Nematodes
Roundworms

(phyllum \textit{Nematoda})

- non-segmented roundworms
- digestive system is like a tube at both ends
- among most abundant life forms on earth
- majority are free living (e.g. \textit{Caenorhabditis elegans})
  - inhabit soil & fresh & salt water niches
- a fraction are parasitic & some infect humans
- most parasitic nematodes depend on \textit{specific} host species
  - \textit{incapable of survival in any other organism}

- \textit{Trichinella spiralis}
  - parasitic nematode
  - more total DNA & 60\% homologous with \textit{C. elegans}
  - parasites may need more \text{\textit{not}} fewer genes to survive inside host
Nematode Parasites

Most common are 3 soil-transmitted helminths:
- Roundworm *Ascaris lumbricoides*
- Whipworm *Trichuris trichiura*
- Hookworms *Necator americanus* & *Ancylostoma duodenale*

Children are susceptible to acquiring a large number of parasites in developing countries.
Children frequently harbor all 3 nematode types.
Childhood malnutrition
- Physical growth retardation
- Deficits in cognitive & intellectual development

Nematode Reproduction

- Usually sexual
- Males are usually smaller than females
- Eggs passed by the female may be embryonated (containing embryo) or (depends on species) unembryonated (further development in environment)

- Free-living roundworms: eggs → larva → adults
- Parasitic roundworms: *life cycle is often much more complicated.*
Eggs ingested → Larvae hatch in small intestine

Indirect: bloodstream to liver, heart, lung, trachea, GI tract

Direct from small intestine to colon

Adults in colon → Mating & egg production, eggs released in feces

Larvae invade skin via hair follicle → Bloodstream to liver, heart, lung, trachea, GI tract

Mating & egg production, eggs released in feces

Larvae introduced by biting insect vector → larvae mature to adults in bloodstream, produce new larvae vector, develop & are introduced to new host

Larvae ingested in copepods (small crustaceans) → GI tract to bloodstream

Blister ruptures & larvae are released in water

Copepods swallow larvae

Aberrant nematode infection: nematodes that complete their lifecycle in a different host infect humans. They cannot complete their lifecycle in humans, but the larval stages cause tissue damage.
### Neglected tropical diseases:

- **Buruli ulcer (bacteria, Mycobacterium ulcerans)** ▶
- **Chagas disease (protozoan, American trypanosomiasis)** ▶
- **Dengue/dengue haemorrhagic fever (virus)** ▶
- **Dracunculiasis (worm, guinea-worm disease)** ▶
- **Fascioliasis (trematode worms)** ▶
- **Human African trypanosomiasis (protozoan)** ▶
- **Leishmaniasis (protozoan)** ▶
- **Leprosy (bacteria, Mycobacterium leprae)** ▶
- **Lymphatic filariasis (worm, elephantiasis)** ▶
- **Onchocerciasis (worm, river blindness)** ▶
- **Schistosomiasis (trematode worm, bilharzia)** ▶
- **Soil transmitted helminthiasis (worm)** ▶
- **Snakebite (toxin)** ▶
- **Trachoma (bacteria, Chlamydia trachomatis)** ▶
- **Yaws (bacteria, Treponema pallidum pertenue)** ▶

### Neglected tropical diseases:

**Diseases of poverty, largely preventable.**

These typically decrease capacity for work, maintain poverty and kill slowly over time.

- *The big three* - research, prevention and treatment of AIDS, TB and malaria in disease endemic countries. The argument for treating NTDs is that decreasing these will help increase life expectancy for people with the big 3. It will also reduce transmission.

**NTDs:** prediction is that after 5 years of treatment, decreased infection will decrease transmission so that these diseases are no longer significant.

**Debate over limited resources:** do we treat diseases that kill quickly (the big 3) or those that decrease life expectancy and maintain poverty?
Neglected Disease
Season 3 Episode 11
Every year billions of pounds are spent on HIV, Malaria and TB. Now an increasingly vocal group of scientists is challenging the way we allocate spending on disease. They say that while the world battles the Big 3 diseases, nearly half of all human misery is caused by diseases that can be cheaply and easily treated – but which don’t grab the headlines.
http://www.rockhopper.tv/programmes/61/

Enterobius vermicularis
(Linnaeus 1758)
**Enterobius vermicularis**

known as **pinworm**
affect nearly all children under 12 years
frequent transmission in **elementary schools & daycare centers**
no reservoir hosts

**Infection**: embryonated eggs swallowed →
- hatch into 2\(^{nd}\) stage larvae in small intestine
- 3\(^{rd}\) & 4\(^{th}\) stages develop in small intestine
- adult worms in large intestine
  - cycle completed 4-6 weeks after egg ingestion

**Retro-infection**: eggs hatch on skin at site of deposition & 2\(^{nd}\) stage larvae crawl through anus into rectum colon → develop into reproducing adults

**Enterobius vermicularis**

adult pinworms feed on **E. coli** & other bacteria in stool
adult worms live in **transverse & descending colon & rectum**
  - females are bigger than males
    - females 8-13 mm long
    - males 5 mm long
adult worms mate
  - males die after copulation
  - female ~10,000 fertilized **non-embryonated** eggs (~6 weeks)

- **gravid** female migrates out of anus onto perianal skin at night
  - stimulated to do so by drop in host body temperature
  - uterus prolapse → expels all eggs & dies
  - explosion can be so intense that eggs become airborne
  - eggs rapidly embryonate (**infectious in 6 hours**)

**Gravid**: pregnant or full of eggs.  **Non-embryonated**: further development required before egg contains embryo.
Enterobius vermicularis Pathogenesis

aberrant infections:
- pelvic peritonitis & granuloma in liver or appendix
female patients:
- larvae that hatch near anus can crawl into vagina
  → infect fallopian tubes & ovaries
  → vaginal itching & discharge
all stages of the worm develop in gut
host does not experience systemic immune reactions
parasite elicits a mild local inflammatory response
can be associated with a low-grade eosinophilia
develop pruritus from response to worm proteins (rare)

Pruritus: an unpleasant sensation that evokes the desire to scratch.

Peritonitis: an inflammation of the peritoneum (membrane lining part of the abdominal cavity & viscera).
Granuloma: a spherical mass of immune cells formed when the immune system attempts to wall off inclusions (such as parasites) that it recognizes as foreign but cannot eliminate.

Enterobius vermicularis Clinical Disease

• majority of infected individuals are free of symptoms
• few experience intense itching of perianal area
  can lead to cellulitis (rare)

Diagnosis: infection detected by examination of tape applied to perianal region as soon as patient awakens
eggs readily detected on tape
eggs usually not found in feces

Cellulitis: bacterial infection of the connective tissue under the skin

Treatment:
pyrantel pamoate, albendazole or mebendazole
drugs don’t kill eggs or larvae → re-treatment 2-3 weeks later

Prevention & Control:
no effective means are currently available
easy transmissibility
Enterobius vermicularis

- GI route without wandering
- Eggs are ingested
- Larvae hatch in small intestine
- Larvae migrate to colon
- Adults mature in colon
- Adults migrate out of anus
- Embryonated eggs

Adult female Enterobius vermicularis - 10 mm.

Cross section of adult in appendix.

Trichuris trichiura

(Linnaeus 1771)
known as “whipworm” due to characteristic shape
serious morbidity in children in developing countries
    heavy infection $\rightarrow$ colitis & stunted growth
    chronic infection $\rightarrow$ physical & cognitive deficits
~795 million infections
    Asia, sub-Saharan Africa & tropical regions of Americas
no reservoir hosts

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Trichuris trichiura
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\* Deliberate infection with porcine whipworm infection reduces disease symptoms $\rightarrow$ the worm is immunosuppressive!

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**Trichuris & Autoimmune Disease**

**Hygiene hypothesis:** developed countries are too clean
  - Low incidence of autoimmune diseases & allergies in less developed countries
  - Significant increase in autoimmune diseases in industrialized countries

**Helminthic therapy:** treatment of autoimmune diseases by deliberate infection with helminths. This therapy is being investigated to treat diseases including Crohn's disease, multiple sclerosis, asthma & ulcerative colitis.

Crohn's disease: an autoinflammatory bowel disease that can attack any part of the digestive tract, from mouth to anus, causing symptoms ranging from cramping to bloody diarrhea.

*Deliberate infection with porcine whipworm infection reduces disease symptoms $\rightarrow$ the worm is immunosuppressive!*
**Trichuris trichiura Life Cycle**

- Embryonated egg swallowed → 1st stage larva hatch in small intestine & penetrate epithelium
  - 4 molts → immature adult → carried to large intestine
  - Adult worms live in transverse & ascending colon
  - Adult female: 30-50 mm & Adult male: 30-45 mm
- Narrow esophagus embedded in host cell syncytium
- Induced by worm secretions
- Posterior in lumen (allows eggs to escape)
- Parasites grow & mature in large intestine → mating
- 3000-5000 eggs/day & live 1.5-2 years
- Fertilized eggs are deposited in soil with feces
  - Must embryonate before they are infectious
  - High humidity, sandy/loamy soil & warm temperature → rapid embryonic development (18-22 days)
**T. trichiura** Cellular & Molecular Pathogenesis

children (5-15 years) harbor largest whipworm burden
worms induce _structural effects_ in large intestine epithelium
*Trichuris* release pore forming protein
  ➔ pores in epithelial cell membranes
  facilitate invasion
  enable parasite to maintain syncytial environment
infection resembles inflammatory bowel disease (IBD)
  extensive gut damage
  chronic inflammation
  capillary damage & erosion ➔ blood loss (anemia)
adult worms can modulate the immune system

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**Trichuris trichiura** Clinical Disease

only in children (usually)
acute dysentery or chronic _colitis_
diarrhea contains blood & mucus
weight loss
rectum swelling & excess pushing ➔ rectal prolapse
chronic malnutrition, short stature, anemia & finger clubbing
chemotherapy ➔ conditions abate & rapid catch-up
**Trichuris trichiura Clinical Disease**

**Diagnosis:** eggs identified in stool samples  
**Treatment:** benzimidazoles (mebendazole or albendazole)  
**Prevention & Control:** ~80% prevalence in tropical areas  
- eggs resistant to chemical disinfectants  
- eggs survive for long time in raw or treated sewerage  
  *proper disposal of sewerage is primary means of prevention*  
- eggs killed by exposure of eggs to direct sunlight (12 hours) or  
- exposure to temperatures >40°C for (1 hour)

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**Terms from the documentary Intestinal Worms (Season 2 Episode 3)**  
**Vietnam:** easternmost country on the Indochina Peninsula in Southeast Asia.  
- 13th most populous country in the world  
- 1885-1954 colonized by the French, “French Indochina”  
- Vietnam War, ended in 1975  
- Per capita GDP $2,942 (2009)  
**“Unholy trinity”**  
- Hookworms, Ascarus, Trichurus  

“Ground itch” – reaction to lots of hookworm larvae invading skin.  
Pregnancy & hookworms: 44 million pregnant women infected with hookworm. In pregnant women, anaemia resulting from hookworm disease results in low birth weight, impaired milk production, and increased risk of death for both the mother and the child.  
2-tank latrine: having the ability to age human feces before using them as fertilizer. If there is only one tank, fresh feces will always be part of night soil used as fertilizer.
Intestinal Worms blight the lives of an estimated 2 million people. They live in the gut and feed on the nutrients we need to survive leading to retarded growth and anaemia. 'Kill or Cure?' travels to Vietnam to see how improved health education and drugs can help plus it looks at a radical new vaccine being developed in the USA, one of the first vaccine to such a large human parasite.

http://www.rockhopper.tv/programmes/29/

Ascaris lumbricoides
(Linnaeus 1758)
**Ascaris lumbricoides**

- one of largest nematodes to infect humans
- adult lives in small intestine
  
  *grows to >30 cm long*
- developing countries: 1.2 billion people are infected
  
  >800 million cases in Asia alone
- most severe consequences in children
  
  *(higher worm burden than adults)*
- eggs thrive in warm moist soil
  
  highly resistant to environmental conditions
  
  survive in sub-arctic regions
  
  ubiquitous → recovered from surface of paper money!

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**Ascaris lumbricoides Life Cycle**

adult worms occupy upper intestine lumen

- live on predigested food (*chyme*) & host cell debris
- maintain position in small intestine lumen
  
  S-shaped configuration
- press against columnar epithelium
- continually move against peristalsis

thick cuticle & unusual lipids → hydrolase resistance

protease inhibitors → interferes with host digestion

adult female worm produce ~200,000 eggs/day

uterus contains ~27 million eggs at a time

eggs exit in fecal mass

embryonation in soil

- completed in 2–4 weeks

  *embryonated eggs swallowed* → *continued life cycle*
**Ascaris lumbricoides Life Cycle**

1st stage larva develops into 2nd stage inside egg
2nd stage larva stimulated to hatch in host
  alkaline conditions in small intestine
  bile salt-mediated eggshell solubilization
  → larva produce proteolytic enzyme to exit
shift in *Ascaris* metabolism from aerobic to anaerobic
immature parasite in intestinal lumen
penetrates intestinal wall → capillary
carried by circulation to liver
worm feeds on liver parenchymal tissue & grows
bloodstream → heart & pulmonary circulation
larva molts 2x & grows larger (length & diameter)

The parenchyma are the functional parts of an organ in the body, in contrast to the stroma, which refers to the structural tissue of organs (connective tissue).

**Ascaris lumbricoides Life Cycle**

breaks out of alveolar space: causes verminous pneumonia
larvae migrate up bronchi into trachea
swallowed → reach lumen of small intestine
2 additional molts
worms grow & mature to adulthood (~6 weeks)
adult worms occupy upper intestine lumen
  adult worms mate → eggs exit in fecal mass
embryonation occurs in soil
completed 2-4 weeks after being deposited

**Wandering:**
Gut → Liver → Heart → Lung → Trachea → Gut
**Ascaris Pathogenesis**

**GI route with wandering**

**Adult female (upper)** & **male (lower) A. lumbricoides - 13-15 cm long**

**Fertilized, non-embryonated egg of A. lumbricoides - 60 x 40 μm.**

most intense host reactions during *migratory phase*

*Ascaris* antigens released by molting cause → eosinophilic infiltration of tissues

*increased IgE*

infected children

impairs physical growth & intellectual development

*malabsorption* of fat, protein & vitamin K

*lactose intolerance* from damaged intestinal mucosa

*chronic intestinal inflammation* → *anorexia & cachexia*

Adult worms recovered from child after treatment with mebendazole.

Child with distended abdomen (bolus of *A. lumbricoides* adults in small intestines)

**anorexia & cachexia:** weight loss & wasting.
Ascaris Clinical Disease

1. migratory phase (symptoms related to worm number)
   - light infection: clinically invisible infection
   - heavy infection: (ingestion of 100s-1,000s of eggs) →
     - intense pneumonitis (can lead to bronchospasm)
     - liver enlargement
     - generalized toxicity (up to 2 weeks)

2. intestinal phase (few symptoms, from adults in intestine)
   - worms migrate when irritated (high fevers & drugs)
     - perforate intestine & liver
     - obstruct bile ducts
     - cause peritonitis
   - heavy infection → bolus obstructs intestine lumen

Pneumonitis: inflammation of lung tissue.
Bronchospasm: a sudden constriction of muscles in the walls of the bronchioles, causing difficulty in breathing.

Ascaris Clinical Disease

moderate infections → rarely symptomatic
- passage of an adult worm in stool
- regurgitation of adult worm during vomiting

Hepatobiliary ascariasis (HPA)
- common in small children
- adult worms migrate into biliary tree
  - → heptatobiliary & pancreatic ascariasis
  - → hepatic ulcers, hepatic abscesses, pancreatitis & death

Biliary tree: branches of bile duct in the liver. The liver produces bile which is secreted via the ducts to the intestine to aid in digestion of fats.
Pancreatitis: inflammation of the pancreas.

Adult ascaris (arrow) in appendix.
**Ascaris Clinical Disease**

**Diagnosis:**
observation of eggs in stool sample

**Treatment:**
• Albendazole & mebendazole are treatments of choice
• Piperazine citrate: for intestinal obstruction
  - (paralyzes worms allowing expulsion by peristalsis)

**migratory (parenteral) phase**
  - light infection → transitory (seldom diagnosed or treated)
  - heavy infection → *pneumonia-like syndrome*
  - surgical intervention if bolus causes intestinal block

**Prevention & Control:**
95% of population infected in some regions of Africa
45% of population infected in parts of Central & South America
US: prevalent in southern rural communities
sanitation (*highest prevalence in tropical rural situations*)

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**The Hookworms**

*Necator americanus*
*(Stiles 1902)*

*Ancylostoma duodenale*
*(Dubini 1843)*
The Hookworms

2 major hookworms species infect humans

*Necator americanus*

*Ancylostoma duodenal*

no known reservoir hosts for *N. americanus* or *A. duodenal*

adults (both species)

habit small intestine

feed on host intestinal mucosa & blood

blood loss from worms in intestine

protein deficiency

iron deficiency anemia

**hookworms infect ~740 million in developing nations of the tropics**

one of most prevalent human infections worldwide

one of most common causes of iron deficiency anemia

*burden: more deaths & disability than other helminths*

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The Hookworm Life Cycle

hookworm infected children ➔
physical & cognitive development deficits
increased susceptibility to other infections

hookworm infected women ➔

~40 million pregnant women infected
iron deficiency & malnutrition during pregnancy
affects intrauterine growth & birth weight
increases likelihood of premature birth
may contribute to maternal mortality

• *N. americanus* is pre-dominant worldwide
  *sub-Saharan Africa, tropical Americas & Southeast Asia*

• *A. duodenale* focally endemic
  *China, India, Africa & Americas*
• *infection* through skin
  *filariform* larvae actively penetrate cutaneous tissues
  via hair follicle or abraded skin
  releases hydrolytic enzymes in subcutaneous tissues

• *migratory phase* of life cycle
  larvae enter capillaries
  carried in bloodstream to lung capillaries
  3rd stage larvae break out of alveolar capillaries
  crawl up bronchi & trachea into pharynx
  swallowed → stomach → intestine

• *parenteral* part of lifecycle
  2 molts in small intestine
devolution of adults

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**The Hookworm Life Cycle**

adult worms
* *A. duodenal* lives ~1 year
* *N. americanus* lives 3-5 years

*A. duodenal* larvae are orally infectious
  in some areas oral ingestion may be major transmission mode
  orally infectious larvae → 2 molts to adult within G.I. tract
  later maturation & copulation (40 days)
  female worm lays eggs → complete life cycle

*A. duodenal* larvae can delay development →
  larvae penetrate skeletal muscles & become dormant
  resume development & complete lifecycle later

larval arrest occurs during pregnancy & development resumes at birth:
larvae in breast milk → vertical transmission in neonates
adult worms feed on intestine mucosa & blood species differentiated by adult mouth parts
   A. duodenal: cutting teeth
   N. americanus: rounded cutting plates

A. duodenal generally more virulent
   larger (more blood loss)
   produces more eggs
   duodenal ~28,000 eggs/day
   americanus: ~10,000

modes of transmission other than skin penetration
   orally infectious
   vertical transmission

eggs embryonate immediately after being passed
   (warm, moist, sandy or loamy soil favorable)
   develop to 1\textsuperscript{st} stage rhabditiform larvae in soil (48 hours)
   larvae feed on debris in immediate surroundings
   grow & molt 2x
   develop into infective 3\textsuperscript{rd} stage filariform larvae
   do not consume food
   developmentally arrested
   seek highest point in environment (tops of grass)
   more likely to come into contact with human skin

\textit{rhabditiform larvae:} early developmental larval stages (1\textsuperscript{st} & 2\textsuperscript{nd}) of soil-borne nematodes which precede infectious 3\textsuperscript{rd}-stage filariform larvae.

\textit{filariform larvae:} infective 3\textsuperscript{rd}-stage larva of nematodes with penetrating larvae or with larvae that migrate through body to reach the intestine.
Hookworm Pathogenesis

3rd stage hookworm larvae penetrate skin
secrete metalloprotease
repeated infection → immediate hypersensitivity
migration to lungs →
pulmonary inflammation (*pulmonitis, pneumonia*)
most pathology from adult worms in small intestine
adults feed on villous tissue
suck blood from attachment site in intestine
secrete anticoagulant
(*blocks action of host factor Xa & Vlla*)
blood loss continues after worm moves
A. duodenal: each worm sucks 0.1-2.2 mL blood/day
N. americanus: each worm sucks 0.01-0.02 mL blood/day
worms rupture ingested RBCs with hemolysins & break down hemoglobin with proteases
Hookworm Clinical Disease

- previously uninfected individuals: penetration of skin by filariform larvae does not result in symptoms
- individuals experiencing repeated infections: develop a pruritic papular vesicular dermatitis at larval entry site (known as ground itch or dew itch)
- heavily infected individuals: symptoms of pneumonia during migratory phase of worms

migrating stages induce intense circulating eosinophilia
intestinal phase
- can be asymptomatic
- can result in gastric pain & abdominal discomfort

Pruritic = itchy; papular = round bumps; vesicular = blistered; dermatitis = inflammation of the skin.
Eosinophils: immune cells responsible for combating multicellular parasites. Along with mast cells, they control allergy & asthma.

Hookworm Clinical Disease

Wakana disease: when a large number of larvae are ingested. Associated with nausea or vomiting, dyspnea & eosinophilia
~60-75% of infections are clinically silent (asymptomatic)
acute disease in individuals who harbor large numbers of worms
major clinical feature is iron deficiency anemia
due to blood lost in intestinal tract
proportional to hookworm number in intestine
severe anemia associated with
lassitude, palpitations & external dyspnea
leads to angina pectoris & congestive heart failure
during pregnancy → prematurity or low birth weight

Dyspnea: shortness of breath or painful breathing;
Lassitude: Lack of energy; Palpitations: abnormal heart beat
Angina pectoris: chest pain due to coronary heart disease; it occurs when the heart muscle doesn’t get enough blood (ie oxygen).
physical signs of hookworm anemia (signs of iron deficiency)
koilonychia: pale sclera & fingernail concavities
chlorosis: yellow-green discoloration of skin

children with severe infection show signs of protein malnutrition
(abdominal distention, facial edema & hair loss)

children with chronic hookworm anemia
physical growth retardation
deficits in child cognition and intellectual development.
reversed by administration of anthelminthic drugs

Hookworm Clinical Disease

Diagnosis:
identification of eggs in stool

Treatment:
adult worms usually susceptible to albendazole & mebendizole
children & pregnant women: drugs are toxic → trade-off
between side effects & improvements in anemia

Prevention & Control:
sanitary disposal of feces
health education
use of footwear
Trichinella spiralis
(Railliet 1896)

Trichinella spiralis infect a broad spectrum of mammalian hosts.
Most widely distributed group of nematode infections belong to the family Trichurata (roundworms).
Unusual -- partly intracellular parasites.
Disease is trichinellosis or trichinosis.
US prevalence is low (scattered outbreaks).
Domestic pig is main reservoir host for Trichinella spiralis.
Prevalence higher in Europe & Asia than US.
Endemic in Japan and China.
Trichinella spiralis Life Cycle

infection initiated by ingesting raw/undercooked infected meat
meat has nurse cell-larva complex in muscle
larvae released by digestive enzymes in stomach → upper part of small intestine
outermost cuticle layer (epicuticle) partly digested
- enables the parasite to receive environmental cues
- select infection site within small intestine
- penetrate columnar epithelium at base of villus
- live within a row of these cells
- considered intra-multi-cellular organisms

larvae rapidly molt 4 times (30 hours) → develop into adults
female: 3 mm long
male: 1.5 mm long

Trichinella spiralis Life Cycle

adult females produce live offspring
newborn larvae: 0.08 mm long
produces offspring until host immunity develops
immune responses interfere with embryogenesis
worm expulsion is final stage of immunity (several weeks)

newborn larvae has a sword-like stylet in oral cavity
used to create entry hole in potential host cells
larvae enter circulation → distributed throughout body
migrating newborns leave capillaries & enter cells
remain or leave based on environmental cues
no cell type tropism (most cell types die after infection)
- if cells don’t form nurse cells (worms re-enter circulation or die)
striated skeletal muscle cells survive
parasites induce changes in muscle
→ cell supports growth & development of larva
**Trichinella spiralis Nurse Cell Formation**

Parasite & muscle host cell develop in coordinated fashion. Intimate & permanent worm-host cell association. Muscle cell components are replaced by 14-16 days clustered dysfunctional mitochondria → *host cell switches from aerobic to anaerobic metabolism*. Host cell nuclei in nurse cell → genome amplification. Nurse cell-parasite complex can live for as long as the host remains alive for lifecycle to continue. Infected host must be eaten by a mammal. Wild mammal scavenging maintains *Trichinella*.

**Oral route with wandering**

*Trichinella spiralis*

- Adult female T. spiralis. Note fully formed larvae in uterus. 3 mm x 36 μm.
- Adult male T. spiralis. 1.5 mm x 36 μm.
- Newborn larva of T. spiralis. 70 μm x 7 μm.

*Nurse cell-parasite complex*
**Trichinella spiralis Pathogenesis**

- **enteral** (intestinal) phase (~3 weeks)
  
  - (larval stages 1-4 & immature & reproductive adult stages)
  
  - Developing worms damage columnar epithelium
  
  - Newborns → intensify inflammation
    
    - Eosinophils, neutrophils & lymphocytes infiltrate
    
    - Villi flatten → less absorbent
  
  - Larval penetration into lymphatic circulation/bloodstream
    
    - May introduce bacteremia
      
      - Due to enteric flora -- death due to sepsis reported

- **parenteral** phase induces most pathologic consequences
  
  - Dose-dependent & due to migrating newborn larvae
  
  - Increased invasion → increased pathology
  
  - Search for striated skeletal muscle
    
    - Cell penetration → cell death
      
      - Damage to brain, liver, kidney & heart
      
      - Cardiomyopathies & CNS abnormalities common

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**Trichinella spiralis Clinical Disease**

dose-dependent severity of disease

- First few days of infection:
  
  - Gastroenteritis, diarrhea, abdominal pain & vomiting
    
    - Transitory (abates ~10 days after ingestion)

- Parenteral phase (~1 week after infection, several weeks long)
  
  - Fever & myalgia
  
  - Bilateral periorbital edema
  
  - Petechial hemorrhages
  
  - Muscle tenderness
  
  - Penetration of non-muscle → more serious outcome
    
    - Cardiovascular involvement → myocarditis
    
    - Invasion of diaphragm muscles → dyspnea
    
    - Invasion of CNS → neuro-trichinellosis
**Trichinella spiralis Clinical Disease**

convalescent phase follows acute phase
many nurse cell-parasite complexes are destroyed

**Diagnosis:**
nurse cell-parasite complex in muscle biopsy

**Treatment:**
no specific anthelminthic therapy
mebendazole (given early) may reduce number of larvae
unlikely that diagnosis is made in time for this
anti-inflammatory corticosteroids are recommended
*rapidly destroying larvae with anthelminthics without use of steroids may exacerbate host inflammatory responses & worsen disease*

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**Trichinella spiralis Prevention & Control**

Trichinellosis in US now rare & sporadic
no meat from commercial sources associated with infection
infection from with raw/undercooked game meats
*bear, fox & cougar* often infected
hunters should cook all meat thoroughly
prevent *Trichinella spiralis* by
  *cooking meat thoroughly or freezing it for 30 days*

other species of *Trichinella*
found in *wild animals* (*bears & raccoons*)
hibernating animals: special proteins in muscles to
prevent ice crystals from forming during winter → these permit
survival of larvae at temperatures below freezing -- *the only way to make those meats safe is to cook them thoroughly*
Lymphatic Filariae

*Wuchereria bancrofti* (Cobbold 1877)

*Brugia malayi* (Brug 1927)

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**The Lymphatic System**

*Structures dedicated to production & circulation of lymphocytes*

- spleen, thymus, bone marrow
- network of vessels
  - carry lymph (*clear fluid*)
  - one-way (*flows towards heart*)

**Blood does not directly contact tissues**

- constituents exit blood vessels
  - = interstitial fluid in tissues
  - = lymph in lymphatic vessels

**Lymph moved in network**

- *intrinsic contractions* of vessels
- *extrinsic compression* of vessels
  - e.g. muscle contraction

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**Lymphedema**: swelling → accumulation of lymph; occurs when lymphatic system is damaged.

**Elephantiasis**: infection of lymphatic vessels causes skin thickening & enlargement of underlying tissues, especially in the legs & genitals.
Lymphatic Filariae

*Wuchereria bancrofti* & *Brugia malaya*

threadlike nematodes
adults live in lumen of lymphatic vessels
~120 million people in 83 countries are infected

**Elephantiasis:** disfiguring disease caused by blockage of the lymphatic vessels affects large numbers of individuals living in endemic area

1970-80: Chinese parasitologists discovered **diethylcarbamazine** (DEC) dramatically reduced filarial prevalence in infected populations → all salt supplies supplemented with DEC

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Lymphatic Filariae

Worms are **ovoviviparous** (live larvae are born)

microfilariae = larvae form transmitted by mosquitoes (*microfilariae taken up in blood*)

• *W. bancrofti:*
  humans are exclusive host
  widely distributed in topics
  South Asia, Africa & tropical regions of Americas
  most strains are **nocturnal**
  (time of microfilaria appearance in peripheral circulation)

• *B. malayi*
  zoonosis (feline & monkey reservoirs)
  Indonesia, Malaysia & parts of Southeast Asia

• other minor members of *Brugia* genus can cause disease
adult worms in lumen of lymphatic vessels throughout lymphatic circulation also in adjacent subcutaneous tissues commonly in lymphatics of extremities & male genitalia both species same size female: 4-10 cm long & male: 2-4 cm long mating → female worm releases 10,000+ offspring/day released offspring are 1st stage larvae (microfilariae) migrate from lymphatics to bloodstream in peripheral blood at night (10 pm to 6 am) aggregate in lung capillaries during daytime nocturnal periodicity: microfilariae prefer low O₂ tension & sense pH change in pulmonary venous circulation during sleep Experiment: sleep of infected volunteers reversed → reversed microfilariae periodicity

Microfilariae live ~1.5 years must be ingested by mosquito to continue life cycle penetrate stomach wall of female mosquito locate to thoracic flight muscles 3 molts → 3rd stage larvae infective after 10-12 days of growth in insect muscle infective larvae move to biting mouthparts deposited onto skin adjacent to bite during blood meal larvae crawl into bite wound immature worms migrate to lymphatic vessels worms develop into mature adults → ~1 year mating → shed microfilariae adult longevity: ~ 5-8 years infections lasting 40 years have been reported
**Filarial Pathogenesis**

**Immunopathologic events**
- *living adults & microfilariae suppress immune response*
- unknown mechanism
- *microfilariae produce prostaglandin E₂ (immunomodulatory for leukocytes)*
- *adult worms secrete anti-mitotic & immunosuppressive factors*

**Lymphangitis/elephantiasis**
- response to dead & dying adults in lymphatics
- develops after years
- *dying/dead adult worms can’t suppress host immune response*
  - → inflammation → intense lymphocytic infiltration
  - → alteration of lymphatics → lumen of vessel closes
  - → remnants of adult worms calcify
Filarial Pathogenesis

heavily infected individuals → blocked lymphatic circulation
lymphedema in affected region of body
smooth muscle hypertrophy in area surrounding site

elephantiasis pathology
secondary bacteremia & fungal infections worsen
worms harbor Wolbachia bacterial symbionts
Wolbachia endotoxin contributes to inflammation

Lymphatic filariasis: elephantiasis is the last consequence of the swelling of limbs & scrotum.

Filarial Clinical Disease

spectrum of clinical manifestations asymptomatic to elephantiasis
pathogenesis leading to advanced disease begins early
asymptomatic infection → lymphatic dilation
chronic clinical manifestations
lymphedema & hydrocele
dilated vessels rupture
chy luria & chylocele
acute lymphadenitis & filarial fevers
death of adult worms →
acute inflammatory response (acute lymphadenitis)
fever & painful swelling of lymph nodes
secondary bacterial infections exacerbate

Hydrocele: a pathological accumulation of serous (serum-like) fluid, can be the result of a plugged inguinal (groin) lymphatics caused by repeated chronic infection with filarial worms.
Chyluria: urine containing chyle (milky bodily fluid consisting of lymph & emulsified fats formed in small intestine & taken up in lymph).
Chylocele: a cystic lesion containing chyle.
Filarial Clinical Disease - Elephantiasis

subgroup of patients with acute lymphadenitis
lymphedema of arms, legs, breasts & genitalia → elephantiasis → loss of elasticity in skin
scrotum is frequently affected in the form of hydroceles may become gigantic -- weighing up to 10 kg

Patient suffering from long-term infection with W. bancrofti. Most worms have died & calcified, blocking lymphatic drainage from the groin to cause elephantiasis of both legs.

Calcified adults of W. bancrofti in blocked lymphatic vessel.

Filarial Clinical Disease

Diagnosis:
- microscopy (microfilariae in blood smear)
- nocturnal periodicity: best to draw blood during hours of sleep

Treatment: all patients should be treated
- asymptomatic patients have abnormal lymphatics
- early treatment prevents subsequent lymphatic damage

• DEC is treatment of choice
  - kills adult & microfilaria
  - decreases incidence of filarial lymphangitis
    - associated with fever (adult worm disintegration)
• ivermectin kills microfilariae but no effect on adults
• treatment of secondary bacterial infections
  - critical for worsening lymphedema & elephantiasis
  - possibly kills Wolbachia
Filarial Clinical Disease

Prevention & Control:
control of mosquito vectors
yearly dose of DEC to interrupt transmission

Use of DEC:
regions of epidemiological overlap with loa loa or *Onchocerca*
Sub-Saharan Africa & Yemen
*DEC toxicity* to *Loa loa* or *Onchocerca* infections
*substitution of ivermectin is essential*

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*Onchocerca volvulus*
(Leukart 1893)
**Onchocerca volvulus**

cause of "river blindness"
vector-borne filarial nematode parasite
blackfly *Simulium* species is vector
adult worm lives in subcutaneous tissues
*microfilariae migrate & induce injury to variety of body sites*
no reservoir hosts
West Africa, Northern South America & Latin America

disease causes blindness & disfiguring dermatitis
(\textit{previously}) major cause of blindness in Africa
people could not live in riverbank areas
infected >50% of the inhabitants of endemic areas
dramatic reduction in disease incidence
vector control
donation/administration of ivermectin (Mectazan)

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**Onchocerca volvulus Life Cycle**

males & females are entwined
adult female \(~40\) cm long
adult male \(\sim 3\text{-}5\) cm long
located in \textit{onchocercomas}
subcutaneous fibrous nodules
size depends on number of adult worms inside
*microfilariae migrate to subcutaneous tissues*
blackfly acquires larvae during blood meal
immature worms penetrate insect
invade hemocele & thorax flight wing muscle fibers
6-8 days of development \(\rightarrow\) larvae molt 2x
larvae migrate from muscles to \textit{proboscis} cavity
deposited onto skin with fly bite

\textit{Black flies that bite heavily infected people die from excess infection!}
Onchocerca volvulus Life Cycle

larvae enter bite wound → invade subcutaneous tissues
→ adults → produce ~700 microfilariae/day for 8-10 years
growth & molting of worms in subcutaneous tissue
formation of fibrous nodules
angiogenic response (production of vessel network)
(supplies nutrients & carries away metabolic wastes)

Body region affected differ according to geography
Africa: nodules predominate in lower part of body
Central America: found on upper portion of body
differences due to biting habits of insect vectors & styles of clothing worn by inhabitants of each endemic area

Onchocerca volvulus

Vector-borne, no GI stages

Adults shed microfilariae into subcutaneous tissues
Adult worms mature in subcutaneous tissues
Blackfly takes second blood meal
Larvae crawl into bite wound
Infective larvae develop in blackfly
Blackfly takes first blood meal, ingests larvae
Normal eye
Damaged eye
PATHOLOGY

Cross section of nodule induced by Onchocerca volvulus with numerous adults worms. 2.5 cm in diameter

Skin section with numerous O. volvulus microfilariae.
**Onchocerca Pathogenesis**

larval migration
→ *tissue degradation, angiogenesis & proteolysis*
immunomodulatory properties →
*biased host response increases leprosy susceptibility*
dead microfilariae induce inflammatory reactions

lesions in skin & eyes
  - cell mediated immunity to parasite
    - onchodermatitis
    - ocular lesions (produce keratitis in cornea)

*Individuals with most vigorous cell mediated immune responses develop most severe disease manifestations.*

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**Wolbachia**

Antibiotics might be therapeutic for *Onchocerca* patients!

*Onchocerca volvulus* contains a bacterial symbiont (*Wolbachia*)
  - *Rickettsia*-like organisms (*obligate intracellular pathogens*)
in oocyte body wall & all stages of worm
  - *essential for fertility*
transmitted *transovarially* to next generation
  - *similar to mitochondrial inheritance*

*Wolbachia* contain pro-inflammatory endotoxin-like products
  → may contribute to skin & eye pathology
*Wolbachia* endosymbionts are required for
  - parasite embryogenesis & fertility
donoxycycline blocks *Onchocerca* embryogenesis
inflammatory progression (eye & skin changes)
Onchocerca Clinical disease

• dermatitis, eye lesions & onchocercomas
• Mild infection: (<5 nodules/individual) *usually asymptomatic*
• Moderate to severe infection: (10+ nodules in head/neck region) *more serious & numerous symptoms*
  • skin involvement characterized by *intense itching*
    numerous circular elevated papules 1-3 mm diameter
    *puritis* can be intense → *suicide due to extreme discomfort*
  • affected skin becomes thickened & edematous
    atrophies, especially on buttocks
    depigmentation, especially over shins

[Higher magnification of O. volvulus microfilaria. 310 µm x 7 µm.]

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Onchocerca Clinical disease

Lymphadenopathy: lymph node involvement

Ocular lesions:
• *initial infection:*
  *conjunctivitis with irritation, lacrimation & photophobia*
  cornea has punctate lesions *(keratitis)*
  motile or dead microfilariae in conjunctiva
• *long-term infection: sclerosing keratitis causes blindness*
  sclerosis & vascularization
  develops over 20-30 year period
  anterior chamber of eye also invaded
  *iritis, iridocyclitis, glaucoma, optic neuritis & papilitis*
  blindness in 30-40 year olds (responsible for taking care of families)
**Onchocerca Clinical disease**

**Diagnosis:**
- microfilariae in skin sample from affected body part
- **Mazzotti test:**
  - low dose of diethylcarbamazine (DEC)
  - 3 hours → infected patients develop *puritis*
  - *patch test* -- DEC on a small region to elicit a local reaction

**Treatment:**
- ivermectin is drug of choice (*mectazan donation program*)
  - inhibits microfilariae release from females
  - does not kill adult worms in nodule
- communitywide chemotherapy → interrupt transmission

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**Smear of a skin snip from a patient heavily infected with O. volvulus.**

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**Onchocerca Clinical disease**

- **Ivermectin toxicity (not from drug)**
  - increased antigen load from dead & dying parasites
  - fever, angioedema & *puritis*
  - symptoms within 24 hours of treatment
- concurrent loa-loa infection (*West & Central Africa*)
  - epidemiologic overlap between 2 helminth infections
  - ivermectin → severe reaction (*encephalopathy*)

**Prevention & control:**
- distribution related to *dipertan* vectors
  - fast running water of mountain streams
  - long flight range (*parasites miles from nearest breeding site*)

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Loa loa
(Cobbold 1864)

Filarial nematode infection
(African eyeworm, loaiasis, Calabar, Fugitive or Tropical swelling)
Central & West Africa
~13 million individuals infected
~40% prevalence in hyperendemic regions
no reservoir hosts

rubber plantations alter rain forest ecology → emerging infection
infection in travelers returning from rural Africa

Vectors: dipteran flies of genus Chrysops (mango fly)
Loa loa Life Cycle

adults migrate & live in subcutaneous tissues
- female adults: 0.5 mm
- male adults: 0.4 mm
- adult worms can live in host tissues for ~17 years
deposit microfilariae while migrating in subcutaneous tissues

microfilariae (880 µ long)
penetrate capillaries & enter bloodstream (during day)
circulate until ingested by mango fly
larva penetrate stomach of fly & locate to fat body
- 8-10 days → 3rd stage larvae
- migrate to biting mouth parts
- released into bite when fly feeds
larvae in subcutaneous tissues of host → develop into adults (1-4 years) → mate → microfilariae
**Loa loa Clinical Disease**

*adults (subcutaneous) or microfilariae (bloodstream) → no pathology*

Calabar swellings (20-30 cm) on extremities or face
- caused when worms are injured by trauma to skin
- localized site of parasite antigen release
- worm proteins are exposed to immune system
- immune system does not detect worm until it is injured
- pain & itching & for a few days
- •Passage of adult worm across eye subconjuctival space
- •serious complications → **immune complex deposition**
  - some only after administration of DEC
  - cardiomyopathy, nephropathy & pleural effusion
- •**encephalitis** *(high microfilariae levels)* - microfilariae in CSF
- •**endomyocardial fibrosis** - rare --eosinophil infiltration of heart

**Immune complex:** formed between an antibody & soluble antigen. These complexes may cause disease when they are deposited in organs such as the kidneys.

**Diagnosis:**
- Calabar swellings *(angioedema)*
- worm beneath conjunctiva
- microfilariae in a blood smear
- adults in subconjunctival space or subcutaneous tissues

**treatment:**
- diethyl carbamazepine (DEC) for 21 days
  - destroys adult worms & microfilariae

**treatment associated complication:** **encephalopathy**
- due to mass destruction of microfilariae
**Loa loa Clinical Disease**

*iatrogenic* complications of loiasis
- increased risk with high numbers of blood microfilariae
- *apheresis* lowers microfilariae prior to drug treatment
- ivermectin reduces microfilariae
- *antihistamines* or *corticosteroids* decrease allergic reaction

hyperendemic in Central Africa
- 95% of population has *Loa loa* antibodies by age 2
- mass DEC therapy to reduce transmission
- insecticide spraying of mango groves (DDT)
- periodic chemotherapy for filariasis & onchocerciasis
- concern about *Loa loa* infections & *encephalopathy*
- complication of unmonitored DEC treatment of loiasis
- alternative ivermectin & albendazole also have risk

**Terms from the documentary-Guinea Worms (Season 3 Episode 2)**

- **Worm** causes painful large ulcers on lower legs & feet that can become infected by other pathogens.
- **Rural subsistence farmers** - no money for medicine.
  - Also, no reliable medicines to kill worm!
  - Immune system can’t detect, therefore no vaccines
- **15-75 km distance to hospital** - can’t walk that far with an injured foot or leg. Any treatment must be brought to remote villages.
- **Gravid female worm** reaches outer skin by ulcerating tissues. Contact with water disseminates motile larvae. These are eaten by copepods (microscopic shrimp-like fresh water organisms. Humans are infected by drinking water contaminated with infected copepods.
- **Water** can be boiled or filtered. Which is better?
Scientists are on the verge of eradicating one of the oldest parasites that has been infecting humans for thousands of years – guinea worm. This will be the first time that humans have succeeded in the planned extinction of an animal from the planet. This programme, shot on location in Sudan, meets patients of this horribly debilitating disease and looks at the efforts to eradicate it for good.

http://www.rockhopper.tv/programmes/52/

*Dracunculus medinensis*

*(Linnaeus 1758)*
**Dracunculus medinensis**

“guinea worm” or “fiery serpent”  
*formerly in Central Africa, Yemen, India, Pakistan & Latin America*

WHO global eradication campaign (1986)  
prevalence fell >99% (eradicated in 8 countries)  
remaining cases Sudan, Ghana & Nigeria  
most in southern Sudan (*war limits public-health*)

*Dracunculus medinensis* infection  
disfigures skin & subcutaneouse tissues  
serious secondary bacterial infections

reservoirs: cats, dogs, monkeys, horses, cattle, raccoons & foxes  
“therapy” → slow extraction by pulling on worm anterior & winding on stick until removed (used throughout world)

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**Dracunculus medinensis** Life Cycle

adults live in subcutaneous tissues, *usually in lower extremities*  
have acutely curved tails (*to anchor in tissues*)  
adult female parasite is long & thin (>100 cm)  
adult male is 40 mm  
  *female induces vesicular ulcerated lesion*  
host skin lesion surrounds worm vulva  
water contact → worm uterine prolapse  
motile larvae releases into water  
larvae eaten by *copepods* (*small crustaceans in ocean & freshwater*)  
penetrate hemocele of crustacean intermediate host  
develop into infective 3rd stage larvae (2-3 weeks)
**Dracunculus medinensis Life Cycle**

copepods ingested by humans (*usually in drinking water*)

- infective larvae released in small intestine
- penetrate small intestine & migrate in connective tissues
- molt 2x more → mature to adults
- gravid females
  - migrate through subcutaneous tissues to extremities of trunk
  - indurated papules eventually become ulcerated
- life cycle complete when ulcer in contact with water

---

**Dracunculus medinensis. The large circular blister, from which the worm is emerging, will heal leaving a disfiguring scar.**

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**Oral route with wandering**

- Copepods ingest larvae
- Blister ruptures, releasing larvae
- Larvae inside copepods are swallowed
- Larvae are freed from copepods in small intestine
- Larvae penetrate small intestinal wall
- Larvae migrate to lower extremities
- Larvae enter subcutaneous tissues
- Adults mature and live in subcutaneous tissues
- Larvae enter abdominal wall
- Life cycle complete when ulcer in contact with water
**Dracunculus Pathogenesis**

primary infection: no host response to worm
if worms do not complete their migration
die, disintegrate & become calcified
causes problems if calcification in joints
at conclusion of successful migration
worm secretes toxin → local inflammation & ulcer formation
most frequently on lower body (legs & feet)
also on upper extremities & trunk
patients can become sensitized to worm secretions
allergic reactions of urticaria & pruritus
anaphylactic reactions
untreated ulcers
secondarily infected (leads to tetanus, gangrene & death)
1% of cases are fatal

Urticaria = hives; Pruritus = itch

**Dracunculus medinensis Clinical Disease**

characteristic cutaneous blisters & ulcers
secondary infections common
 cellulitis along worm track (~20% permanent disability)
(ankylosing of joints, arthritis or contractures)

Diagnosis:
• identification of adult worm head in skin lesion
• identification of larvae released in freshwater
• radiographs of calcified adult worms

Treatment:
• ancient treatment: winding worm on a stick until it is extracted
• surgical removal of worm (exaggerates allergic reactions)
• metronidazole or niridazole treatment of infection
• anti-inflammatory drugs for allergic worm death symptoms

Contractures: a permanent tightening of muscle, tendons, ligaments, or skin that prevents normal movement of the body part & can cause permanent deformity: Ankylosing = joining
Dracunculus medinensis Clinical Disease

Successful eradication of Dracunculus medinensis possible

1. no human carrier state beyond a 1-year incubation
2. few animal reservoirs
3. seasonal transmission
4. cases easily detected (protruding worms)
5. simple methods for transmission control

prevention & eradication
1. filter drinking water to remove copepods
2. treat water with a larvicide
3. prevent infected individuals from entering water
4. clean water from wells

Aberrant Nematode Infections

Cutaneous Larva Migrans (CLM)
Visceral Larva Migrants (VLM)

Toxocara canis
(Johnston 1916)

Toxocara cati
(Brumpt 1927)
Aberrant Nematode Infections

zoonotic \(\rightarrow\) \textit{occasionally infects humans}

\textit{symptoms from larvae}

\textit{incapable of maturing to adult parasites in humans}

2 diseases caused by this type of parasites

- cutaneous larva migrans (CLM)
- visceral larva migrans (VLM)

• CLM - cutaneous larva migrans (worldwide distribution)
  caused by larvae of dog & cat hookworms
  \textit{Ancylostoma braziliense} & \textit{Uncinaria stenocephala}

other less common \textit{Nematoda} may also be responsible for CLM

raccoon transmitted \textit{Strongyloides procyonis} “duck hunter's itch”

![A. braziliense 3rd stage larva](image1)

“A Creeping eruption” in a
patient who stepped on
larva of \textit{A. braziliense}.

Aberrant Nematode Infections

filariform larvae of \textit{A. braziliense}

in sandy moist soil

(beaches where dogs & cats defecate)

Southeast Asia, Caribbean & Puerto Rico, US coasts

human infection

- filariform larvae penetrate skin
- lack proper environmental cues (cannot develop)
  survive for \(~10\) days
- intense inflammatory reaction with itching
- induced by larval secretions (\textit{hydrolytic enzymes})
- \textit{serpiginous lesions} “creeping eruption” at 1 week
- secondary bacterial infections caused by scratching
  eosinophilia or elevated IgE

Treatment: oral albendazole or ivermectin
Aberrant Nematode Infections

VLM - Visceral larva migrans
OLM - Ocular larva migrans
caused by larvae of
Toxocara canis & Toxocara cati
aberrant migration of larvae through viscera
far more serious than CLM
human infection by ingestion of embryonated eggs of Toxocara
children in Toxocara egg-contaminated sandbox, etc.

Pathology:
larvae migrate through body organs, then die
degree of host damage varies with tissues invaded
(liver, lungs, CNS, eyes)
eyes are most seriously affected organ
marked immune hypersensitivity responses

Toxocara canis and Toxocara cati
Adults live in dog
and cat small intestine
Animals eat embryonated
eggs, acquires adults
Eggs pass in feces and
embryonate in soil
Eggs are ingested
Tissue larva migrate
to all organs via
bloodstream
Larvae hatch in small
intestine and penetrate wall

Embryonated egg of
Toxocara canis.

Toxocara canis
adults: female = 9
cm & male = 6 cm.
**Aberrant Nematode Infections**

dying *Toxocara* larvae
    in _viscera_ (lungs, liver & brain) results in _CLM_
    in _eye_ results in _OLM_

ocular disease occurs in absence of systemic involvement & vice versa

**visceral larva migrans**

mainly a disease of young children under 5 years
fever & enlargement of liver & spleen
respiratory symptoms (bronchospasm resembles asthma)
eosinophilia & IgM & IgG _hypergammaglobulemia_
myocarditis, nephritis & CNS involvement
seizures, neuropsychiatric symptoms, encephalopathy
eosinophilic _meningoencephalitis_

"covert toxocariasis" _spectrum_ = subtler manifestations

larvae in lungs → **asthma**
larvae in brain → “idiopathic seizure disorder”
also linked to intestinal disorders, arthritis & skin rashes

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**Aberrant Nematode Infections**

Diagnosis: pediatric patient should be suspected of VLM if
fever, eosinophilia & hepatosplenomegaly
history of _pica_ (eating soil, feces, paper, etc.)

• **ocular larval migrans (OLM)**
    in older children (5-10 years)
    unilateral vision impairment & *strabismus*
    invasion of retina
    blindness is common

*Strabismus*: condition in which the eyes are not properly aligned with each other

*Procyonis larvae in brain of child who died of VLM.*

*Granuloma in retina of patient with OLM.*

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Granuloma in retina of patient with OLM.
Aberrant Nematode Infections

VLM treatment:
- albendazole is choice for *Toxocara cati* patients
- thiabendazole (older drug) less effective
- mebendazole poorly absorbed outside GI tract
- corticosteroids (suppress allergic manifestations)

OLM treatment:
- vitrectomy (surgery)
- anthelminthic therapy
- corticosteroids

Prevention & Control:
*Toxocara* common in young pets (puppies often harbor worms)
- children with *pica* at risk of ingesting embryonated eggs in soil
- treatment of dogs & control of feces are major control