cause no acute symptoms.
- High worm burdens may cause abdominal pain and intestinal obstruction.
- Migrating adult worms may cause symptomatic occlusion of the biliary tract or oral expulsion.
- During the lung phase of larval migration, pulmonary symptoms can occur (cough, dyspnea, hemoptysis, eosinophilic pneumonitis).
- Abdominal complications—penetration of intestine or appendix, peritonitis leads to death
- Tx with albendazole, mebendazole, ivermectin

Ascariasis

- Dx—eggs in stool
- Proper sanitation
- Chemotherapy at regular intervals
- Health education
- Avoiding areas fertilized with pig or human feces
  - Eggs can be long lived and resistant to chemicals, UV light

Diagnosis/Prevention/Control

Ecology of infection with *Ascaris* and *Trichuris*
Baylisascaris procyonis

- Large intestinal nematode of raccoons
- Transmitted by fecal-oral contamination
- First infection reported in 1984
- Humans and other mammals are accidentally infected and disease can be fatal
  - Young children
- Over 50 species of birds and mammals can act as intermediate or paratenic host

Geoelastic Distribution

- U.S.-infected raccoons are common in the Middle Atlantic, Midwest, Northeast regions, and are well documented in California and Georgia.
- Proven human cases have been reported in California, Oregon, New York, Pennsylvania, Illinois, Michigan, and Minnesota, with a suspected case in Missouri.
- *B. procyonis* has a widespread geographic distribution, with infection rates as high as 70% in adult raccoons and exceeding 90% in juvenile raccoons
- Predator animals may become infected by eating a smaller animal that has been infected with *Baylisascaris*.

Baylisacariasis

- The severity of the disease depends to a large extent on how many eggs are ingested.
- Human infections can be asymptomatic, yet infections often result in severe disease manifestations
  - Larvae that continue to grow and wander in body
    - Penetrate the gut wall and migrate to a wide variety of tissues (liver, heart, lungs, brain, eyes)
  - Infection can result in visceral larva migrans (VLM) or ocular larva migrans (OLM)
  - Larvae tend to invade the spinal cord, brain, and eye of humans, resulting in permanent neurologic damage, blindness, or death
    - Symptoms appear 1-3 weeks after infection, can take as long as 2 months

Baylisacariasis: OLM, CNS involvement

Reported human cases of larval *Baylisascaris procyonis* infection in U.S.

<table>
<thead>
<tr>
<th>State</th>
<th>Location</th>
<th>Age</th>
<th>Sex</th>
<th>Clinical</th>
<th>Outcome</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penn.</td>
<td>Penn.</td>
<td>11 m</td>
<td>Male</td>
<td>Encephalitis</td>
<td>Focal</td>
<td>17</td>
</tr>
<tr>
<td>Iowa</td>
<td>Iowa</td>
<td>18 f</td>
<td>Female</td>
<td>Encephalitis</td>
<td>Peri</td>
<td>18</td>
</tr>
<tr>
<td>New York</td>
<td>New York</td>
<td>31 m</td>
<td>Male</td>
<td>Encephalitis</td>
<td>Peri</td>
<td>14</td>
</tr>
<tr>
<td>Calif.</td>
<td>Calif.</td>
<td>20 y</td>
<td>Male</td>
<td>Encephalitis</td>
<td>Peri</td>
<td>21</td>
</tr>
<tr>
<td>Calif.</td>
<td>Calif.</td>
<td>40 y</td>
<td>Male</td>
<td>Encephalitis</td>
<td>Peri</td>
<td>22</td>
</tr>
<tr>
<td>Calif.</td>
<td>Calif.</td>
<td>60 y</td>
<td>Male</td>
<td>Encephalitis</td>
<td>Peri</td>
<td>30</td>
</tr>
<tr>
<td>Calif.</td>
<td>Calif.</td>
<td>5 y</td>
<td>Male</td>
<td>Encephalitis, meningitis</td>
<td>Peri</td>
<td>23</td>
</tr>
<tr>
<td>Calif.</td>
<td>Calif.</td>
<td>2 y</td>
<td>Male</td>
<td>Encephalitis, meningitis</td>
<td>Peri</td>
<td>23</td>
</tr>
<tr>
<td>Calif.</td>
<td>Calif.</td>
<td>11 y</td>
<td>Male</td>
<td>Encephalitis</td>
<td>Peri</td>
<td>2</td>
</tr>
<tr>
<td>Calif.</td>
<td>Calif.</td>
<td>11 y</td>
<td>Male</td>
<td>Encephalitis</td>
<td>Peri</td>
<td>1</td>
</tr>
<tr>
<td>Calif.</td>
<td>Calif.</td>
<td>27 y</td>
<td>Male</td>
<td>Encephalitis</td>
<td>Focal</td>
<td>4</td>
</tr>
</tbody>
</table>
Diagnostics/Treatment

- No widely available definitive diagnostic tests
  - Many cases are not diagnosed
  - Examination of tissue biopsies can be extremely helpful if a section of larva is contained
  - Ocular examinations revealing a migrating larva, or lesions consistent with a nematode larva are often the most significant clue to infection with *Baylisascaris*
- Albendazole recommended
- Laser treatment of the eye for larvae

Prevention

- Avoid environments where raccoons live
  - Young children, hunters, trappers, taxidermists
- Raccoon stuff
  - Do not keep raccoons as pets (illegal)
  - Discourage raccoons from visiting your home or yard by eliminating access to food sources and housing
  - Anti-helminthics for raccoons
- To eliminate eggs, raccoon feces and material contaminated with raccoon feces should be removed carefully and burned, buried
- Boil water
- Potential for bioterrorism?

Hookworm spp.

- *Necator americanus* ("American killer")
  - Was widespread in the Southeastern U.S. early in the 20th century.
  - Most common hookworm worldwide
- *Ancylostoma duodenale*
- WHO: 740 million affected globally
- Filariform juvenile worms penetrate skin
- Hookworm infection leads to anemia, protein deficiency, malnutrition
- Hookworm disease is a leading cause of morbidity in children and pregnant women, and can have adverse results for the mother, the fetus and the neonate.

Hookworm spp. life cycle

Disease caused by hookworms

- Iron deficiency anemia is the most common symptom of hookworm infection
  - Caused by blood loss at the site of intestinal attachment of the adult worms
  - Worms continuously move to new places exacerbating bleeding
  - Can be accompanied by cardiac complications
- Gastrointestinal and nutritional/metabolic symptoms can also occur
- Local skin manifestations during penetration by the filariform (L3) larvae
- Respiratory symptoms can be observed during pulmonary migration of the larvae
Diagnosis and Treatment

- Examination of the eggs cannot distinguish between *N. americanus* and *A. duodenale*
- Larvae can be used to differentiate between *N. americanus* and *A. duodenale*
- Need to distinguish between the rhabditiform larvae of hookworms and those of Strongyloides stercoralis
- Treatment: Albendazole, with mebendazole and pyrantel pamoate as alternatives

Control

- Mass drug tx campaigns cannot eradicate worms, but reduce loads in environment and prevalence
- Education
- Sanitary disposal of human waste

Trichuris trichiura

- Human whipworm
- Second most common nematode parasite of man
- Worldwide distribution
- WHO - 795 million affected globally
- 2.2 million infected in U.S. (mostly Southern)

Trichuris Life Cycle

- Most frequently asymptomatic
- No tissue migration
- Heavy infections, especially in small children, can cause gastrointestinal problems (abdominal pain, diarrhea, rectal prolapse)
  - Possible growth retardation
- Treatment
  - Mebendazole
  - Albendazole

Trichuris: Clinical features

- Children are continuously exposed to infection
- Children grow rapidly and are especially susceptible to infection and the associate morbidity
- Chronic helminth infection seems to have a negative impact on cognitive development
- 10 cents annually per child covers drug cost
- The program is heavily based on drug treatment
**Capillaria spp.**

- Similar in morphology to Trichuris spp.
- Three species reported in humans, but *Capillaria philippinensis* most common
- Ingestion of raw or undercooked fish
- *C. philippinensis* is endemic in the Philippines and also occurs in Thailand, Taiwan.
  - Rare cases reported from other Asian countries, the Middle East, and Colombia.
- Rare human infections with *C. hepatica* (hepatic capillariasis) and *C. aerophila* (pulmonary capillariasis) have been reported worldwide.

**Life Cycle**

*Capillaria philippinensis* is currently considered a parasite of fish-eating birds, which seem to be the natural definitive host.

**Disease, etc.**

- Intestinal capillariasis (*C. philippinensis*) manifests as abdominal pain and diarrhea
  - A protein-losing enteropathy can develop which may result in death from loss of electrolytes, heart failure, secondary bacterial infection
- Hepatic capillariasis (*C. hepatica*) manifests as an acute or subacute hepatitis with eosinophilia, with possible dissemination to other organs.
- Pulmonary capillariasis (*C. aerophila*) may present with fever, cough, asthma, and pneumonia, and also may be fatal.
- Dx: eggs, larvae and/or adult worms in the stool, also intestinal, liver, lung biopsies/necropsies.
- Tx: Mebendazole, albendazole is an alternative.

**Taiwan: New Focus of Disease?**

- More than 2,000 cases of intestinal capillariasis have been reported from the Philippines and Thailand
- Since the first case in Taiwan was reported in 1983, subsequent cases have continued to appear.
  - Some with no history of fish consumption
- Taiwan is also a key rest stop on the north-south migratory routes for many fish-feeding migratory birds, which are thought to be the major carriers of *Capillaria philippinensis*.
- More than 200,000 foreign laborers living in Taiwan who originally came from major epidemic areas in any given year, and it could potentially facilitate the spread of this disease.

**Strongyloides stercoralis**

- Threadworm
- Exists as a free-living animal and also as a parasite
  - Filariform infective larvae and a free-living rhabditiform larvae
- Autoinfection is important
- 3-100 million people estimated to be infected

**Strongyloides life cycle**

*Strongyloides stercoralis* is a threadworm that exists as both a free-living animal and a parasite, with filariform and rhabditiform stages in its life cycle.
Distribution of Strongyloides

Tropical and subtropical areas, but cases also occur in temperate areas (including the South of the United States). More frequently found in rural areas, institutional settings, and lower socioeconomic groups.

Disease, dx, tx

- Frequently asymptomatic
- Gastrointestinal symptoms include abdominal pain and diarrhea
- Pulmonary symptoms occur during pulmonary migration of the filariform larvae
- Dermatologic manifestations
- Disseminated strongyloidiasis occurs in immunosuppressed patients

Diagnosis
- Identification of larvae in the stool or duodenal fluid (compare to eggs of other worms)
- Larvae may be detected in sputum from patients with disseminated strongyloidiasis

Treatment: Ivermectin, Albendazole

Hyperinfection syndrome (HS)

- Hyperinfection and disseminated disease occur during amplification of the autoinfective life cycle.
- Occurs in chronically infected people after immunosuppressive therapy is initiated for an underlying condition.
- Other risk factors: transplantation, human T-lymphotropic virus type 1 (HTLV-1) infection, HIV, malnutrition, diabetes, chronic renal failure, chronic alcohol consumption.
  - With diminished T-cell immunity, larvae migrate in frequently massive numbers to the lungs and often to other tissues, triggering local inflammation and antigen stimulation.
  - Bacteremia, meningitis, and gram-negative sepsis can occur, as intestinal flora attached to the larvae also migrate throughout the body.
- Delays in making a diagnosis, errors in empiric treatment and facilitating the development of HS by initiating steroids for asthma occur all too frequently where healthcare providers are not familiar with immigrant/travel medicine
- Hyperinfection and disseminated disease occur during amplification of the autoinfective life cycle.
- Occurs in chronically infected people after immunosuppressive therapy is initiated for an underlying condition.
- Other risk factors: transplantation, human T-lymphotropic virus type 1 (HTLV-1) infection, HIV, malnutrition, diabetes, chronic renal failure, chronic alcohol consumption.
  - With diminished T-cell immunity, larvae migrate in frequently massive numbers to the lungs and often to other tissues, triggering local inflammation and antigen stimulation.
  - Bacteremia, meningitis, and gram-negative sepsis can occur, as intestinal flora attached to the larvae also migrate throughout the body.
- Delays in making a diagnosis, errors in empiric treatment and facilitating the development of HS by initiating steroids for asthma occur all too frequently where healthcare providers are not familiar with immigrant/travel medicine

Angiostrongylus spp.

- *Angiostrongylus cantonensis*, the rat lungworm, is the most common cause of human eosinophilic meningitis.
  - The first described case of human *A. cantonensis* infection occurred in Taiwan in 1945.
- *Angiostrongylus costaricensis* causes abdominal, or intestinal angiostrongyliasis.
  - Reported from Costa Rica, and occurs most commonly in young children.

Angiostrongylus spp. Life Cycle

Sources of infection: slugs, land snails, fresh water prawns, other paratenic (transport) hosts; larvae in slime on produce or in planarians that are in produce

Distribution of *A. cantonensis* and human *A. cantonensis* infections or outbreaks worldwide
Outbreaks

- Several outbreaks of A. cantonensis disease in humans have been reported in the Pacific islands and more than 2800 cases have been documented worldwide.
  - >47% cases in Thailand
  - Custom of eating raw/undercooked snails (Pila spp) with alcohol
- In the past 10 years, several major outbreaks of the disease have been reported in endemic regions, especially in China (nine outbreaks in mainland China and three in Taiwan).
- Caribbean islands
  - First case of human angiostrongyliasis was reported in Cuba in 1973
  - Increasing numbers of A. cantonensis cases, most notably in Costa Rica and Jamaica.

Hawaii Outbreak

1-6-09: ANGIOSTRONGYLUS MENINGITIS - UNITED STATES: (HAWAII): ProMED-mail
- 3 residents of Hawaii (big island) contracted Angiostrongyulus meningitis
  - 2 people in comas
  - Home-grown produce suspected as source of infection
- More cases suspected, but others have not gone to the hospital because they do not have medical insurance.
- Angiostrongyulus cantonensis is spreading in countries of the Pacific rim including Hawaii probably spread by rats carried on ships.

Angiostrongyliasis: Clinical Features

- Eosinophilic meningitis
  - Ingested larvae eventually reach the CNS in ~2 weeks where they usually die shortly thereafter.
  - Severe headaches, nausea, vomiting, neck stiffness, seizures, and neurologic abnormalities.
  - The incubation time is highly variable, ranging from 1 day to several months, depending on the number of parasites involved.
  - Occasionally, ocular invasion occurs and surgery is required to remove worms
- Abdominal angiostrongyliasis mimics appendicitis, with eosinophilia
- Most cases of human angiostrongyliasis are mild and self-limiting, but death can occur in severe cases without prompt and proper treatment.

Dx of Angiostrongyliasis

- In eosinophilic meningitis, the cerebrospinal fluid (CSF) is abnormal (elevated pressure, proteins, and leukocytes; eosinophilia).
- In abdominal angiostrongyliasis, eggs and larvae can be identified in the tissues removed at surgery.
- CT scan detecting lesions in meninges, serologic confirmation by ELSA

Treatment/Prevention of Angiostrongyliasis

- Thiabendazole for early, invasive stages
- Relief of symptoms for A. cantonensis infections can be achieved by the use of analgesics, corticosteroids, and careful removal of the cerebral spinal fluid at frequent intervals.
- Avoid eating raw or undercooked intermediate and paratenic hosts (snails, other mollusks) or potentially contaminated vegetables.
- Eradicating molluscan hosts and rats near houses and vegetable gardens

Anisakis simplex

- Common worm parasite encountered in fish with marine mammals as definitive hosts
- Accidental ingestion of larvae
- Common in Japan, where over 2,000 cases of parasitism are registered annually, constituting 95% of the world-wide total.
- First case reported in 1955 in Holland
- First case in U.S. in 1975
**Anisakis: Miscellaneous**

**Geographic Distribution**
- Worldwide, with higher incidence in areas where raw fish is eaten (e.g., Japan, Pacific coast of South America, the Netherlands).
- Emerging in Spain

**Laboratory Diagnosis**
- Gastroscopic examination during which the 2 cm larvae are visualized and removed, or by histopathologic examination of tissue removed at biopsy or during surgery.

**Tx:** surgical or endoscopic removal

---

**Anisakiasis**

- Within 6 hours after ingestion of infected larvae, they penetrate stomach or intestine, causing violent abdominal pain, nausea, and vomiting may occur.
- If the larvae pass into the bowel, a severe eosinophilic granulomatous response may also occur 1-2 weeks following infection

**Anisakis simplex allergy**
- Allergic reactions to *A. simplex* should be suspected when allergic-like reactions occur after eating seafood, yet the results of skin tests to seafood are negative.
- Allergic reactions may be triggered by dead parasites.
- Since the allergens are not always destroyed by heat, allergic reactions may even occur after food is cooked.

---

**Prevention**

- Caution with raw, salted, pickled fish
- FDA guidelines for retailers who sell fish intended to be eaten raw.
  - Freezing fish to -31°F for 15 hours or -4°F for 7 days to kill parasites and physical examination
- Commercial blast-freezing can render juveniles harmless