Hymenolepis nana

- Dwarf tapeworm
- **Definitive Host:** Humans, rodents
  - Most common tapeworm of humans in the world
  - 1% rate of infection in the southern U.S.
  - 97.3% rate of infection in Moscow, Russia
- **Intermediate Host:** Larval and adult beetles (but optional)
  - Larval stage, cysticercoid, can develop in D.H. if it eats the eggs
    - Probably a recent evolutionary event?!?
Hymenolepis nana

- **Geographic distribution:** Cosmopolitan.
- **Mode of Transmission:**
  - Ingestion of infected beetle
  - Ingestion of food contaminated with feces (human or rodent)
  - Fecal/oral contact
- **Control:**
  remove rodents from house
- **Pathology and Symptoms:**
  Generally none because worm is so small (about 40 mm).

Cysticercoid
Hymenolepis nana life cycle

1. Embryonated egg in feces
2. Egg ingested by insect
3. Humans and rodents are infected when they ingest cysticercoid-infected arthropods.
4. Embryonated egg ingested by humans from contaminated food, water, or hands
5. Oncosphere hatches Cysticercoid develops in intestinal villus
6. Adult in ileal portion of small intestine
7. Autoinfection can occur if eggs remain in the intestine. The eggs then release the hexacanth embryo, which penetrates the intestinal villus continuing the cycle.
8. Eggs can be released through the genital atrium of the gravid proglottids. Gravid proglottids can also disintegrate releasing eggs that are passed in stools.
9. Scolex
Hymenolepis diminuta

- Rat tapeworm
- **Definitive Host:** Humans and rats
  - Human infections are uncommon
- **Intermediate Host:** grain beetles (*Tribolium*)
  - Required
- **Geographic Distribution:** Cosmopolitan
- **Mode of Transmission to D.H.:** Ingestion of infected beetle.
Hymenolpeis diminuta

- **Pathology**: Usually asymptomatic
  - because worms are relatively small (90 cm maximum).
- Heavy infections are rare.
  - No fecal/oral infection
- **Diagnosis**: Eggs in feces. Eggs do not have polar filaments.
- **Treatment**: Praziquantel
- **Prevention**: Remove rats from home.
- **Notes**: Easily maintained in laboratories so has been used as the “model” tapeworm to study metabolism, reproduction, genetics, physiology, etc.
*H. diminuta* human infections are rare
Echinococcus granulosis

- A.K.A – Sheep Tapeworm
- **Definitive Host:** Carnivores including dogs, wolves, and coyotes
- **Intermediate Host:** Herbivores including sheep and mice.
- **Geographic Distribution:** Most common in sheep raising countries
  - New Zealand and Australia highest incidence
Echinococcus Life Cycle
Hydatidosis

- Caused by the larval stage.
  - After egg hatches, oncosphere leaves intestines and goes to another location
  - Divides to create more worms
  - Forms a hydatid cyst.
    - Single chamber filled with fluid and larvae
    - Tough, outer wall
- Grows very slowly.
  - May take 20 years for symptoms to start
The cyst is lined by a multilayer parasite tissue with the innermost layer being the **germinal layer**.

This layer is a undifferentiated “stem cell” layer that can spawn the formation of “brood capsules” which are themselves lined by GL.

The **daughter cysts** (the encircled body) "bud" into the center of the fluid-filled cyst.

Thousands of **protoscolices** can fill the hydatid (hydatide sand).

Protoscolices are the infective stage for dogs (each one will grow into an adult worm).

Hydatides usually grow slowly but steadily (1-5 cm per year).

They are usually well tolerated until their size becomes a problem or they rupture.

Cyst rupture or leakage can result in allergic reactions and metastasis.
Hydatidosis

- Cyst can reach large size
  - Holds up to 15 quarts of fluid
  - Fluid contains remains of dead larvae and worm waste
- **Symptoms:** Depends on location.
  - Most common location are lungs, liver, abdominal cavity
    - Asymptomatic
  - CNS – causes problems very quickly
  - If cyst ruptures, host dies of anaphylactic shock
Hydatidosis

- **Prevention:** Most U.S. cases are from improper handling of dog feces or accidental egg ingestion while handling dog.

- In Kenya, transmission between humans and dogs are frequent.
  - Humans become intermediate host by eating roasted dog intestines.

- In Lebanon, most human cases in leather workers.
  - Dog feces are used in tanning solutions.
Comparative Egg Size

- Metagonimus yokogawai
- Heterophyes heterophyes
- Opisthorchis felineus
- Clonorchis sinensis
- Taenia
- Hymenolepis nana
- Enterobius vermicularis
- Trichuris trichiura
- Ascariis lumbricoides
  - fertile
  - Hookworm
- Diphyllobothrium latum
- Hymenolepis diminuta
- Paragonimus westermani
- Trichostongylus
- Ascaris lumbricoides
  - fertile
  - Schistosoma japonicum
  - Schistosoma haematobium
  - Schistosoma mansoni
  - Fasciola hepatica
  - Fasciolopsis buski
Carbohydrate Metabolism in Eukaryotes

Hexose → Pyruvate → CO₂ + Acetate

No compartmentalization → Substrate level phosphorylation

Hexose → Pyruvate → CO₂ + H₂ + Acetate

Hydrogenosomal compartmentalization → Substrate level phosphorylation

Hexose → Pyruvate + O₂ → CO₂ + H₂O

Mitochondrial compartmentalization → Oxidative phosphorylation

Hexose → Malate (O₂) → CO₂ + Acetate, Propionate, Succinate

Mitochondrial compartmentalization → Anaerobic metabolism
Helminth Carbohydrate Metabolism

- **Homolactate fermentors** - Schistosomes and Filarial worms
  - Production of lactic acid by anaerobic glycolysis and excretion of lactic acid
  - 2 moles of ATP formed per mol of glucose

- **Mixed fermentation** - adult worms, later larval stages

- **Respiration** - free-living and early larval forms
General Platyhelminth Metabolism

- **Facultative Anaerobes**
  - glucose is main energy source

- **Glucose** is taken down to pyruvate and PEP through *glycolysis* (NAD is recycled by reduction of pyruvate to lactate, succinate and acetate)

- **Malate dismutation**
  - CO2 fixation step - PEPCK
  - 3 enzymes in common
  - MDH  FH  FR

- The adult cestode store large amounts of GLYCOGEN to provide energy between host meals
Aerobic to Anaerobic transitions
Fig. 1. Anaerobic fumarate-respiration in the mitochondria of Fasciola hepatica. The oxidative branch of malate dismutation is indicated in purple and the reductive branch in green. Electron transport to and from NADH/NADPH and rhodoquinone is indicated in blue. Note that the enzyme complexes 8 and 9 are part of the electron transport chain and in fact located in the mitochondrial inner membrane. The dashed arrow through enzyme complex 9 is symbolic for proton translocation over the mitochondrial inner membrane. The numbers indicate the following enzymes: (1) phosphoenolpyruvate carboxykinase, (2) malate dehydrogenase, (3) malic enzyme, (4) pyruvate dehydrogenase, (5) acetate: succinate CoA-transferase, ASCL (6) succinyl-CoA synthetase, (7) fumarase, (8) fumarate reductase, (9) NADH-dehydrogenase. Complex I, (10) propionate:succinate CoA-transferase, PSCL, (11) methylmalonyl-CoA mutase + methylmalonyl-CoA epimerase; (12) propionyl-CoA carboxylase. Abbreviations: AcCoA, acetyl-CoA; FUM, fumarate; MAL, malate; Methylmal-CoA, methylmalonyl-CoA; OXAC, oxalacetate; PEP, phosphoenolpyruvate; PROP, propionate; prop-CoA, propionyl-CoA; PYR, pyruvate; RQ, rhodoquinone; RQ-H2; reduced rhodoquinone; SUCC, succinate; Succ-CoA, succinyl-CoA.
Platyhelminth Treatments

- Quinoline derivatives
  - Praziquantel
  - Oxamniquine
- Benzimidazole derivatives
  - Mebendazole
  - Albendazole
  - Thiabendazole
- Other drugs
  - Niclosamide
  - Metrifonate

- Why Praziquantel?
  - Early 20th century relied heavily on antimonials
  - Effective against a number of species
  - Most widely used drug
  - Safe, fairly cheap to make
# Common agents for helminth infestations

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<th>Drug(s) of choice</th>
<th>Alternative(s)</th>
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<td><em>Taenia saginata</em> (beef tapeworm)</td>
<td>Niclosamide or Praziquantel</td>
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<td><em>Taenia solium</em> (pork tapeworm)</td>
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<td><strong>TREMATODES</strong></td>
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<td><em>Schistosoma haematobium</em></td>
<td>Praziquantel</td>
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<td><em>Schistosoma mansoni</em> (bilharzia)</td>
<td>Praziquantel</td>
<td>Oxamnique</td>
</tr>
</tbody>
</table>
A little history on praziquantel

- Large number of pyrazino isoquinoline compounds were synthesized by Merck as potential tranquilizers (~late 1960s)

- Partnership between Merck and Bayer led to the first screening of the compounds as possible anthelmintics (mid-1970s)

- EMBAY 8440 - now known as praziquantel - was an effective antitrematode and anticestode compound.

- First human volunteers tested in 1978, by 1980 praziquantel had become the drug of choice to treat schistosomiasis as well as a number of other worm infections
Praziquantel (Biltricide)

- Broad spectrum helminth chemotherapeutic
- Drug of choice for treating Cestode and Trematode infections
- Effective single dose treatment
- Inexpensive - ~$0.25/dose
  - Decreasing still - $0.075/tablet
- Minimal side effects
  - Nausea, vomiting, abdominal pain - brief period
Tegument is a syncytium

- absorb nutrients (drugs) through the tegument
- praziquantel causes vacuolization of the syncytial distal tegument
- Processes can be observed in flukes or tapeworms, both in vivo and in vitro
- The tegumental vacuoles finally burst leading to parasite death

Trematode and Cestode tegument structure is similar (not identical)
Praziquantel - mode of action

- Influx of Ca²⁺ results in muscle contractions of entire body
  - Appears non-selective
- Spastic contraction of musculature
- Vacuolization and blebbing of the tegument
- Increased exposure of worm antigens
- Leads to changes in glucose uptake
- Accelerated depletion of energy stores
- Host-immune response is necessary for complete activity of PZQ
Widespread use

**Eastern Nishikigoi**

- **Breed**: GINRIN SHOWA
- **Sex**: Female
- **Price**: $14000.00
- **ID**: 060004

Please call or email for availability or ordering information.

**Eastern Nishikigoi**
14700 Goldenwest Street
Westminster, CA 92683
(714) 890-1989 - phone
(714) 895-7958 - fax

Close Window
Mebendazole

- Broad spectrum
- Binds tubulin and disrupts microtubules
- Low toxicity, however poorly absorbed
Thiabendazole

- Introduced in 1961
- Blocks fumarate reductase
- Also binds tubulin
- High incidence of nausea, vomiting, anorexia
Mebendazole & Thiabendazole

- High affinity binding effectively irreversible

Mebendazole

- Glucose
- Fumarate reductase
- Tubulin \( \alpha, \beta \)
- Microtubules
- MTOC
- Nucleus
Benzimidazole binding to tubulin

A growing microtubulin

B tubulin-benzimidazole complex

Unfolding region of carboxy terminus induced by benzimidazole

Abnormally unfolded loop of β-tubulin prevents further addition of α, β-subunits; inhibition of microtubule polymerization
Applied parasitology:

During the Paris Olympics, sprinter Gilbert Velox was disqualified for "illegal use of his tapeworm".
One of the worst jobs in science?

**Worm Parasitologist**  
By William Speed Weed

Certainly, studying worm parasites isn’t nearly as bad as playing host to them. But here’s an essential distinction: The medicos who go into this line—God bless ’em—do it by choice. Supported by the World Health Organization and various international charities, they travel to the tropics to eradicate diseases that afflict millions of people. Yet although we’re regularly treated to tales of Ebola warriors, we rarely hear about the tribulations of the worm docs.

For instance . . . [consider these ellipses a pause to enable the faint of stomach to flee the page] . . . *Ascaris lumbricoides* eggs hatch in the small intestine, then migrate to the lungs; they’re coughed into the mouth and swallowed back to the gut, where each worm will grow as long as 16 inches and where each female will lay billions of eggs to be defecated forth so that a new cycle of life can begin. (The adults can exit this way too, in a large bolus that resembles a tangle of spaghetti.) The *Wuchereria bancrofti* worm sometimes settles in the scrotum, where it blocks the flow of lymph. This can result in elephantiasis, a wretched condition that features scrotal swelling to jack-o’-lantern proportions and an infection that reeks of death. Moving right along . . . [see helpful ellipsis-related note, supra] . . . the female *Dracunculus medinensis* migrates from the gut to a point just under the skin of, say, a leg, where she then commences growth to a length of as great as three feet, and where, ultimately, she lays her eggs.

When the thousands of babies make their joyous arrival, they blister the skin and pop through, leaving Mom behind. The traditional way to get rid of her is to wrap her head around a stick and twist very slowly—one turn of the stick per day—for weeks or months, depending on how long she is. (This treatment is so old that it inspired the ancient snake-and-pole aesculapius symbol of medicine.) And so worm parasitologists are unsung heroes—and decorum dictates that unsung they shall remain. “We can’t show pictures or even really talk about these diseases,” says parasitologist Eric Ottesen of Emory University. “Society just isn’t ready for it.”