Lecture 5: Emerging Parasitic Helminths part 2: Tissue Nematodes
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Readings-Nematodes
• Ch. 11 (pp. 290, 291-93, 295 [box 11.1], 304 [box 11.2])
• Ch.14 (p. 375, 367 [table 14.1])

Monsters Inside Me
• Toxocariasis, larva migrans (Toxocara canis, dog hookworm):
  Background: http://animal.discovery.com/invertebrates/monsters-inside-me/toxocariasis-toxocara-roundworm/

Learning Objectives
• Understand how visceral larval migrans, cutaneous larval migrans, and ocular larval migrans can occur
• Know basic attributes of tissue nematodes and be able to distinguish these nematodes from each other and also from other types of nematodes
• Understand life cycles of tissue nematodes, noting similarities and significant difference
  • 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 drugs (always available) that are used to treat parasites
• Describe factors of tissue nematodes that can make them emerging infectious diseases
• Be familiar with Dracunculiasis and status of eradication

Lecture 5: On the Menu
Tissue Nematodes
• Cutaneous Larva Migrans
• Visceral Larva Migrans
• Gnathostoma spp.
• Trichinella spiralis
• Dracunculus medinensis

Problems with other hookworms
• Cutaneous larva migrans or Visceral larva migrans
• Hookworms of other animals frequently fail to penetrate the human dermis (and beyond).
  • Ancylostoma braziliense (most common in Gulf Coast and tropics),
  • Ancylostoma caninum, Ancylostoma ceylonicum,
• They migrate through the epidermis leaving typical tracks
• Eosinophilic enteritis-emerging problem in Australia
Outbreak of Cutaneous Larva Migrans at a Children’s Camp --- Miami, Florida, 2006

On July 20, 2006, the director of a children’s camp noted that many of the Miami-Dade County Health Department (MDCHD) children who had received a diagnosis of cutaneous larva migrans (CLM), or “creeping eruption,” a skin condition typically caused by dog or cat hookworm larvae of the genera *Ancylostoma* and *Dermatophagoides*, respectively, also had diarrhea on the first day of treatment. MDCHD repeated anthelmintic treatment on day 3 of their treatment regimen. The target population for the MDCHD surveillance program included all children younger than 18 years of age who attended a day camp in Miami-Dade County. The presence of hookworm larvae in the soil was confirmed by the Miami-Dade County Environmental Health Division. The director of the camp decided to provide anthelmintic treatment on day 3 of the children’s treatment regimen.

The camp property, which is located in Miami, includes a swimming pool and a tennis court, both of which are played on by the children. The camp required that all children receive a stool sample at the beginning of the camp season.

On July 20, camp administrators noted 40 diarrheic children, most with symptoms lasting 1–2 days, and 1 child with symptoms lasting 2–3 days, and 1 child who had no symptoms the day before.

MDCHD conducted a total of 31 stools of persons (5 staff members and 26 campers) who were exposed to the camp environment. All stool specimens were negative for human enteric pathogens.

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5649a2.htm

**Visceral Larva Migrans (VLM)**

- Caused by juveniles of several species of nematodes that gain entry to improper host
- Larvae begin tissue migration, but become arrested and migrate throughout body
- *Toxocara canis*, *Toxocara cati*, *Ascaris suum*
- No maturation to adults

**Toxocara canis**

- Dog roundworm
  - Transmitted maternal-fetal
- Infects very high % puppies
- Distributed worldwide
- Worms release massive amounts of eggs that are environmentally stable
- Causes VLM, OLM
- Albenbazaldehyde+inflammatory drugs

**Diseases**

- VLM
  - Larvae invade multiple tissues (liver, heart, lungs, brain, muscle) and cause fever, anorexia, weight loss, cough, rashes, hepatosplenomegaly
  - Death can occur rarely, by severe cardiac, pulmonary or neurallogic involvement.
- OLM
  - Larvae produce various ophthalmologic lesions, sometimes misdiagnosed as retinoblastoma
  - Often occurs in older children or young adults, with only rare eosinophilia or visceral manifestations.
- Dx: For both VLM and OLM, the diagnosis rests on clinical signs, history of exposure to puppies, laboratory findings, and detection of antibodies to *Toxocara.*
  - Remember, no eggs in stool

**Gnathostoma spp.**

- *G. spinigerum*
  - Transmitted in Asia, especially Thailand and Japan; recently emerged as an important human parasite in Mexico
  - Humans infected by eating undercooked fish or poultry containing third-stage larvae, or by drinking water containing infected copepods
  - Disease due to migrating, immature worms
  - Emerging imported infections
  - Adults and larvae have numerous spines for encysting in host tissue
  - Note collar of spines of adult worm, used for sticking in host tissue

**T. canis life cycle**

- Larval stages in soil mature to infective larvae
- Ingested by puppy, infective larvae mature to adult worms
- Adults migrate to small intestine
- Eggs released by adults mature in small intestine
- Released in feces, infective stage when ingested by dog
- Dog can contaminate soil for life
- Eggs infective after 2–4 weeks
- Eggs can remain infective for years
Within 24-48 h of ingestion of larvae, patients may develop fever, vomiting, epigastric pain.
Migration in the subcutaneous tissues causes intermittent, migratory, painful, pruritic swellings (cutaneous larva migrans).
Migration to other tissues (visceral larva migrans) can result in ocular involvement, more serious manifestations such as eosinophilic meningitis with myeloencephalitis.
Removal and identification of the worm is both diagnostic and therapeutic.
Tx: Surgical removal or combination with albendazole or ivermectin.

First case of clinical gnathostomiasis was reported in Mexico in 1970.
Over 1,000 cases reported along Gulf/Pacific Coasts from 1980-1996.
Linked to eating ceviche.
Mass production and commercial distribution of tilapia has been implicated.

Zoonotic infections
Humans are accidental, dead-end hosts.
Multiple species of Trichinella infect humans depending on climate and reservoir hosts.
- T. spiralis, T. pseudospiralis, T. nativa, T. nelsoni, T. britovi
- T. spiralis is cosmopolitan, most pathogenic.
Emerging in China, Russia, other European countries.
In 2008, morbidity due to trichinellosis doubled in Russia: 312 cases in 2008 vs. 155 in 2007.
779 human cases in EU Member States during 2007.

Domestic cycle
Domestic pigs are considered the dominant reservoir host, but there are many different typical hosts throughout the world.

Sylvatic (wild animal) cycles
- Temperate regions (carcass and live prey): pig, wild boar, horse, dog, bear, fox
- Arctic regions (carcasses): polar bear, walrus, wolf, fox
- Tropical regions (carcasses): warthog, hyena

Infection is maintained primarily in rats and other rodents which may be eaten by other animals such as pigs and bears.
**T. spiralis Distribution**
- Emerging in China, Russia, other European countries
  - In 2008, morbidity due to trichinellosis doubled in Russia: 312 cases in 2008 vs. 155 in 2007.
  - 779 human cases in EU Member States during 2007
- Lithuania, June 2009: outbreak due to wild boar meat sausages - affected 107 people

**Nurse Cell Complex**
- Larvae encysted in striated muscle
- Subversion and redirection of host cell activities
  - Alteration of gene expression of host cell from contractile fiber to cell that nourishes worm
  - Synthesis of collagen by neighboring fibroblasts encloses nurse cell
- Juveniles absorb nutrients while in nurse cell and increase 1mm in 4-8 weeks, infective to hosts
- Juveniles enter developmental arrest and live for years
- Calcification of nurse cell and worms by host reactions

**Disease**
- The first few days of the infection are characterized by gastroenteritis associated with diarrhea, abdominal pain, vomiting.
- Pathology is due to migrating newborn larvae as they randomly penetrate cells (e.g., brain, liver, kidney, heart) in their search for striated skeletal muscle cells.
  - Fever and myalgia, bilateral periorbital edema, and petechial hemorrhage
- Heavy infection results in generalized edema, cardiomyopathies and CNS abnormalities

**Trichinosis Dx and Tx**
- Dx based on symptoms of stage of life cycle and larvae in feces, blood, other secretions
- Muscle biopsy for larvae, PCR, antibody detection
- Steroids are used for infections with severe symptoms
- Mebendazole or albendazole can be used to treat infections in the intestines
- Treatment should begin as soon as possible and the decision to treat is based upon symptoms, exposure to raw or undercooked meat, and laboratory test results.
  - No specific treatment for trichinosis once the larvae have invaded the muscles

**Prevention**
- Curing (salting), drying, smoking, or microwaving meat does not consistently kill infective worms.
- Cook meat products until the juices run clear or to an internal temperature of 170°F.
- Freeze pork less than 6 inches thick for 20 days at 5°F to kill any worms.
- Cook wild game meat thoroughly-harder to kill worms than in pork.
- Cook all meat fed to pigs or other wild animals.

**Outbreak: Crazy turtles**
- In July 2008, four teaching hospitals in northern Taiwan reported 8 patients in 2 groups with fever, myalgias, and eosinophilia of unknown cause developed after they shared a common food source in May 2008.
  - Group A: 20 Taiwanese, participated in a festive meal at a Japanese food restaurant, and were served raw meat, blood, liver, and eggs of 3 of 5 soft-shelled turtles
  - Group B: A group of 3 Japanese customers was served the other 2 turtles
- Extensive serologic testing for helminths by ELISA, hits against *Trichinella* spp.
- The incubation period, clinical features, and laboratory findings in this outbreak were similar to those of other reported trichinosis outbreaks associated with eating mammals
  - *T. papuae* and *T. zimbabwensis* are the most likely parasites causing this outbreak because of their ability to infect mammals and reptiles.
- Serum specimens from 6 of the 8 case-patients reacted most strongly to the 53 kDa recombinant protein of *T. papuae.*
- Significance:
  - Not yet determined how soft-shelled turtles were infected by *T. papuae* in this outbreak, so further investigation of the potential infectious source is warranted.
  - Further investigations are urgently needed to assess the epidemiology of reptile trichinosis and the human risk for trichinosis from reptiles.
This little piggy……

I don't each pork as much as I used to will you?

Egyptian texts suggest that it was common during the middle of the second millennium BC.

“Guinea worm”

Eradication efforts have limited areas of disease to many rural communities in Africa, but it is a major public health problem because of dependence upon unprotected water sources for drinking.

Prevents many people from working and leads to food shortages and lower earnings.

**Dracunculus medinensis**

- Juvenile worms stimulate allergic reaction that causes blister, usually on lower limbs where juveniles exit
- Inflammation and frequent secondary bacterial infection
- Calcified worms and arthritis
- Paraplegia due to worms in CNS

**Dx and Tx of Dracunculiasis**

**Diagnosis**
- The clinical presentation of dracunculiasis is so typical, and well known to the local population, that it does not need laboratory confirmation.
- No serologic test is available

**Treatment**
- Local cleansing of the lesion and local application of antibiotics, if indicated because of bacterial superinfection.
- Mechanical, progressive extraction of the worm over a period of several days.
- 10 day treatment with metronidazole is not curative, but decreases inflammation and facilitates removal of the worm
- Mebendazole has been reported to kill the worm directly.

**Removing adult female worms**
Transmission of the disease is most common in very remote rural villages and in areas visited by nomadic groups.

- Drinking water from underground sources free from contamination
- Prevent persons with ulcers from entering ponds and wells used for drinking water
- Filtration of drinking water to remove copepods
- Treatment of water sources with larvicides to kill copepods
- Communities provided with new safe sources of drinking water, or have existing dysfunctional ones repaired

Prevention of Dracunculiasis

Dracunculus Eradication Program

- Originally began at CDC in 1980
- WHO, UNICEF, Carter Center, Gates Foundation collaboration has dramatically reduced the incidence of dracunculiasis
- Goal of global eradication by 2009
- In 1986, there were an estimated 3.5 million cases of Guinea worm in 20 endemic nations in Asia and Africa.
- Due to prevention and health education efforts, by the end of 2008, there were fewer than 5,000 cases in six nations in Africa: Sudan, Ghana, Mali, Ethiopia, Nigeria, and Niger.