Even More Worms!

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Disclosures of Financial Relationships with Relevant Commercial Interests

- None

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Major Helminth Pathogens

TREMATODES

Blood flukes
- *Schistosoma mansoni*
- *Schistosoma japonicum*
- *Schistosoma haematobium*

Liver flukes
- *Fasciola hepatica*
- *Clonorchis sinensis*
- *Opisthorchis viverrini*

Lung flukes
- *Paragonimus westermani*

Intestinal flukes
- *Fasciolopsis buski*
- *Metagonimus yokagawai*

CESTODES

Intestinal tapeworms
- *Taenia solium*
- *Taenia saginata*
- *Dibothriocephalus latus*
- *Hymenolepis nana*

Larval cysts
- *Taenia solium*
- *Echinococcus granulosus*
- *Echinococcus multilocularis*

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- *Strongyloides stercoralis*
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Tissue Invasive
- *Wuchereria bancrofti*
- *Brugia malayi*
- *Onchocerca volvulus*
- *Loa loa*
- *Trichinella spiralis*
- *Angiostrongylus cantonensis*
- *Anisakis simplex*
- *Toxocara canis/cati*
- *Baylisascaris procyonis*
- *Gnathostoma spinigerum*
- *(Dracunculus medinensis)*

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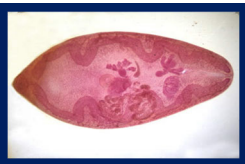
Trematodes (Flukes)

- Flat, fleshy, leaf-shaped worms
- Usually have two muscular suckers
- Usually hermaphroditic (except Schistosomes)
- Require intermediate hosts (usually snails or clams)
- Praziquantel treats all (except *Fasciola hepatica*)



Paragonimus (CDC DpDx)

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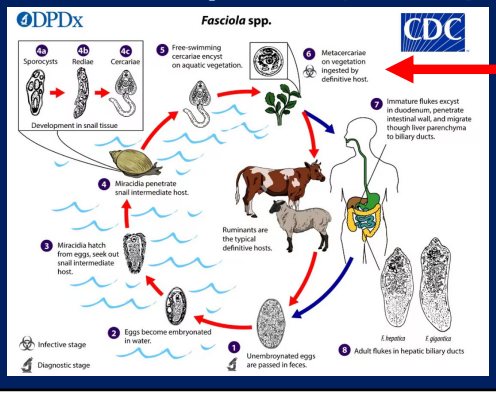
Fasciola hepatica ("Sheep Liver Fluke")



Cercariae have to encyst on vegetation!

F. hepatica (2-3 cm in length)
Worldwide distribution in tropical areas (high prevalence: Bolivia, Peru)

F. gigantica (up to 7.5 cm in length)
Present in Africa, SE Asia, Pacific

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Fasciola hepatica ("Sheep Liver Fluke")

- Acquired by eating encysted larvae on aquatic vegetation (e.g., Water chestnuts)
- Fluke migration through the liver: RUQ pain and hepatitis
- Arrive at biliary ducts in liver and mature over 3-4 months
- Can induce biliary obstruction

Dx: eggs in stool exam (low sensitivity), serology

Rx: triclabendazole (FDA approved in 2019!)

(***Note: fasciola species are the only trematode parasites of humans that don't respond well to praziquantel)

F. hepatica
(CDC DpDx)

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Clonorchis sinensis

"Chinese Liver Fluke"

China, Japan, Eastern Russia, Korea, Vietnam

- Eggs →snails →freshwater fish
- Acquisition by ingestion of undercooked fish
- Flukes develop in duodenum then migrate to liver bile ducts
- Can live for > 15 years, making 2000 eggs/day
- Cats and dogs can serve as reservoirs

Opisthorchis viverrini

"Southeast Asian Liver Fluke"

- Similar lifecycle
- Also acquired by eating fish

Both can cause:

- **Biliary obstruction**
- **Cholelithiasis**
- **Cholangiocarcinoma**

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Paragonimus westermani "Lung Fluke"

Eggs→snails→freshwater crabs and crayfish

Ingestion of undercooked seafood

(China, Japan, Korea, India, Philippines)

Adults migrate to LUNGS, frequent EOSINOPHILIA

Symptoms:

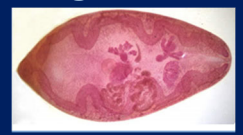
- *Fever, cough, diarrhea during acute migration*
- *Later, may have chest pain as worms migrate through lungs*
- *Can develop chronic pulmonary symptoms*

Dx: Sputum and/or stool exam for eggs, serology

NOTE: Cases of Paragonimus kellicotti acquired in U.S. by ingestion of raw crayfish in rivers in Missouri!

CID 2009 Sep 15;49(6):e55-61.

Clin Microbiol Rev 2013 Jul;26(3):493-504



CDC DpDx

CDC DpDx

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Intestinal Flukes

Fasciolopsis buski

("Giant Intestinal Fluke" 2 cm w x 8 cm)

- Acquisition: eating encysted larval stage on aquatic vegetation
- Symptoms: usually asymptomatic
  - Can cause diarrhea, fever, abdominal pains, ulceration, and hemorrhage

Dx: eggs in stool

Metagonimus yokagawi

(2.5mm x 0.75mm)

- Acquisition: eating larvae in undercooked fish
- Symptoms: diarrhea and abdominal pain

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Cestodes (Tapeworms)

- All (except *D. latum)* have suckers with surrounding hooklets on the scolex (head) to attach to intestinal lining
- Have flat, ribbon-like bodies composed of proglottid segments which contain reproductive organs
- Have no digestive systems (food absorbed through soft body wall of worm)

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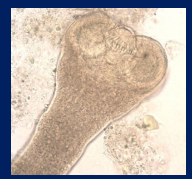
Hymenolepis nana

"Dwarf tapeworm" (4-6 cm long)
Found worldwide → the most common cestode infection of humans
Predator (larval stage): rodents, humans
Prey (tapeworm stage): beetles!
Acquisition: by ingestion of eggs in contaminated food or water
OR by ingestion of infected grain beetle!
Symptoms: Often asymptomatic
With large parasite burdens, can cause
-loose stools, diarrhea
-crampy abdominal pain
-weakness
Diagnosis: finding eggs or proglottid segments in stool
(note: sometimes confused for pinworms)
Treatment: praziquantel 25 mg/kg x 1, repeat dose in 10 days
(higher than for most tapeworm infections)

H. nana egg in wet mount
(note the hooklets)
CDC DpDx



H. nana scolex in stool sample
(note the hooklets and suckers)
CDC DpDx

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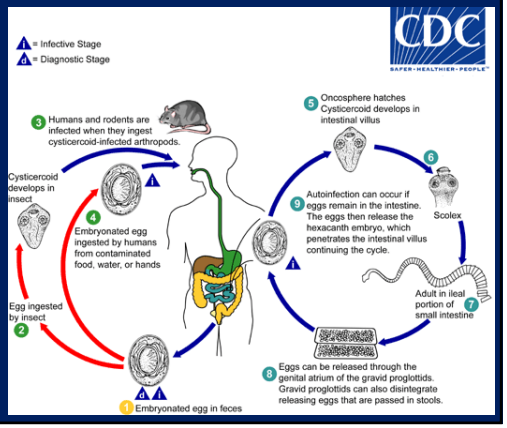
Hymenolepis nana



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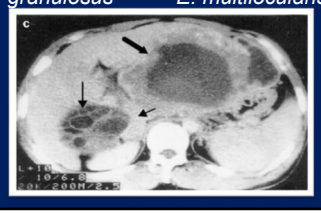
Echinococcus multilocularis

Fox/rodent lifecycle

Causes an infiltrative, tumor-like growth in liver

- → poorly demarcated
- → has a semi-solid nature (does not form large cysts)

E. granulosus *E. multilocularis*



Lancet 2003;362:1295-304

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Nematodes (Roundworms)

- Non-segmented round worms
- Flexible outer coating (cuticle)
- Muscular layer under the cuticle
- Nervous, digestive, secretory, and reproductive systems

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How Do People Get Infected with Nematodes?

1. Eating eggs in fecally contaminated food or soil
   Ascaris, Trichuris, Enterobius, and Toxocara
2. Direct penetration of larvae through skin
   Hookworms, Strongyloides
3. Eating food containing infectious larvae
   Trichinella, Angiostrongylus, Anisakis
4. Vector transmission
   Wuchereria, Brugia, Oncho, Loa

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Paracapillaria philippinensis

Epidemiology: primarily SE Asia

Risk factor: **eating raw freshwater fish**

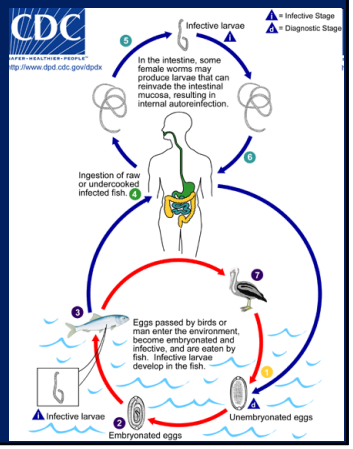
Sxs:

Often initially asymptomatic

Over time develop:

- borborygmus
- abdominal pain
- watery diarrhea

→ If not treated over weeks to months get large electrolyte losses and dehydration which can lead to death



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Paracapillaria philippinensis

Pathogenesis:

Eat infected raw fish

→ larvae released into intestine

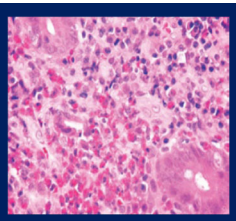
→ grow to adults which burrow in mucosa

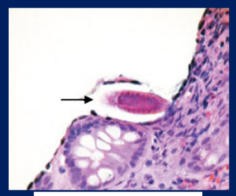
→ female worms lay eggs (oviparous)

→ some female worms are larviparous

→ some larvae burrow into the intestinal lining and develop into adults

→ over weeks to months the worm burden increases (from a few worms to tens of thousands) and symptoms progress





N Engl J Med 2008;359:75-80.

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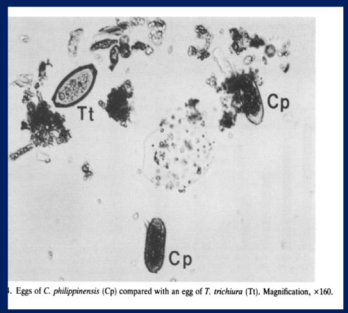
Paracapillaria philippinensis



. Eggs of *C. philippinensis* (Cp) compared with an egg of *T. trichiura* (Tt). Magnification, ×160.

Cross J, Clin Micr Reviews, 1992

N Engl J Med 2008;359:75-80.

Dx: stool o/p (eggs similar to Trichuris)

Rx: 10 d course albendazole + supportive Rx (IVF, replete electrolytes, etc.)

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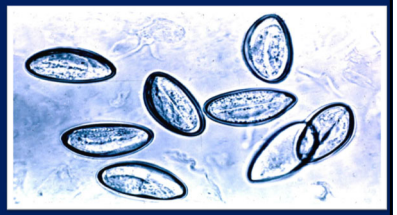
Enterobius vermicularis (Pinworm)



- Found everywhere
- Fecal/oral
- Humans are the only hosts
- Peri-anal itching
- Also: vaginal itching/discharge (vulvovaginitis) nausea/abdominal pain, rare: appendicitis

Dx: stool o&p exams not very helpful
→ "pinworm paddle test" early am before showering or defecating, multiple tests increase sensitivity
→ eggs have one flat side

Rx: pyrantel pamoate, albendazole, or mebendazole single dose
→ **treat all members of household**
→ **retreat everyone in two weeks**
→ careful trimming of fingernails, hand washing, washing of bedclothes to rid house of eggs

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Question #1

A 13-year-old girl developed a pruritic rash on her foot after moving to rural northeast Florida.

Which of the following helminths is the most likely cause of the rash?

A. *Enterobius vermicularis*
B. *Ascaris lumbricoides*
C. *Trichuris trichiura*
D. *Toxocara canis*
E. *Anyclostoma caninum*

Am Fam Physician 2010, 81(2): 203-4.

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Cutaneous Larva Migrans

Creeping eruption caused by dog or cat hookworms

Ancylostoma caninum
Ancylostoma braziliense
Uncinaria stenocephala

- Worms migrate laterally
- Unable to penetrate basal membrane of human skin
- Can occur 2-8 weeks after exposure

Figure 1. Cutaneous Larva Migrans Caused by *Ancylostoma braziliense*.

N ENGL J MED 351;8 WWW.NEJM.ORG AUGUST 19, 2004

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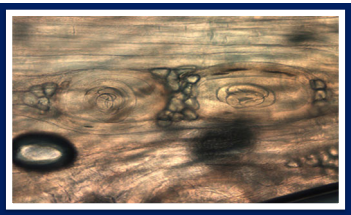
Trichinellosis

(T. spiralis and, in Africa, T. nelsoni)

1. Eat meat containing cysts. (pork, boar, horse, wild game)
2. Larvae are released from cysts by gastric acid
3. Adults invade sm. Bowel, and mature into adults over 1-2wks*
   --> ABDOMINAL CRAMPS,
   DIARRHEA IF HEAVY INFXN
4. Adults (who only live for about a month) produce larvae.
5. Larvae migrate to striated muscle, encyst, and live in "nurse cells
   - **MUSCLE PAIN**
   - **PERIORBITAL EDEMA**
   - **EOSINOPHILIA**
   - OCC CNS AND HEART DAMAGE
     +/- Fever and Urticaria

*Molt four times within 40h and then copulate within hours after final ecdysis. Newborn larvae (NBL, L1 larvae) can be released as soon as 4 days after infection! (4 larval stages, 1 adult stage) PMID: 11895947



CDC DPDx

Diagnosis:
- Serologies are supportive
- + Biopsy is definitive

Treatment:
- Albendazole + steroids

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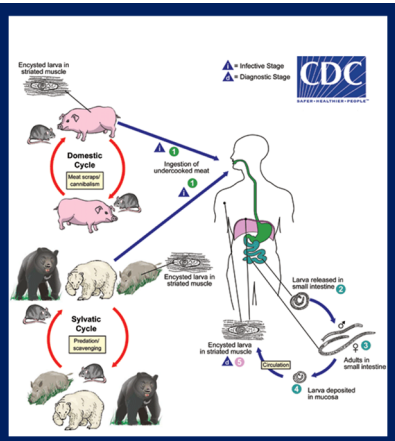
Trichinellosis



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Anisakis

Ingestion of larvae in raw or undercooked seafood (found worldwide)
In humans, parasite buries its head into gastric mucosa. Eosinophilia common.

Symptoms
- Due to invasion of worm (pain, vomiting)
- Due to allergic rxn to worm
  (mild urticaria, itchy sensation back of throat, anaphylactic shock)

Treatment

→ usually simple endoscopic removal
→ for allergic symptoms, avoid contaminated fish

Larvae are typically 1.5-3.0 cm in length

CDC DPDx

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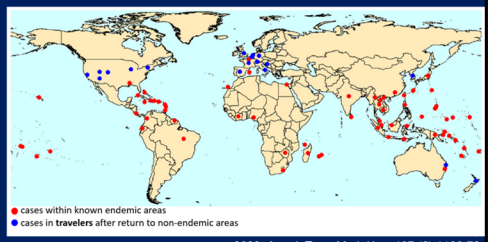
Angiostrongylus

The most common parasitic cause of eosinophilic meningitis worldwide

Appears to be spreading in range

Acquisition by eating raw or undercooked
- Snails or slugs
- Freshwater prawns, shrimps, crabs, frogs
- Contaminated produce (leafy greens)

A. cantonensis



2022, Am. J. Trop. Med. Hyg, 107 (6):1166-72
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Two species cause disease in humans

A. cantonensis – **eosinophilic meningoencephalitis**

→ China, SE Asia, Japan, Australia, Pacific basin, Hawaii, Caribbean, Africa, everywhere

A. costaricensis – **inflammation of the GI tract (abdominal angiostrongyliasis)**

maturation of larvae in intestinal wall

eosinophilic granulomas on histopathology of intestinal biopsies

→ Central and South America

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Angiostrongylus in Florida!

Snails and rodents in Florida have been documented to harbor Angiostrongylus for several years

Between June 2021 and Jan 2022

→ Three pediatric cases of eosinophilic meningitis due to Angiostrongylus were reported in Florida

19-month-oldresented with refusal to walk
- Geophagia sand at beach
- 21-day hospitalization

10-year-old presented with 3 weeks of progressive headache and vomiting
- Had eaten a snail 1 month prior on a dare
- Prolonged hospitalization with intubation

8-month-old presented with fever, vomiting, lethargy, and left-sided esotropia
- No h/o unusual ingestions
- 14-day hospitalization

In all three cases Angiostrongylus was identified by cell-free DNA next-gen sequencing (Karius®) of plasma

Journal of the Pediatric Infectious Diseases Society, Volume 13, Issue 12, December 2024, Pages 639–642, https://doi.org/10.1093/jpids/piae113

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Angiostrongylus cantonensis

Prevention (recommendations from the Hawaii DOH)

→ Do not eat raw/undercooked snails or slugs, freshwater prawns, shrimps, crabs, frogs

→ Inspect and rinse all produce, especially leafy greens

→ Wear gloves when handling snails or slugs and wash hands after handling snails or slugs

Also: rodent eradication and freezing of mollusks and crustaceans

https://health.hawaii.gov/docd/disease_listing/rat-lungworm-angiostrongyliasis/#info_for_clinicians

Diagnosis
- Usually presumptive (eosinophilic meningitis + exposure history)
- Serology (not commercially available)
- CSF PCR (Hawaii DOH State Laboratory, NIH as research assay)

Treatment: corticosteroids + albendazole

(see 2021 Guidelines paper in Parasitology, 148,227-233. PMID:32729438)

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Question #2

A 6-year-old boy from Indiana who has a pet dog and likes to play in a sandbox presents with fever, hepatosplenomegaly, wheezing, and eosinophilia. He has never travelled outside the continental U.S.

What is the most likely causative agent acquired in the sandbox?

A. *Anisakis simplex*
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Toxocariasis (and Baylisascariasis)

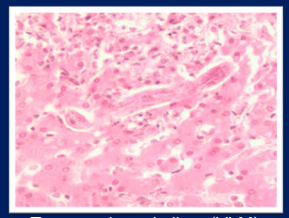
Due to dog (*Toxocara canis*), cat (*Toxocara cati*), and raccoon (*Baylisascaris procyonis*) ascarids.

Humans acquire infection by ingestion of animal feces.
In humans → larvae hatch in intestine and migrate to liver, spleen, lungs, brain, and/or eye.

Symptoms

Visceral Larva Migrans (VLM)
usually 2-5 year olds
fever, eosinophilia, hepatomegaly
also wheezing, pneumonia, splenomegaly

Ocular Larva Migrans (OLM)
often in 10-15 year olds
retinal lesions that appear as solid tumors



Toxocara larva in liver (VLM)

Baylisascaris often more severe and more likely to cause CNS disease (eosinophilic meningitis)

CDC DPDx

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Toxocariasis

Dx: clinical picture + Toxocara antibody testing
(serum and intraocular fluid by ELISA testing)

NOTE: Toxocara IgG is only supportive b/c many individuals have + Ab due to prior exposure

Rx: usually self-limited disease
acute VLM or OLM can be Rx with albendazole and steroids

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Gnathostoma spinigerum and hispidum

Undercooked freshwater fish (ceviche!), frogs, birds, reptiles
Asia (esp. Thailand), Central/South America, parts of Africa

→ Disease due to migrating immature worms
→ Often with peripheral eosinophilia
→ May have initial epigastric pain, nausea, vomiting as worms penetrate GI tract and migrate to tissues

SKIN: migratory, painful subcutaneous swellings (recur every few weeks, can last for years)
creeping eruption/cutaneous larva migrans

TISSUE: visceral larva migrans
eosinophilic meningoencephalitis
radiculomyelitis
ocular disease (anterior and posterior uveitis)

Dx: empiric or by biopsy, no antibody test available in the U.S.

Rx: can be difficult, may require 3 weeks of albendazole

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What is this?

Emerging Guinea Worm.

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Dracunculus medinensis

(fiery serpent, affliction with little dragon)

Emerging Guinea Worm.

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- Acquired by drinking water contaminated with microscopic copepods ("water fleas")
- One year after a person is infected, adult female worms emerge and expel their larvae
- Adult worms can be >2 feet long.
- Worm emergence is excruciatingly painful
  - → predisposes to bacterial superinfection
  - → can lead to disability for months
- No effective medical therapy → treatment is slow manual extraction
- Global eradication campaign since 1980s, down to less than 10 cases per year
- Infection is preventable by
  - → filtering water through fine cloth to remove copepods
  - → not walking in drinking water
  - → killing copepods and larvae with chemicals applied to drinking water
- Complete eradiation has been elusive as some animals, especially dogs, can serve as reservoirs

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Caveat to today's talk – a bit simplistic
Multiple parasites can cause similar diseases

Eosinophilic meningitis

Nematodes
- **Angiostrongylus cantonensis (rat lung worm)**
- **Baylisascaris procyonis (racoon ascarid)**
- **Gnathostoma species**
- Toxocara canis & T. cati
- Trichinella spiralis
- Strongyloides stercoralis
- Loa loa
- Meningonema peruzzi (filaria of monkeys)

Trematodes
- Schistosoma species (larvae or eggs)
- Paragonimus westermani
- Fascioliasis

Cestodes
- Neurocysticercosis
- Echinococcus

Non-helminth infections
- Fungi (esp. Coccidiodes and Cryptococcus
- Myiasis with CNS entry
- Bacteria (very rare; Tb, syphilis, Rickettsia, Strep)
- Viruses (very rare; LCMV, Coxsackie)
- Protozoa (very rare; Toxoplasmosis)

Malignancies
- Hodgkin's
- NHL
- AML
- Meningeal carcinomatosis
- Glioblastoma

Primary Hypereosinophilic Syndromes

Inflammatory/allergic reacitons
Medications (NSAIDS, ciprofloxacin, contrast dye)
VP shunt, other foreign bodies

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Good Luck!

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