Introduction to Parasitology

The basics are just the beginning

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Objectives for Learning

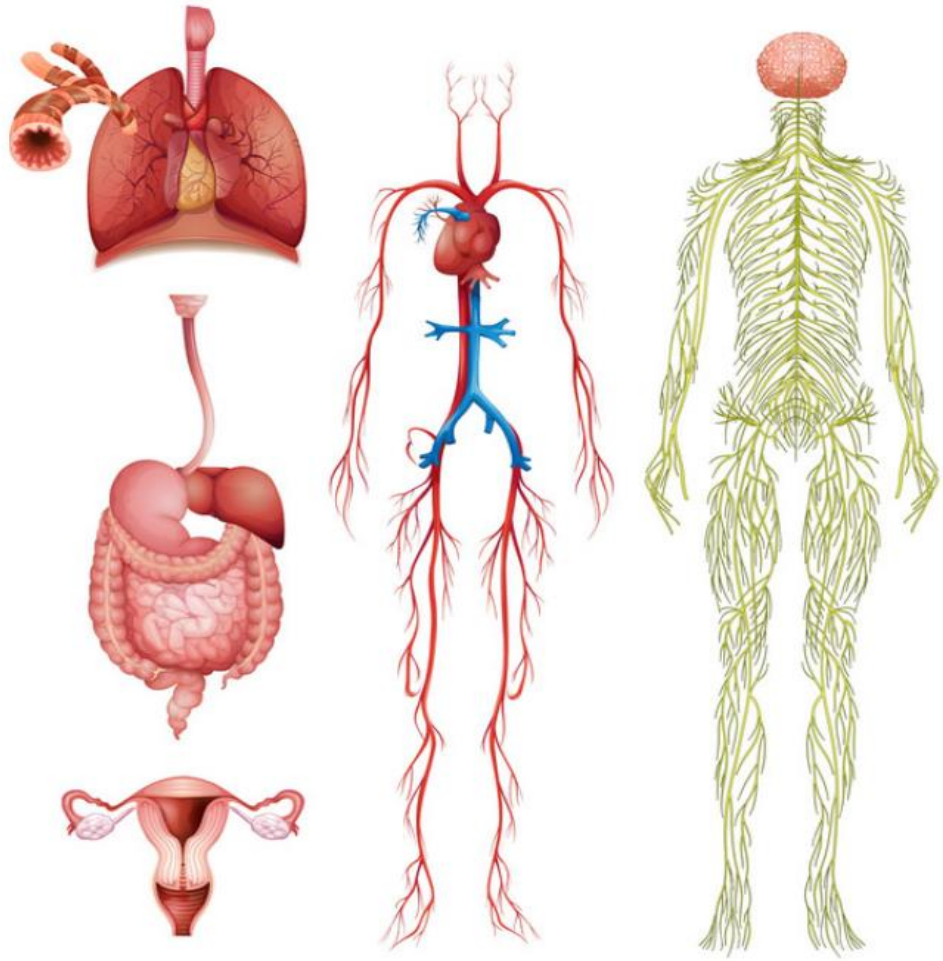
Understand parasite diversity/taxonomy

Recognize clinically relevant parasites found in humans and how to test for them

Understand the impact and role of parasites in human health

Parasitology Structure

- Basic overview of all sites
- Focus on:
  - » Brain/Central nervous system
  - » Skin/Soft tissue
  - » Lungs
  - » Liver
  - » GU
  - » Blood (See separate video)



What is a parasite?

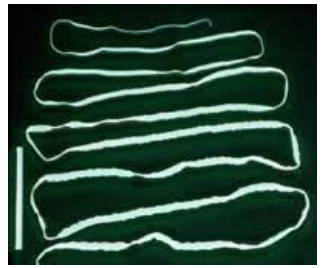
An organism that derives a survival benefit from a host at the expense of the host.

Key Concepts in Parasitism

- Definitive Host –where sexual maturity and reproduction occur for completion of transmission cycles
- Intermediate Host – where asexual or developmental stages occur (e.g. larvae development, excystation, etc). Not competent for development to final lifecycle stages
- Paratenic Host – a host which harbors an immature stage but no further development of the parasite occurs; used for further transmission
- Reservoir Host – a primary host that maintains a parasite in nature
- Dead-end or Accidental Host – where various levels of parasite life cycle can occur, but the parasite cannot complete the entire life cycle and fails to perpetuate gametes/fully mature.

Broad (Medical) Classification of Parasites

- Helminth – worm
  - » Flatworms – Platyhelminths (only 2 parasitic classes)
    - Cestoda – tapeworms
    - Trematoda – flukes
  - » Roundworms – Nematoda



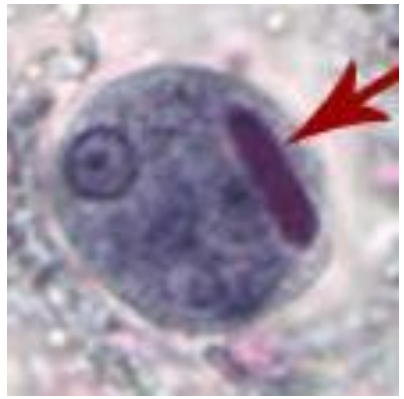
Taenia

Paragonimus

Ascaris

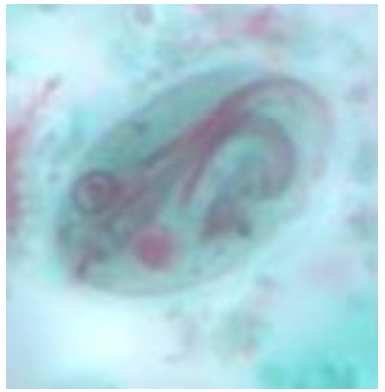
Broad (Medical) Classification of Parasites

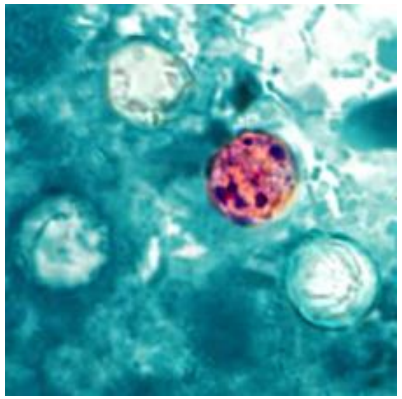
- Protozoa – unicellular eukaryotic free-living or parasitic organisms
  - » Ameba
  - » Coccidia
  - » Flagellates
  - » Ciliates
  - » Stramenopiles
  - » Microsporidia*



Entamoeba

Giardia





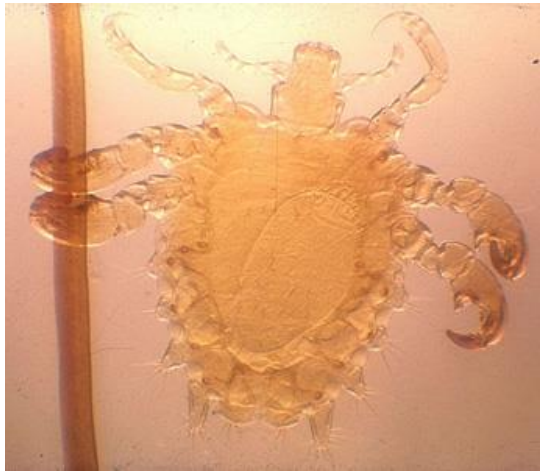
Cyclospora

Balantioides

* Fungi, not protozoa

Broad (Medical) Classification of Parasites

- Arthropods –eukaryotic free-living or parasitic organisms
  - » Mites
  - » Lice
  - » Fleas
  - » Ticks
  - » Fly larvae (myiasis)
  - » True bugs

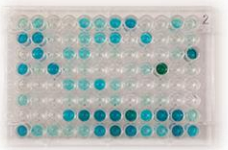


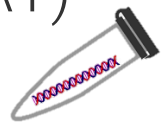
Pubic louse

Scabies mites

Diagnostics

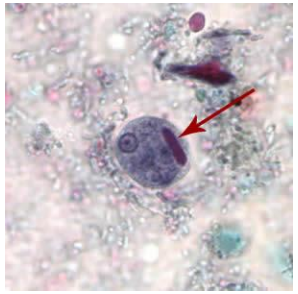
- Specimen dependent/organism dependent
  - » Each organism discussed in more detail within body systems
- Broad types of tests include:
  - » Stool parasite examinations
  - » Body fluid parasite examinations and cytology
  - » Histopathology of tissue
  - » Antigen detection
  - » Antibody detection (serology)
  - » Nucleic acid amplification tests (NAAT)
  - » Culture (very limited use)





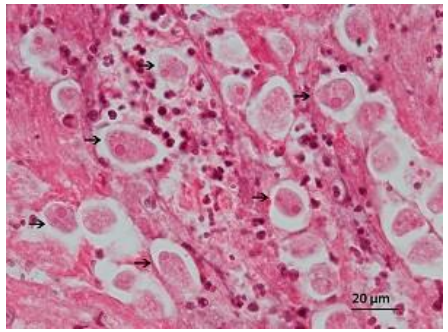
Diagnostics - Microscopy

- Stool examination
  - » Wet mount and permanent stain (trichrome)
  - » Other special stains



- Body fluid examination
  - » Aspirates

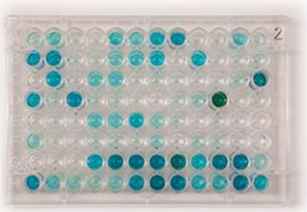
- Tissue
  - » H&E stains



Diagnostics – Antigen detection

- Detection of antigen (immuno-stimulatory component) from a parasite in a patient specimen
- Variable in performance and specimen types
  - » Blood & stool
- Rapid time to result

Diagnostics – Antibody detection

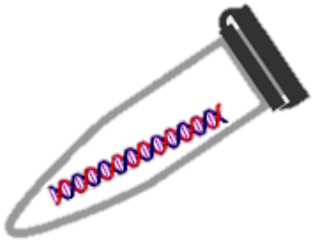


- Detection of antibody from a patient that recognizes antigen(s) from a parasite

- Variable in performance and specimen types
  - » Serum and CSF

- Moderate time to result, limited availability

Diagnostics – NAAT



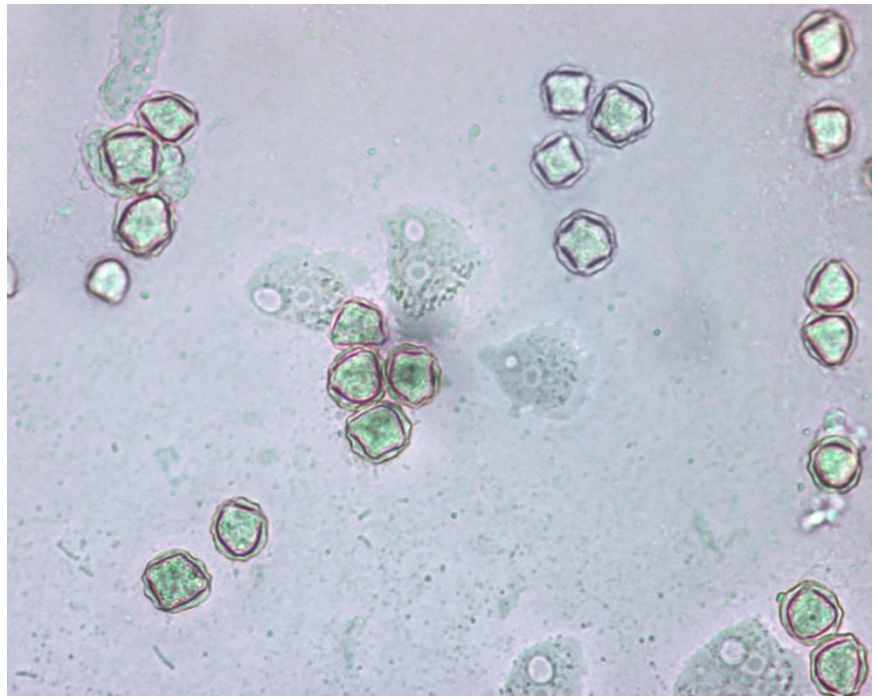
- Detection of nucleic acid from a parasite in a patient specimen

- Variable in specimen types, excellent specificity
  - » Sensitivity depends on organism and biology

- Long time to result for rare parasites, limited availability
  - » Stool parasites can be faster and readily available

Diagnostics – Culture

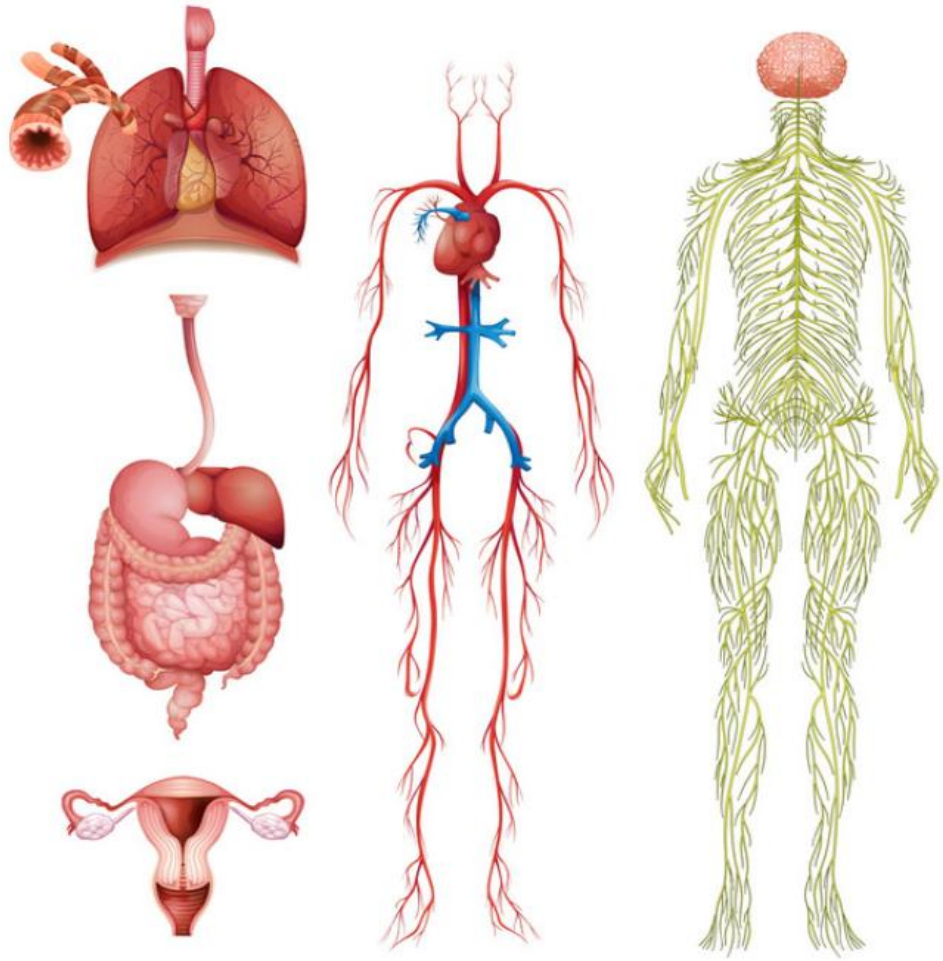
- Limited utility in parasitology
- Insensitive
- Not routinely performed in most labs
- Can be biosafety risk



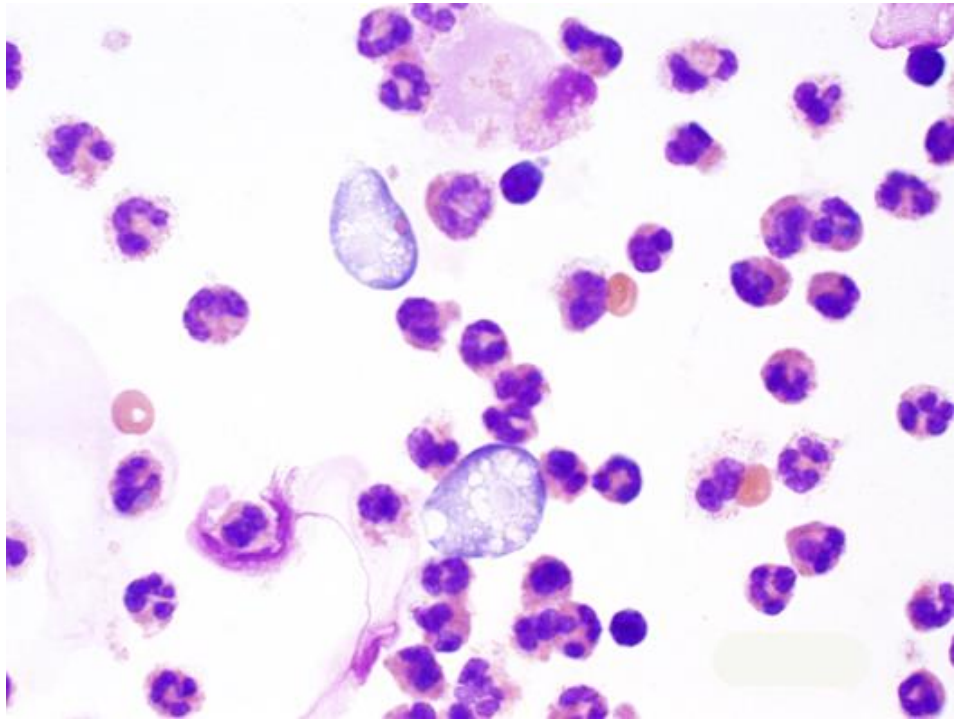
Acanthamoeba in culture

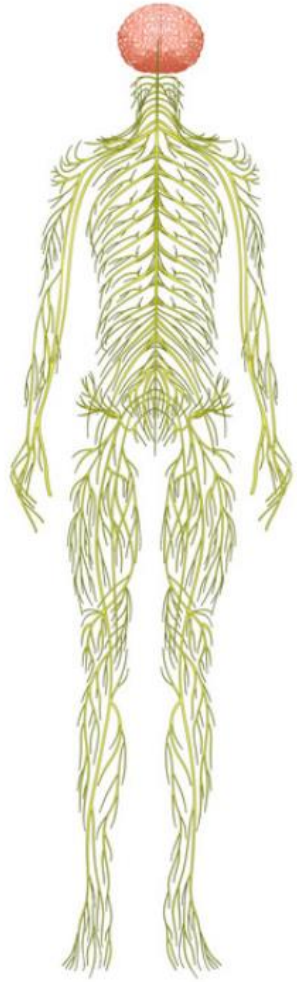
Organ Systems

- Brain/Central nervous system
- Skin/Soft tissue
- Lungs
- Liver
- GU



Parasites of the Brain/Central Nervous System



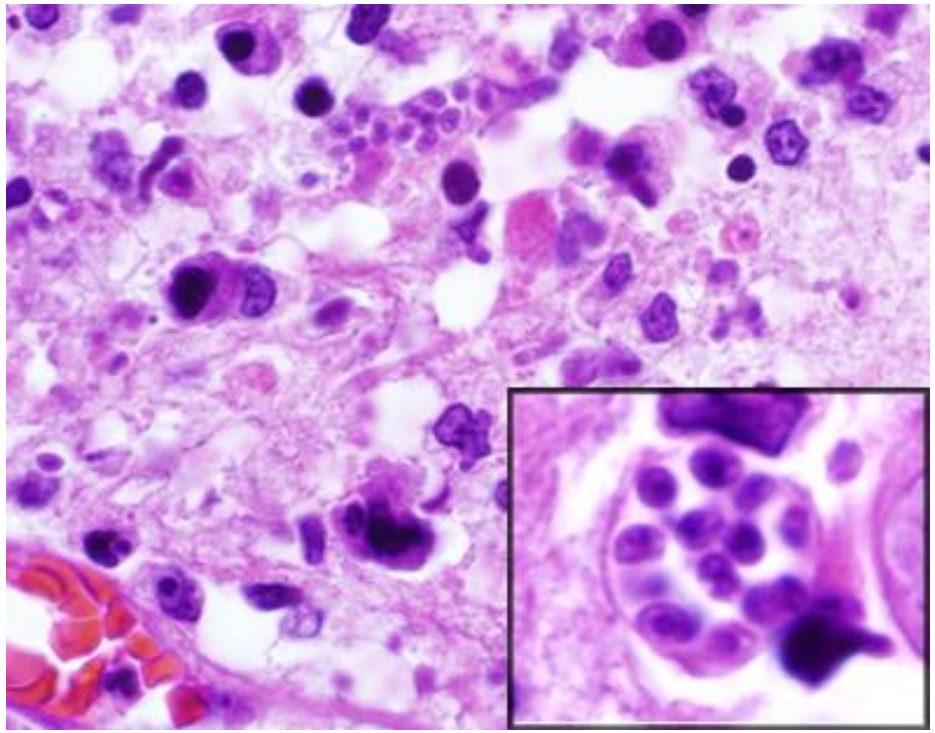


Toxoplasmosis (*Toxoplasma gondii)*

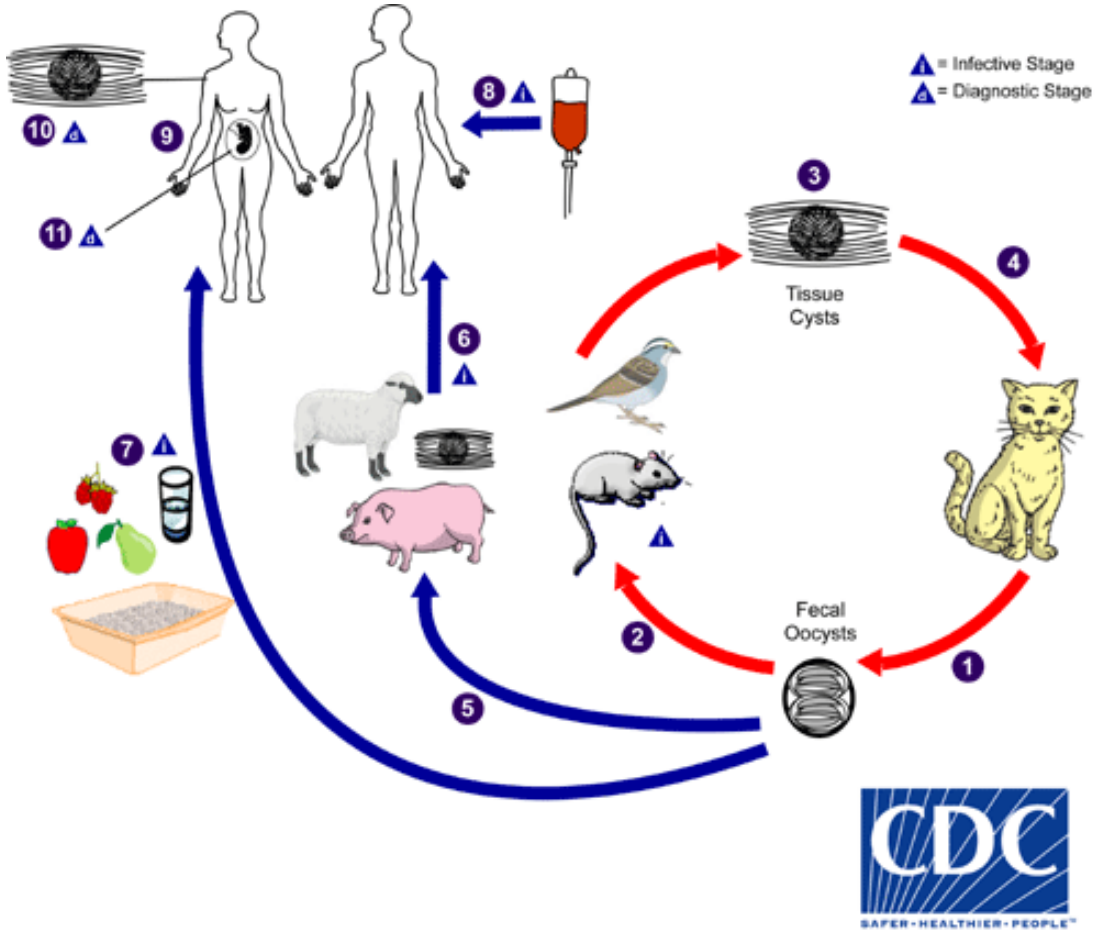
- Caused by apicomplexan parasite, *Toxoplasma gondii*
- Transmission occurs via:
  - » Eating undercooked meat of animals harboring tissue cysts
  - » Food, water, fomites contaminated with cat feces containing infectious oocysts
    - Contaminated soil or changing cat litter box
  - » Blood transfusion
  - » Organ transplantation
  - » Transplacentally from mother to fetus.

Toxoplasmosis (*Toxoplasma gondii*)

- Cats are definitive hosts
- Humans are dead-end hosts



Tachyzoites in brain tissue



Toxoplasmosis (*Toxoplasma gondii*)

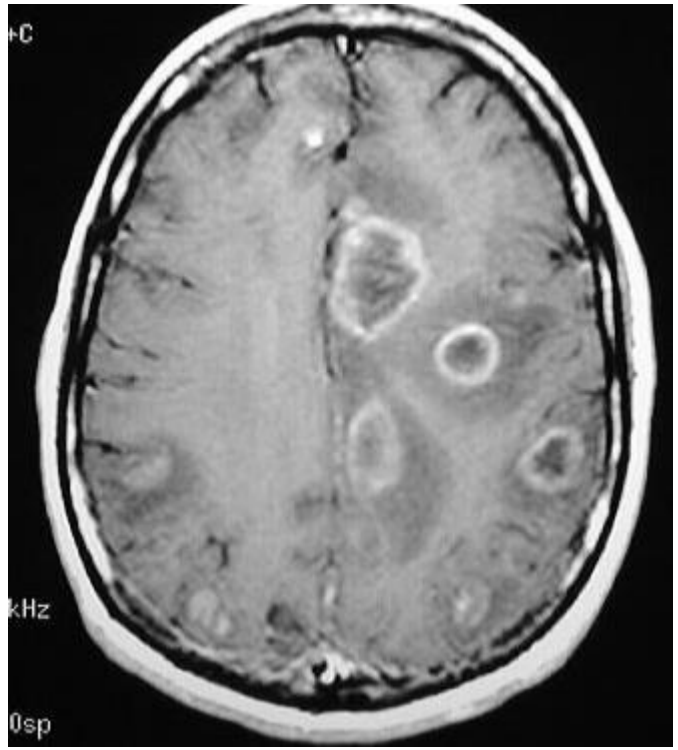
- Common sites of human infection are skeletal muscle, myocardium, brain, eyes.
- Symptoms
  - » Acute disease often asymptomatic; cervical lymphadenopathy and flu-like illness
  - » Immunodeficient patients will have localized symptoms based on body site
  - » Ocular disease: vision loss
  - » AIDS patients: toxoplasmic encephalitis.

Peripheral retinochoroiditis

Toxoplasmosis (*Toxoplasma gondii*)

- Diagnosis is primarily by serology (IFA, IgG/IgM EIA); PCR of aspirates; tissue cysts & tachyzoites may be observed in biopsy specimens & aspirates.
  - » Radiologic findings of: "ring enhancing lesions"
    - Not specific to toxoplasmosis, but supports serology

- Treatment: pyrimethamine, folinic acid (leucovorin), & sulfadiazine in immunocompromised patients & congenitally-infected newborns.

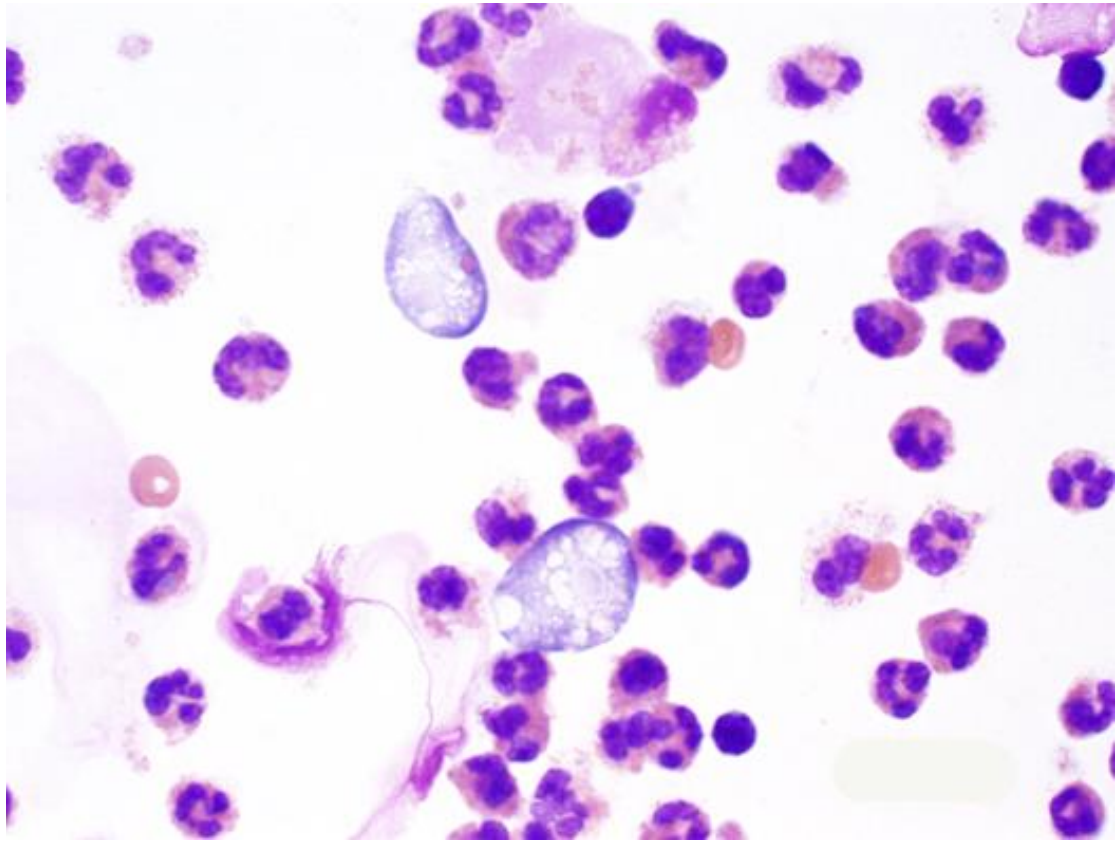


CT Scan showing ring enhancing lesions

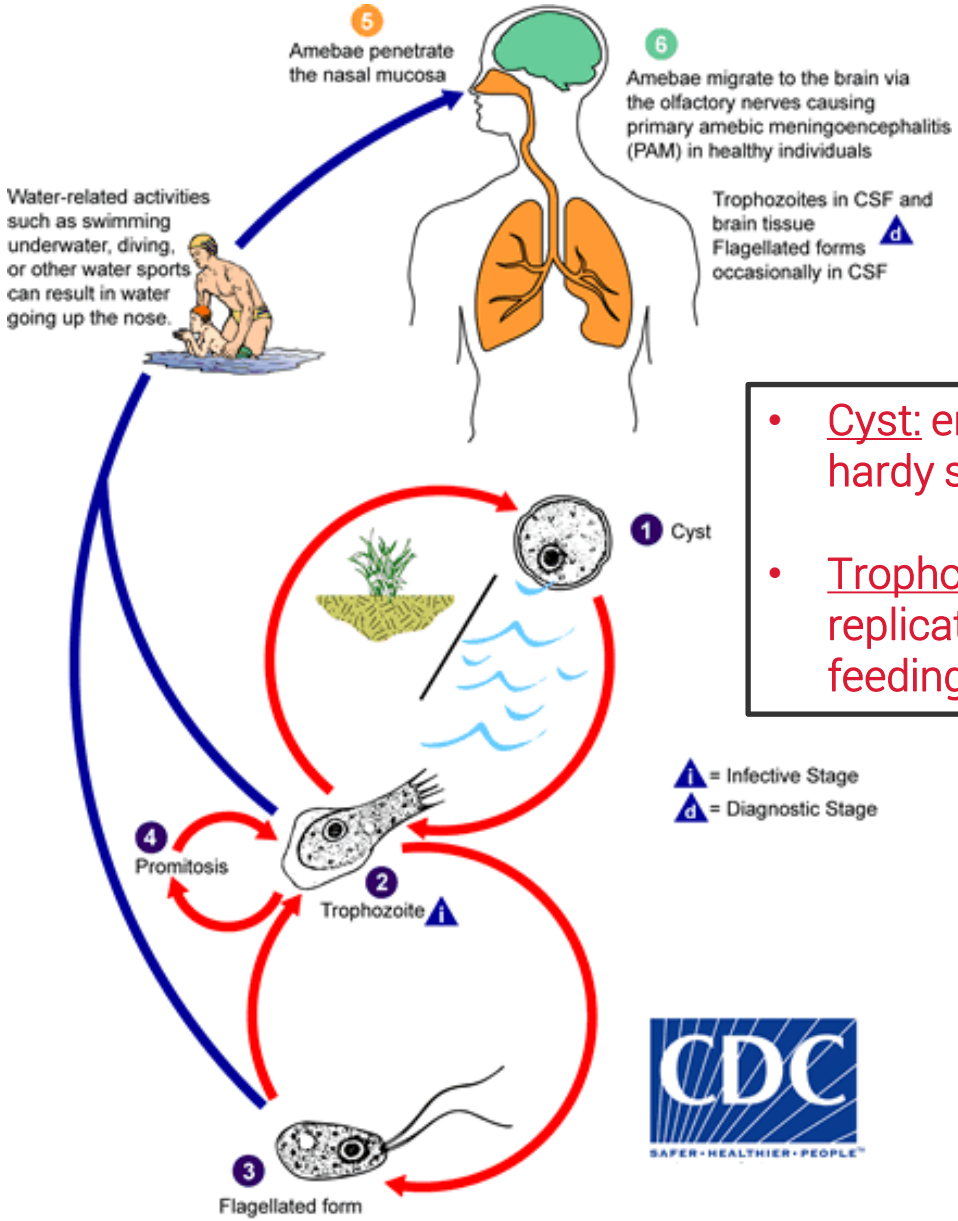
Primary Amebic Meningoencephalitis (PAM)

- Caused by the free-living ameba, *Naegleria fowleri*
- Not a “true parasite”: human infection is incidental & most cases fatal. Part of natural fauna of warm, fresh water.
- Route of infection is through the nasal mucosa
- Typically in children, teens, and young adults
- Symptoms
  - » Hemorrhagic-necrotizing meningoencephalitis
    -> severe CNS dysfunction
  - » Rapid onset
  - » High case-fatality rate

Life Cycle of *Naegleria fowleri*



Trophozoites in CSF



- Cyst: environmentally hardy stage
- Trophozoite: replication and feeding

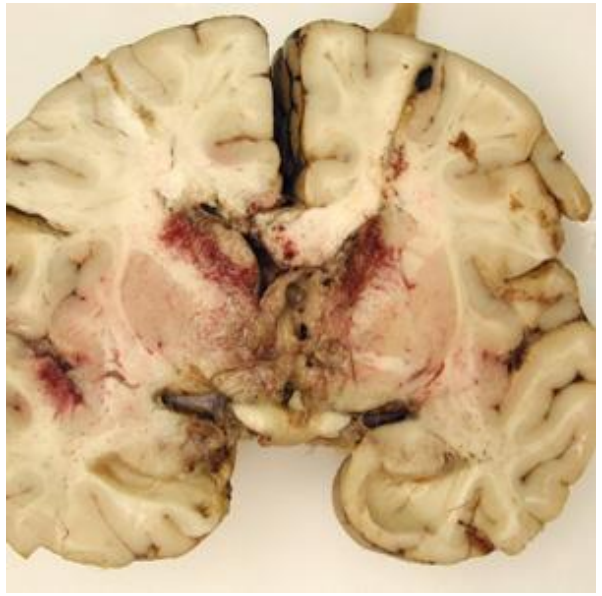
Primary Amebic Meningoencephalitis (PAM)

- Diagnosis usually made on autopsy by histopathology examination of brain tissue
  - » Observation of live trophozoites in fresh wet mount of CSF; confirm with Giemsa, trichrome
  - » PCR of CSF (CDC, large reference labs)
  - » Culture [delay issues]

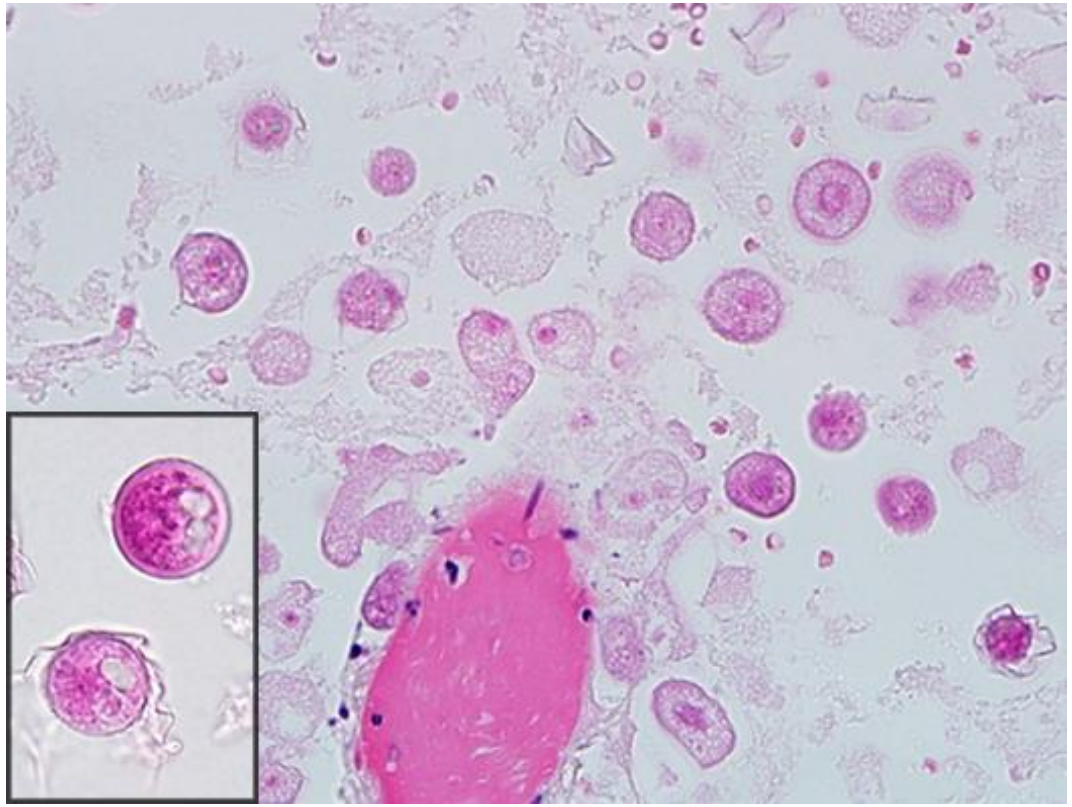
- Treatment: Miltefosine + medically controlled hypothermia

Granulomatous Amebic Encephalitis (GAE)

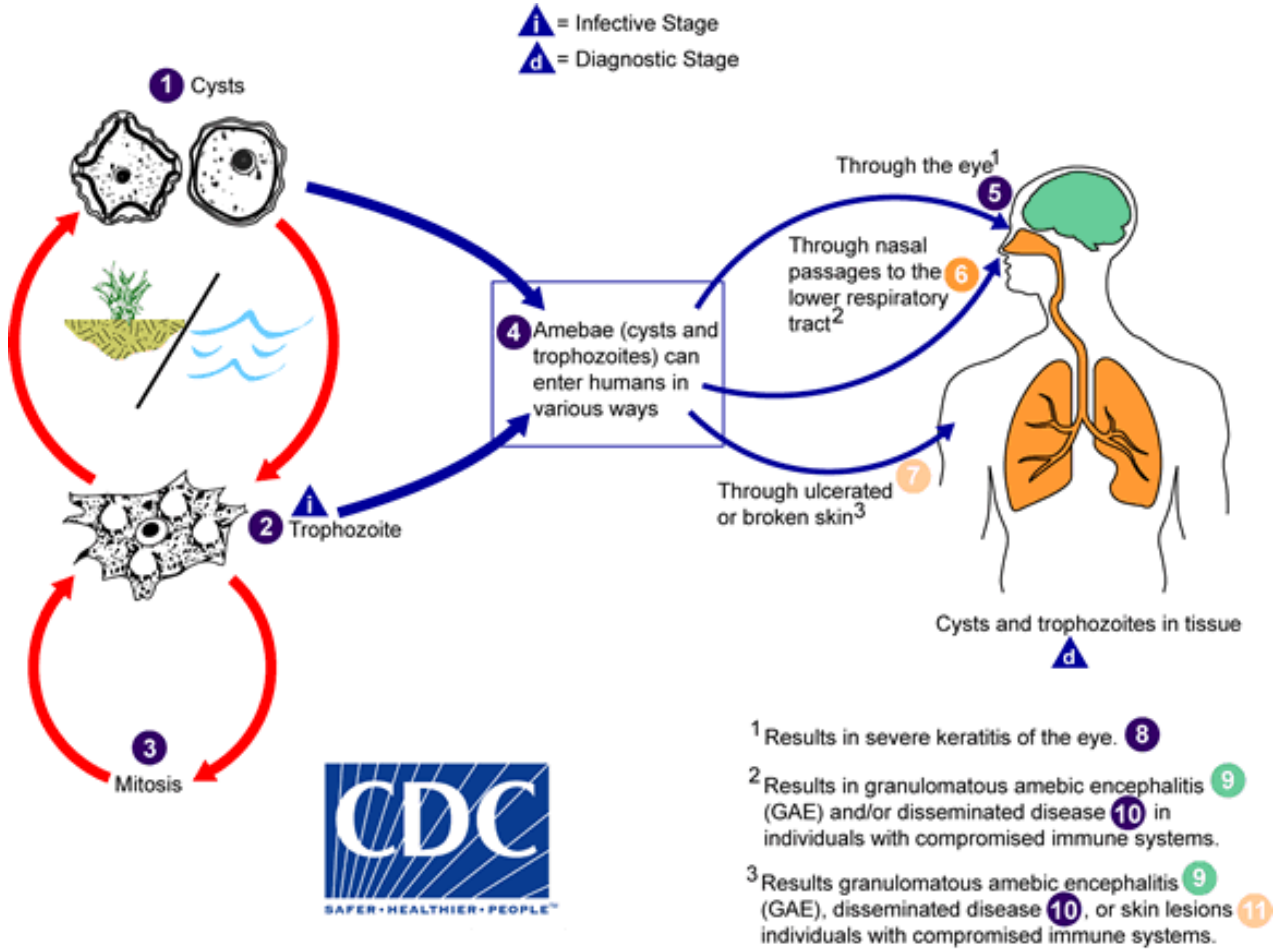
- Caused by free-living amebae *Balamuthia mandrillaris* & *Acanthamoeba* spp.
- Not 'true parasites'; part of normal soil and water fauna. Humans are accidental hosts.
- Route of infection: lower respiratory tract or ulcerated or broken skin.
  - » *Acanthamoeba* species can also enter the eye, causing amebic keratitis (AK)
- Symptoms
  - » Meningoencephalitis/encephalitis
  - » More chronic than PAM



Life Cycle of *Acanthamoeba*/ *Balamuthia*



Balamuthia in brain tissue, H&E stain



Granulomatous Amebic Encephalitis (GAE)

- More commonly seen in immunocompromised patients
- Diagnosis usually made on autopsy by histopathology examination of brain tissue
  - » Giemsa and calcofluor white stain of specimens
  - » Culture
  - » PCR (CDC, large reference labs)
- Treatment: None. Most cases are fatal

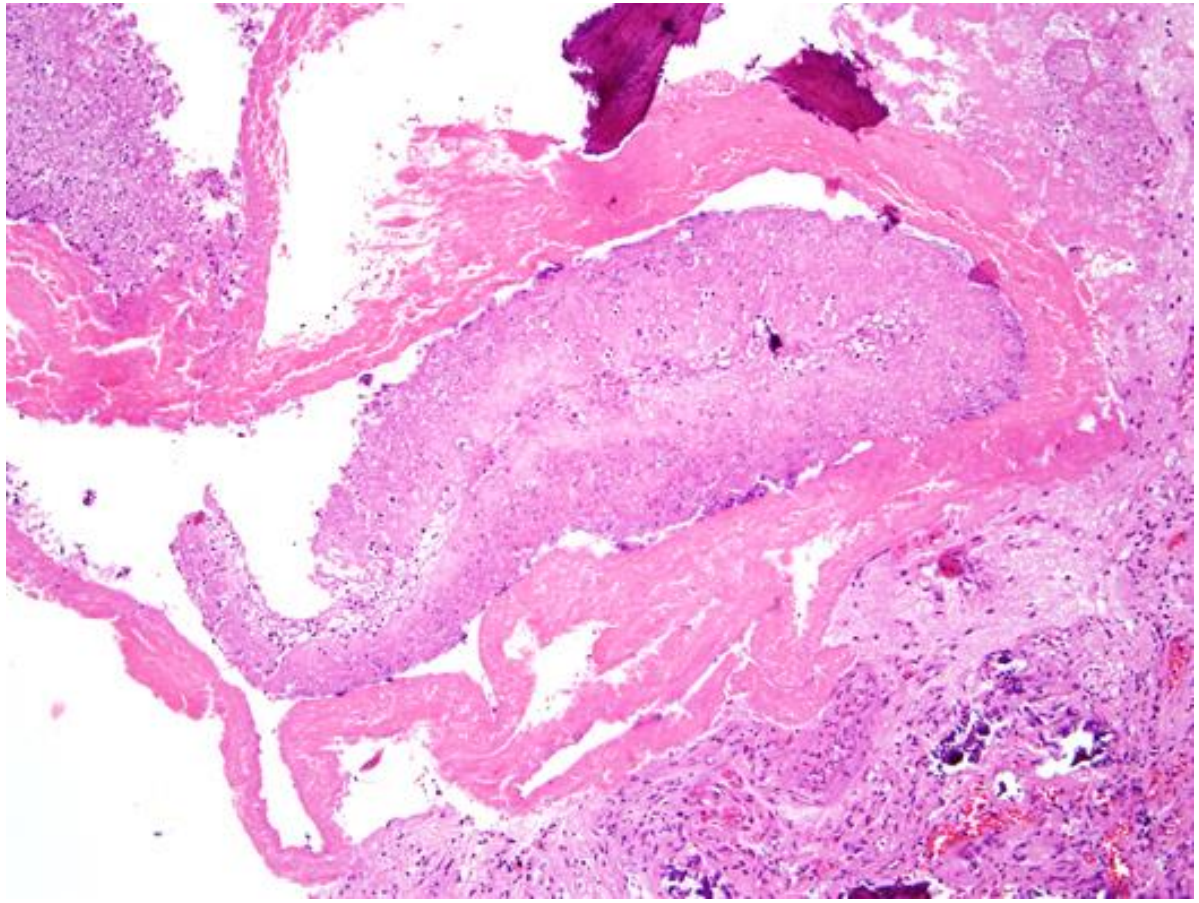
Free-living Amebic Infections

	Primary Amebic Meningoencephalitis	Granulomatous Amebic Encephalitis
Causal Agent(s)	*Naegleria fowleri*	*Acanthamoeba* spp., *Balamuthia mandrillaris*
Source of Infection	Inhalation when water forced into nasal cavity	Inhalation to lower respiratory tract; cuts and abrasions
Route to brain	Olfactory nerve	Hematogenous
Risk groups	Children, teens, young adults	Usually immunocompromised
Diagnosis	Wet mounts/Giemsa stain, PCR, histopathology, [culture]	Giemsa/Calcoflour white stains; PCR; histopathology; [culture]
Stage(s) in human tissue	Trophozoites only	Trophozoites, cysts
Treatment	Amphotericin B, Mitefosine + therapeutic hypothermia	Combos of pentamidine, sulfadiazine, flucytosine, AND fluconazole or itraconaconazole (*Acanthamoeba*) or azithromycin or clarithromycin (*Balamuthia*)

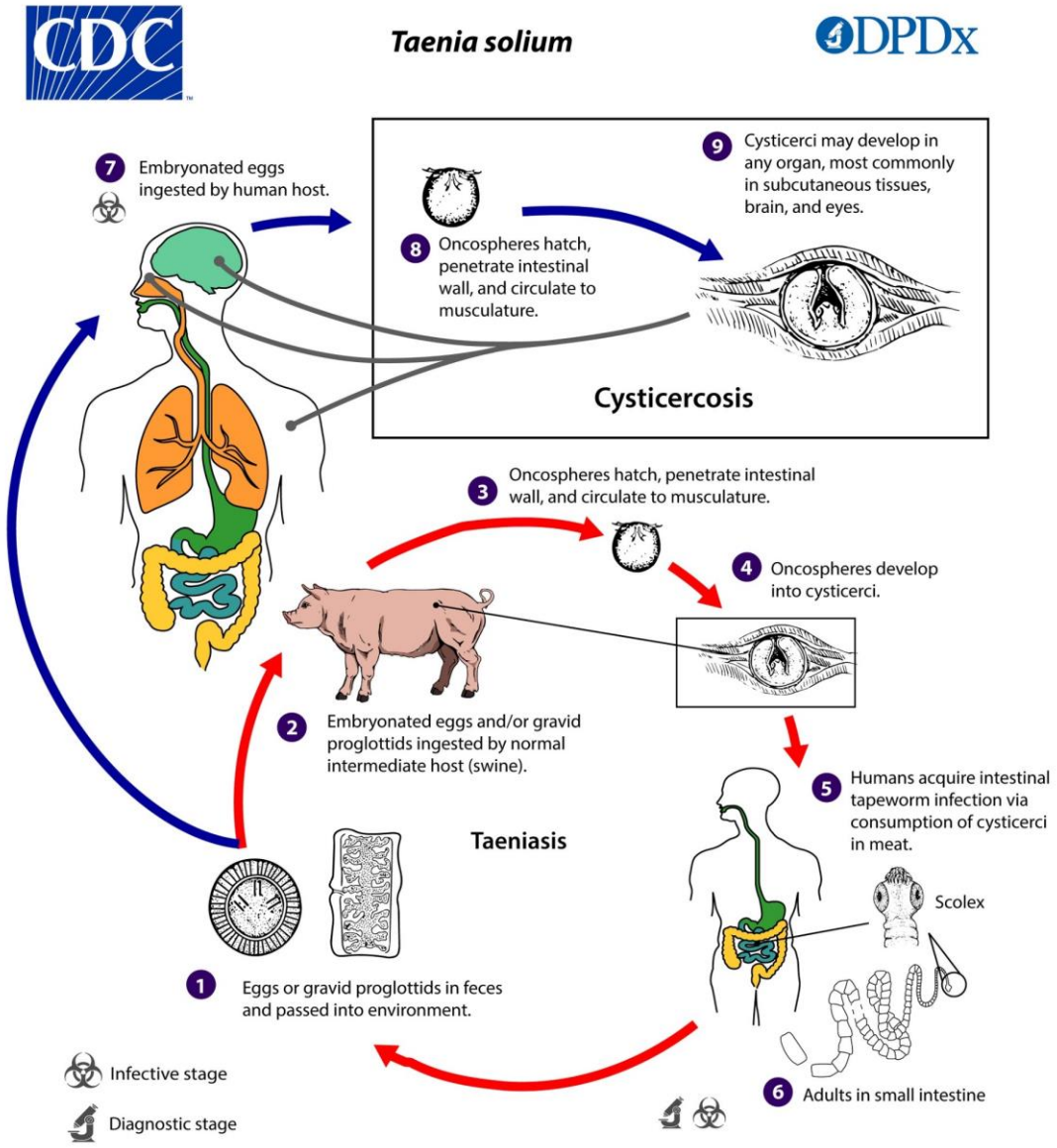
Neurocysticercosis

- Caused by the ***larval*** stage (cysticercus) of *Taenia solium* (the 'pork' tapeworm).
  - » Latin America, SE Asia
- Acquired: eating *T. solium* eggs in food, fomites contaminated with **human** stool.
- Clinical manifestations: vary by number, size, & state of cysticerci & inflammatory response to degenerating cysts.
  - » Epilepsy most-common manifestation, also intracranial hypertension, hydrocephalus, chronic meningitis, & cranial nerve abnormalities

Life Cycle of *Taenia solium*



Degrading cysticercus in brain biopsy



Neurocysticercosis

- Diagnosis primarily by imaging, confirmed w/ antibody detection
  - » EIA for initial screening
  - » CDC immunoblot recommended by WHO & PAHO for confirmation

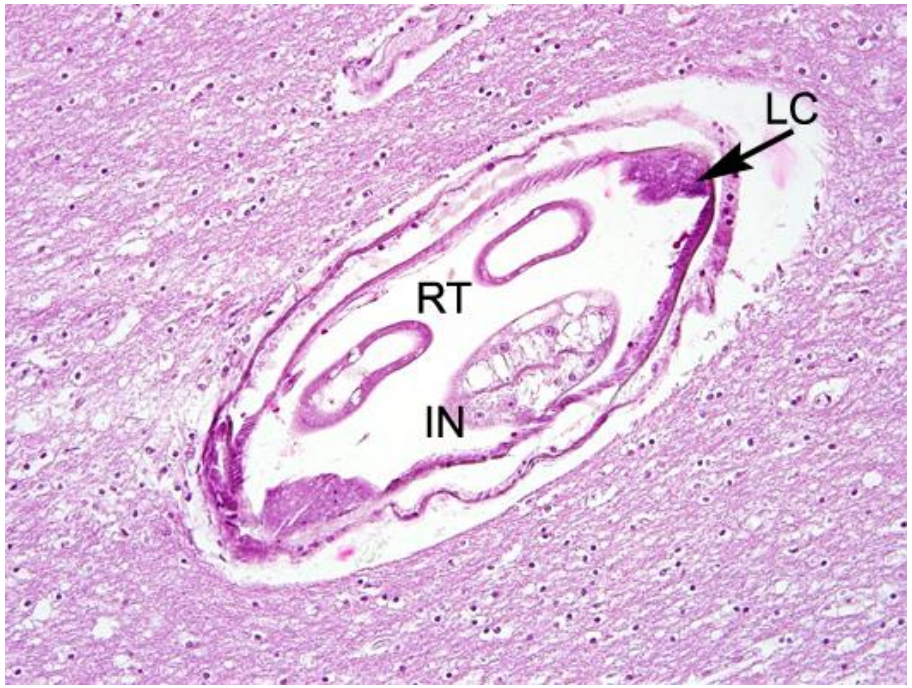
- Larval worms may be seen in biopsy specimens, but undesirable to biopsy the brain

- Treatment: control of symptoms; antihelminthic therapy might increase symptoms!
  - » Corticosteroids usually co-administered to combat these effects.
  - » Albendazole may be better than praziquantel; combined albendazole/praziquantel with corticosteroids if >2 active parenchymal cysts

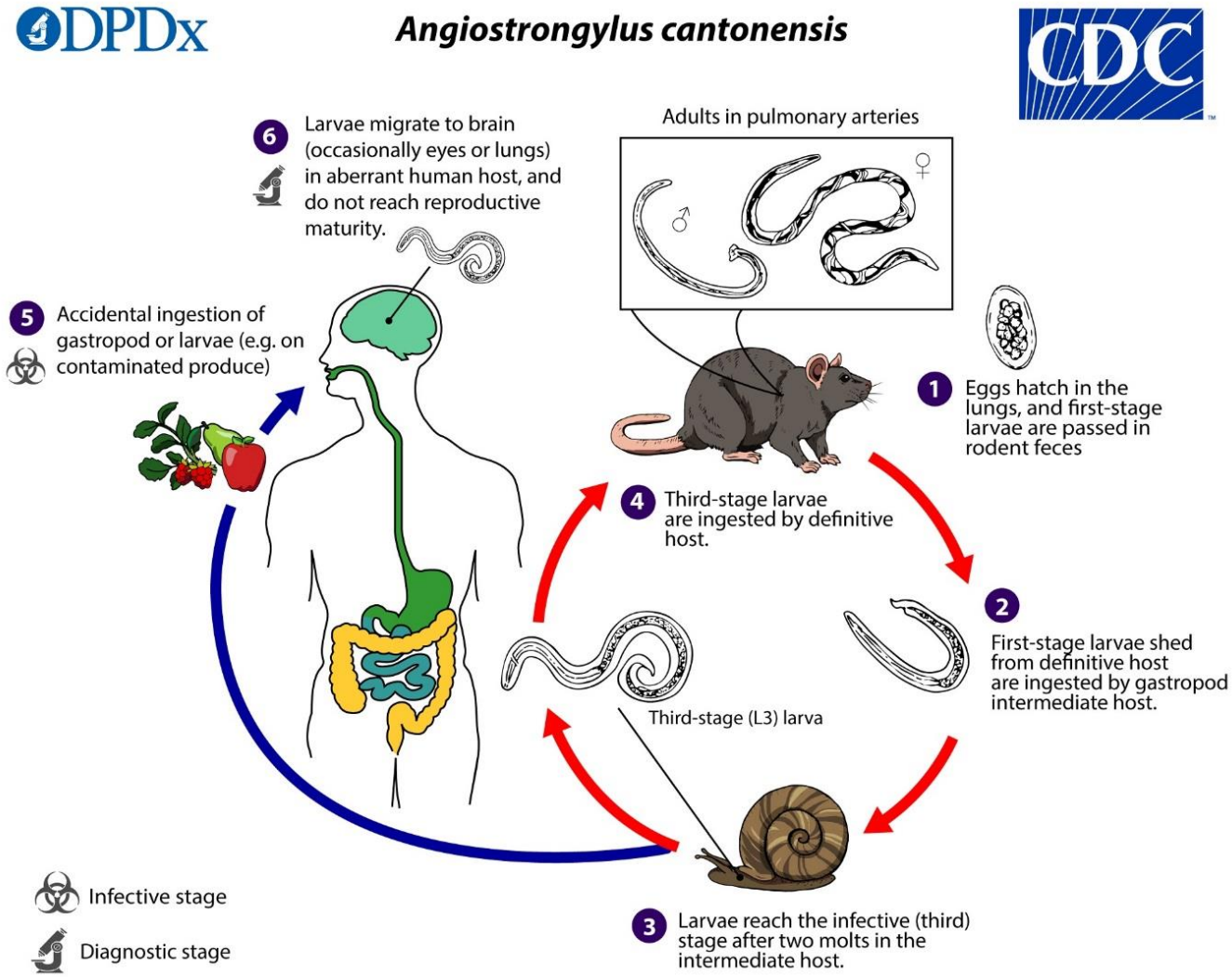
Angiostrongyliasis

- Caused by the nematode, *Angiostrongylus cantonensis*.
  - » Human infection in Asia/South Pacific; Africa, Latin America, Caribbean, Hawaii
- Natural definitive hosts are rats; intermediate hosts are mollusks
- Human infection: ingesting raw or undercooked snails and slugs containing infectious (third stage, L3) larvae
- Clinical symptoms: bi-temporal headache, nausea, vomiting, stiff neck, & eosinophilic pleocytosis of the CSF
  - » Symptoms related to death of larvae in brain and directly proportional to parasite load

Life Cycle of *Angiostrongylus cantonensis*



L4/young adult in brain autopsy specimen



Angiostrongyliasis

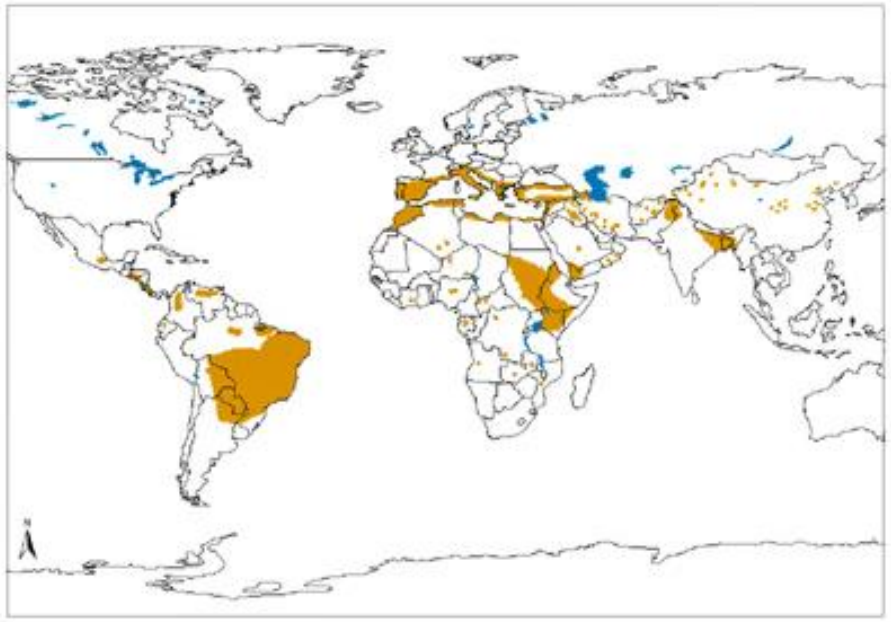
- Diagnosis:
  - » PCR (CDC, HI DOH)
  - » Observations of L4 larvae in CSF or brain biopsy/autopsy specimens
  - » Antibody detection not available in the US

- Treatment usually limited to analgesics for pain and corticosteroids for inflammation; removal of CSF to relieve headache and pressure

Parasites of the Skin and Soft tissue

Leishmaniasis

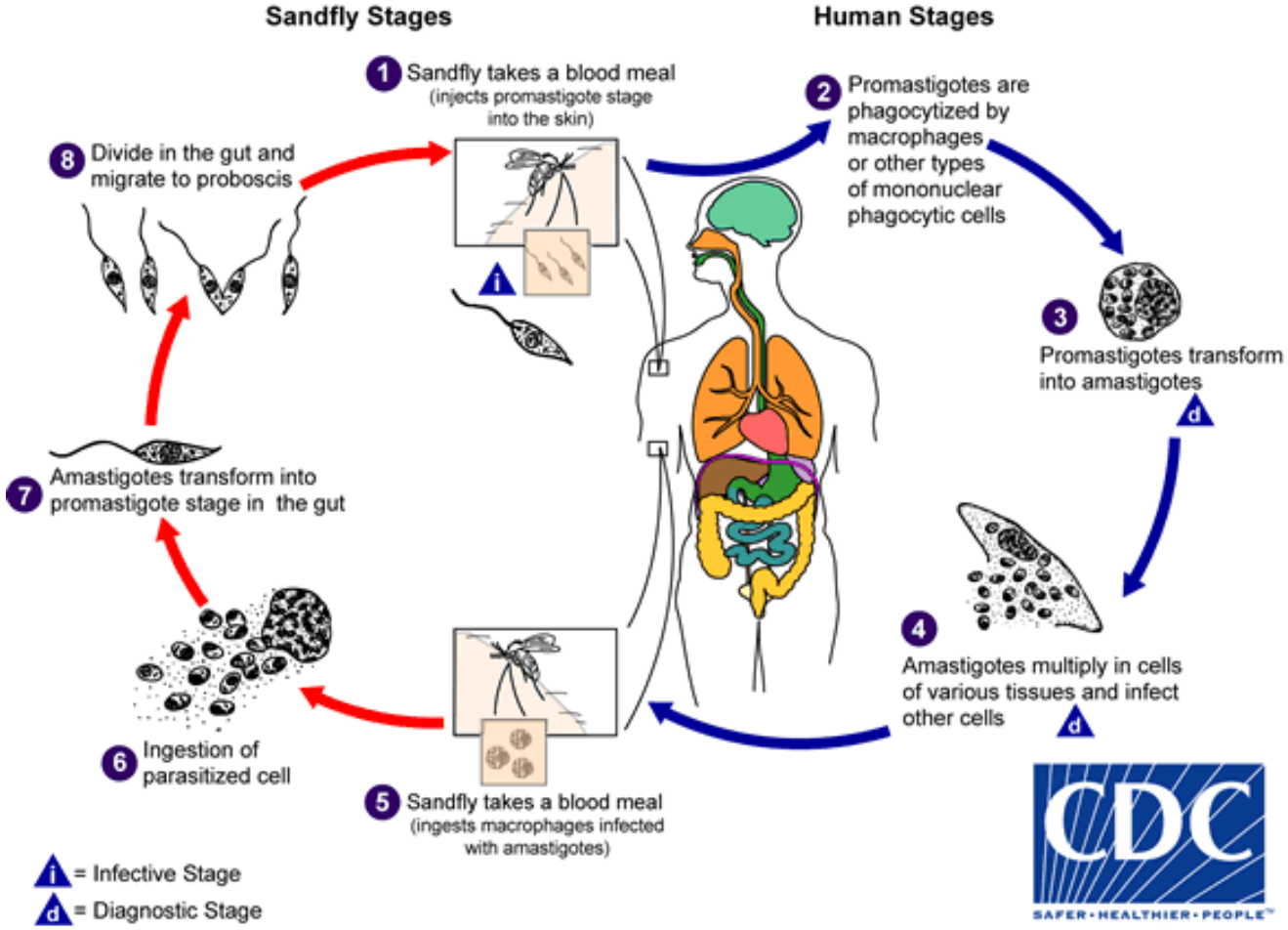
- Caused by hemoflagellate protozoa, *Leishmania*
- Infect many mammals
  - » 21 of 30 known species infect humans
- Vectored to humans by the phlebotomine sand fly
- Geographically dispersed:
  - » Tropic/sub-tropics
    - C. & S. America
    - Africa
    - Asia
    - Middle East
    - S. Europe



www.who.int

Leishmaniasis

- Clinical manifestations
  - » Cutaneous (pizza lesion)
    - Painless or painful
  - » Mucocutaneous
    - Disemination of cutaneous
  - » Visceral (kala-azar)
    - Fever, weight loss, hepatosplenomegaly
    - Anemia
    - Thrombocytopenia
    - Leukopenia
- Different species w/ different clinical manifestations

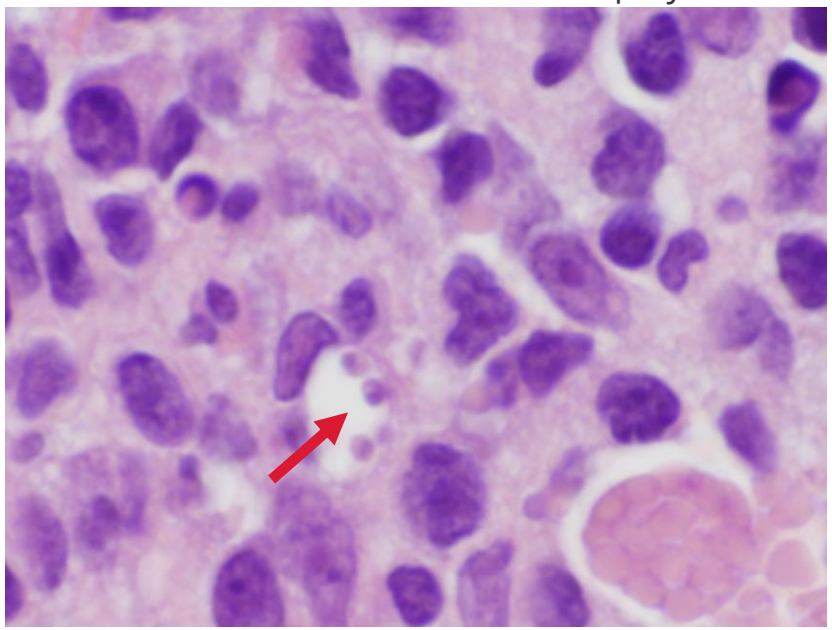


https://www.cdc.gov/dpdx/

Leishmaniasis

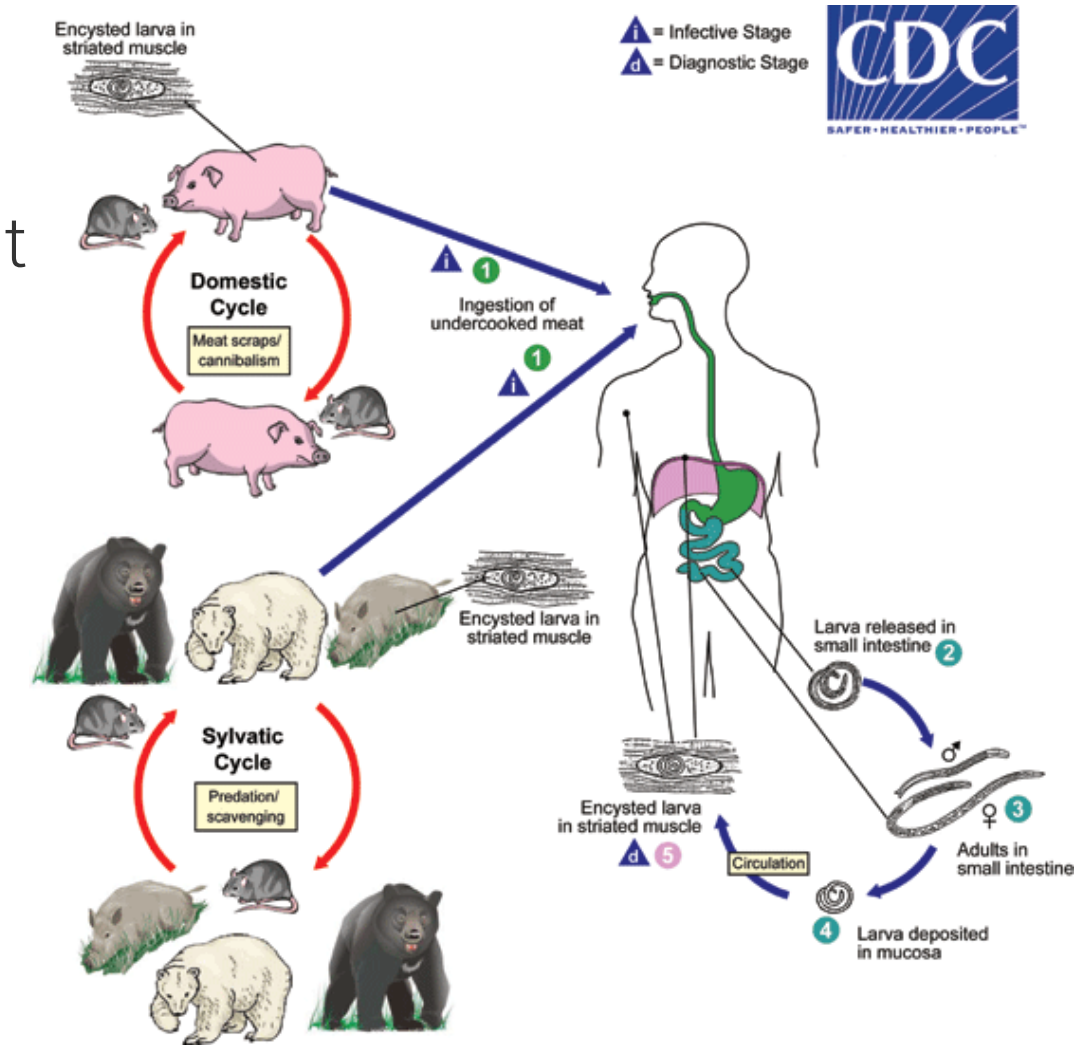
- Diagnosis:
  - » Histopathologic examination of tissue (biopsy, aspirate)
  - » Serology
  - » PCR
- Treatment:
  - » Pentavalent antimony (investigational from CDC)
  - » Liposomal amphotericin B (visceral only)
  - » Miltefosine (cutaneous, mucocutaneous, visceral)

H&E stained skin biopsy



Trichinellosis

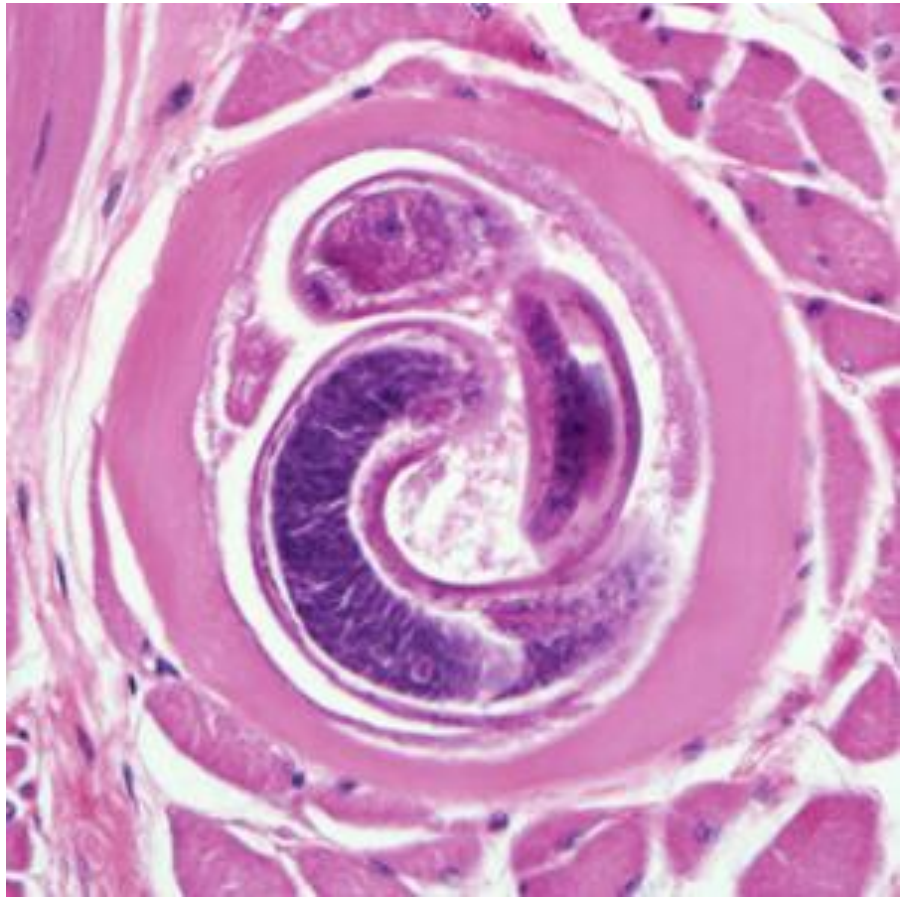
- Caused by nematode, *Trichinella*
- Acquired: ingestion of undercooked meat containing encysted larvae
- Geographically dispersed:
  - » Worldwide with bias towards
    - Europe
    - N. America



Trichinellosis

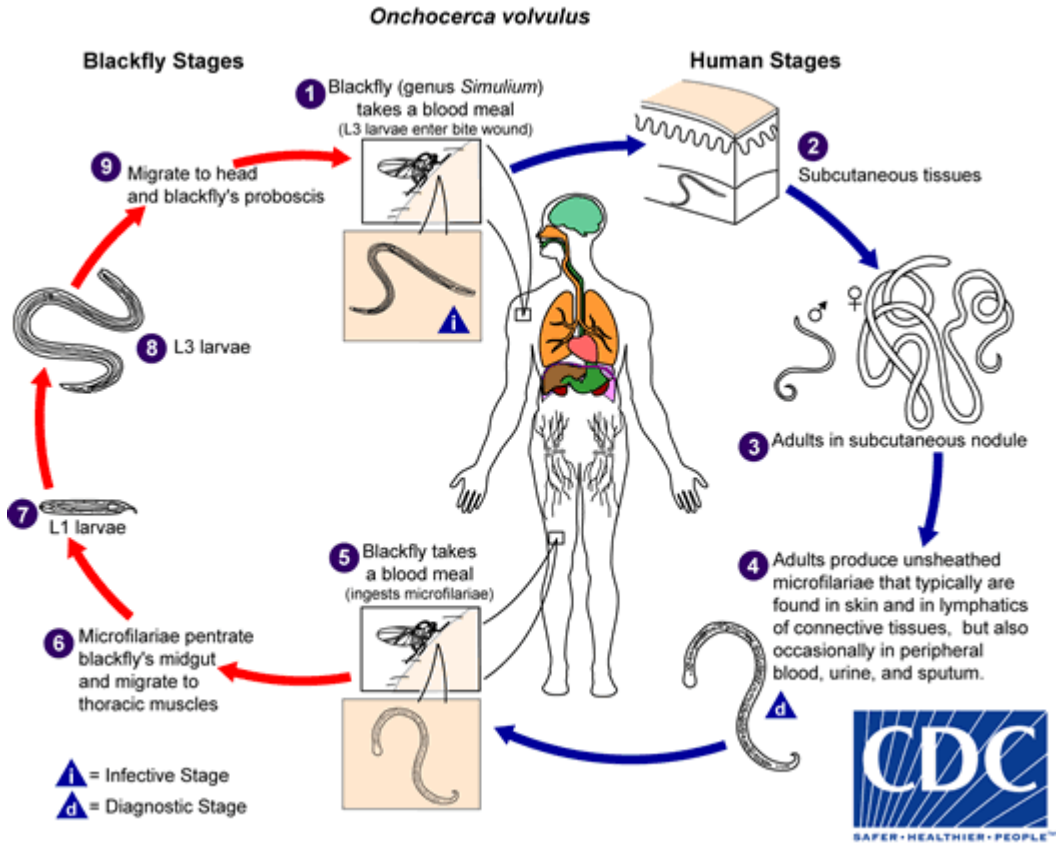
- Symptoms:
  - » May be asymptomatic
  - » Initially GI: diarrhea, cramping, emesis
  - » >1 Week: Muscle invasion
    - Periorbital & facial edema
    - Fever, myalgias, rashes
    - Peripheral eosinophilia
  - » Larvae encyst in muscle: myalgia & weakness → cessation of symptoms
- Diagnosis:
  - » Social history
  - » Serology
  - » Tissue stain & microscopy

Encysted larvae in muscle H&E stain



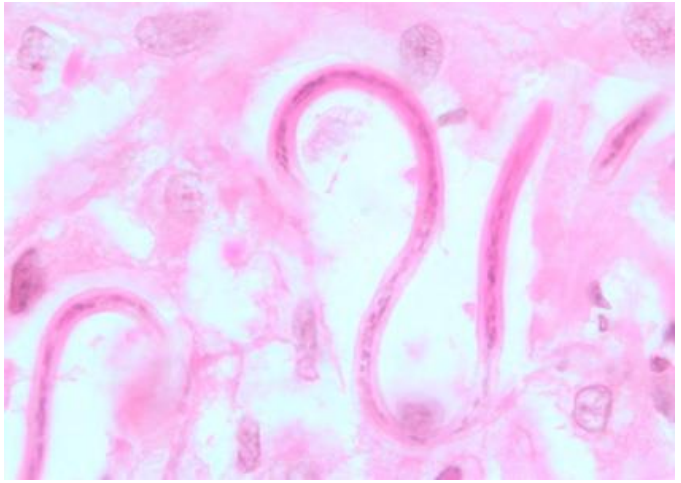
Onchoceriasis

- Caused by the nematode *Onchocerca volvulus*
- Acquired via the bite of *Simulium* (black fly)
- Geographically constrained:
  - » Africa (Sub-Saharan)
  - » Latin America (focal)
  - » Middle East (Yemen)



Onchoceriasis

- Symptoms:
  - » Most symptoms are result of inflammatory reactions to dead or dying worms
    - Itchy skin rash
    - Subcutaneous nodules
    - Vision change
  - » Continued inflammation of cornea and optic nerve results in blindness
    - River blindness
- Diagnosis: skin snip and histology
- Treatment:
  - » Ivermectin



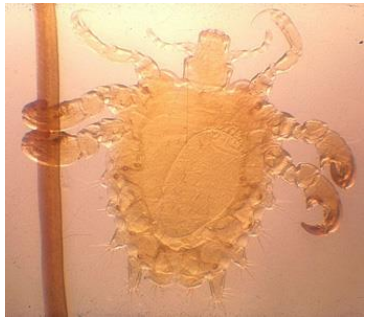
https://www.npr.org/sections/goatsandsoda/2016/01/14/462911189/the-farmer-and-fisherman-who-lost-his-sight-to-river-blindness

Scabies

- *Sarcoptes scabiei* (itch mite)
- Acquired by direct contact with mite infected surfaces
- Symptoms: Severe pruritius serpiginous burrows
  - » Common between digits and behind large joints
- Geographically distributed worldwide
  - » Low socioeconomic status
  - » Institutional settings
- Diagnosis: macroscopic identification of mite
- Treatment:
  - » Permethrin (human)
  - » Cleaning (environment)

Lice

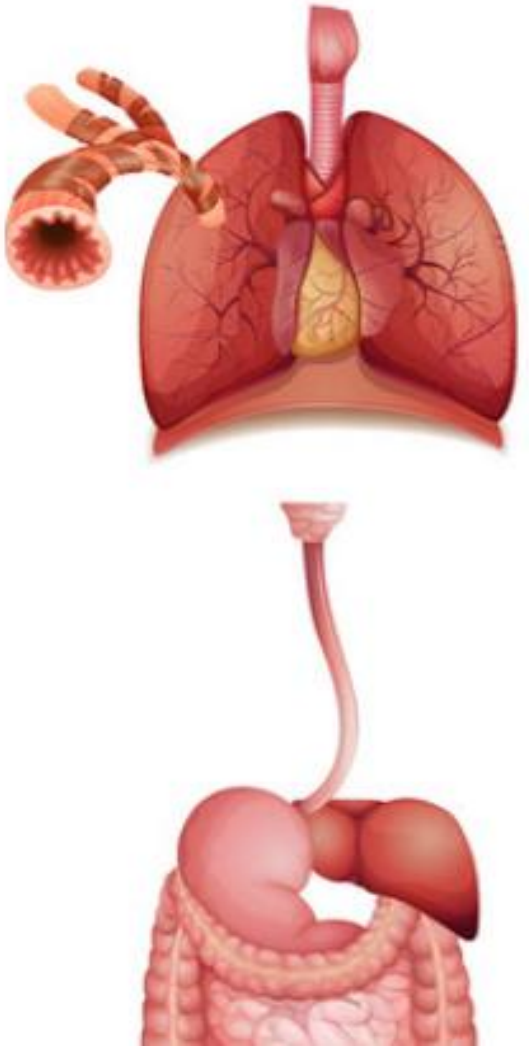
- *Pediculus humanus* (head and body louse)
- *Pthirus pubis* (pubic louse)
- Symptoms: Itching of infected site
  - » Can transmit serious human diseases
    - Epidemic typhus, relapsing fever, trench fever
- Diagnosis: macroscopic identification of louse
- Treatment:
  - » Ivermectin lotion (human)
  - » Nit combing (human)
  - » Environmental cleaning



Pubic louse

Head louse

Parasites of Lung and Liver

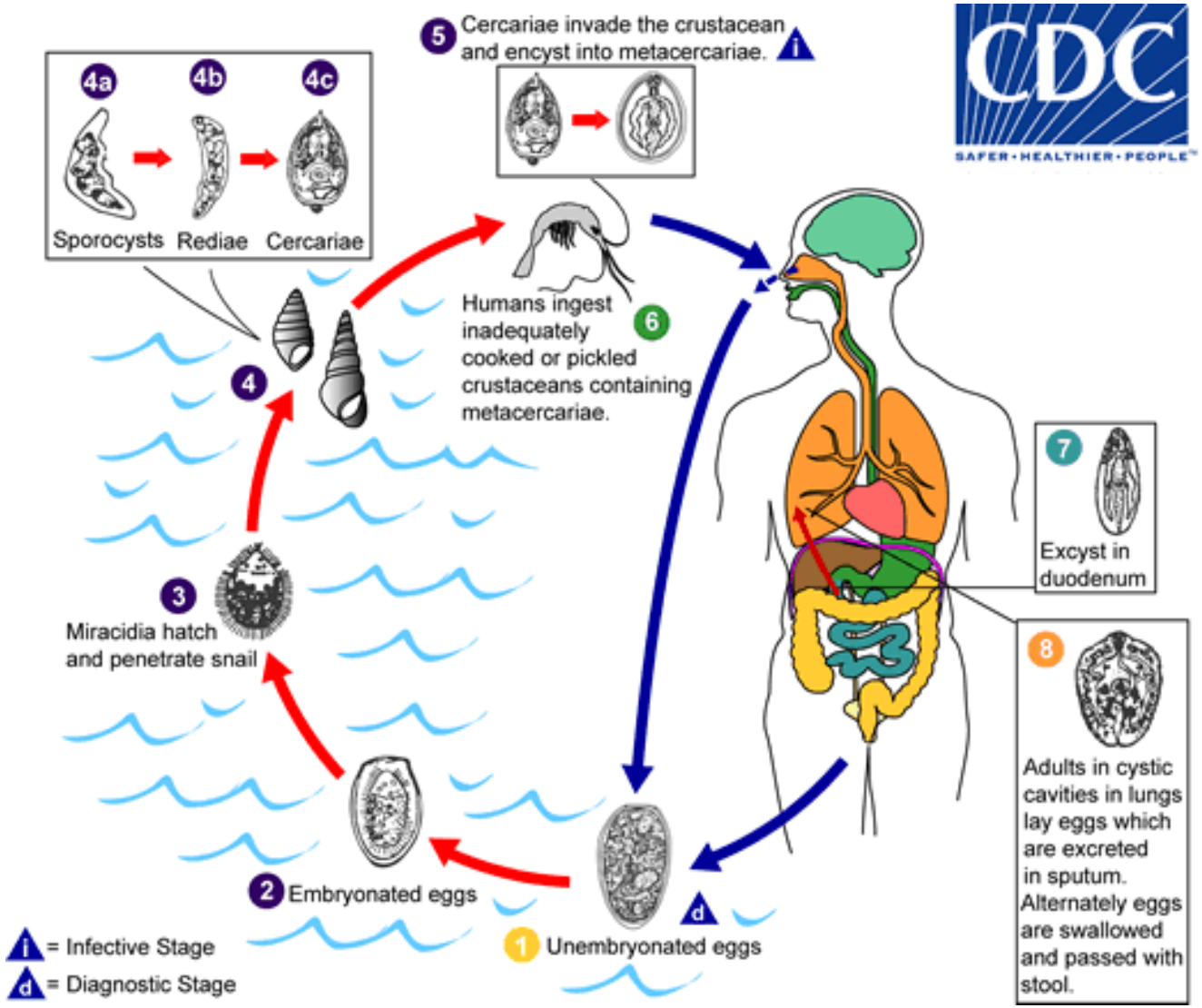


Paragonimiasis

- Caused by lung flukes in the genus *Paragonimus*.
  - » *Paragonimus westermanni* & *P. heterotremus* in southeast Asia
  - » *Paragonimus kellicotti* in the United States.
- Infections occur from the ingestion of raw or undercooked freshwater crustaceans.
- Symptoms:
  - » Acute: diarrhea, abdominal pain, fever, cough, urticaria, eosinophilia
  - » Chronic: cough, expectoration of discolored sputum ("iron fillings"), hemoptysis

'crab martini'

Life Cycle of *Paragonimus* spp.



Paragonimiasis

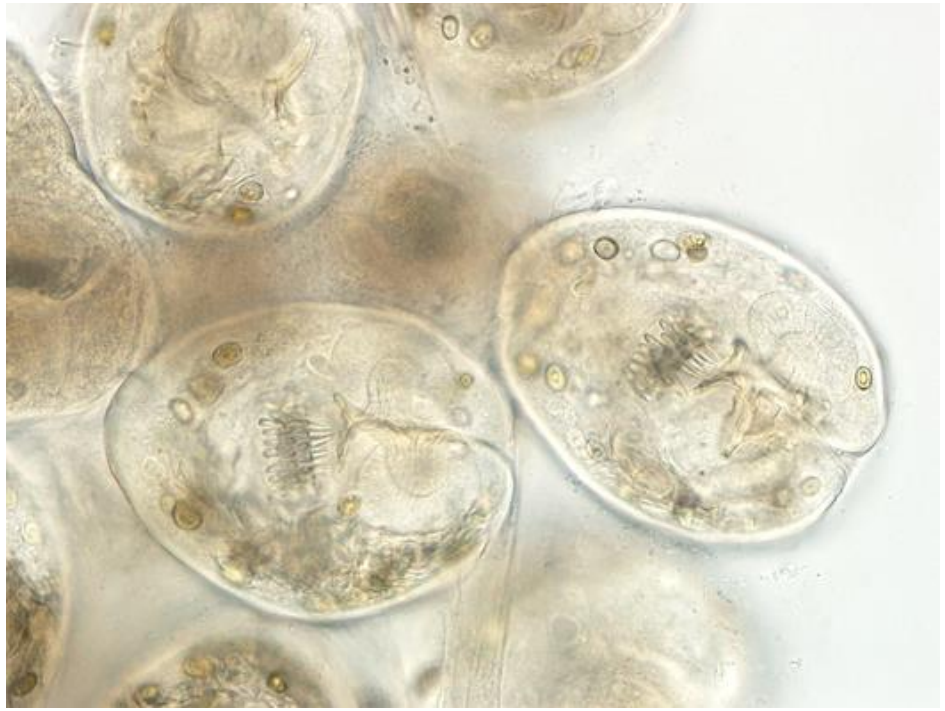
- Diagnosis
  - » morphology (eggs in respiratory specimens & stool)
  - » Serology
- Treatment: praziquantel

Eggs of *Paragonimus* in respiratory specimen

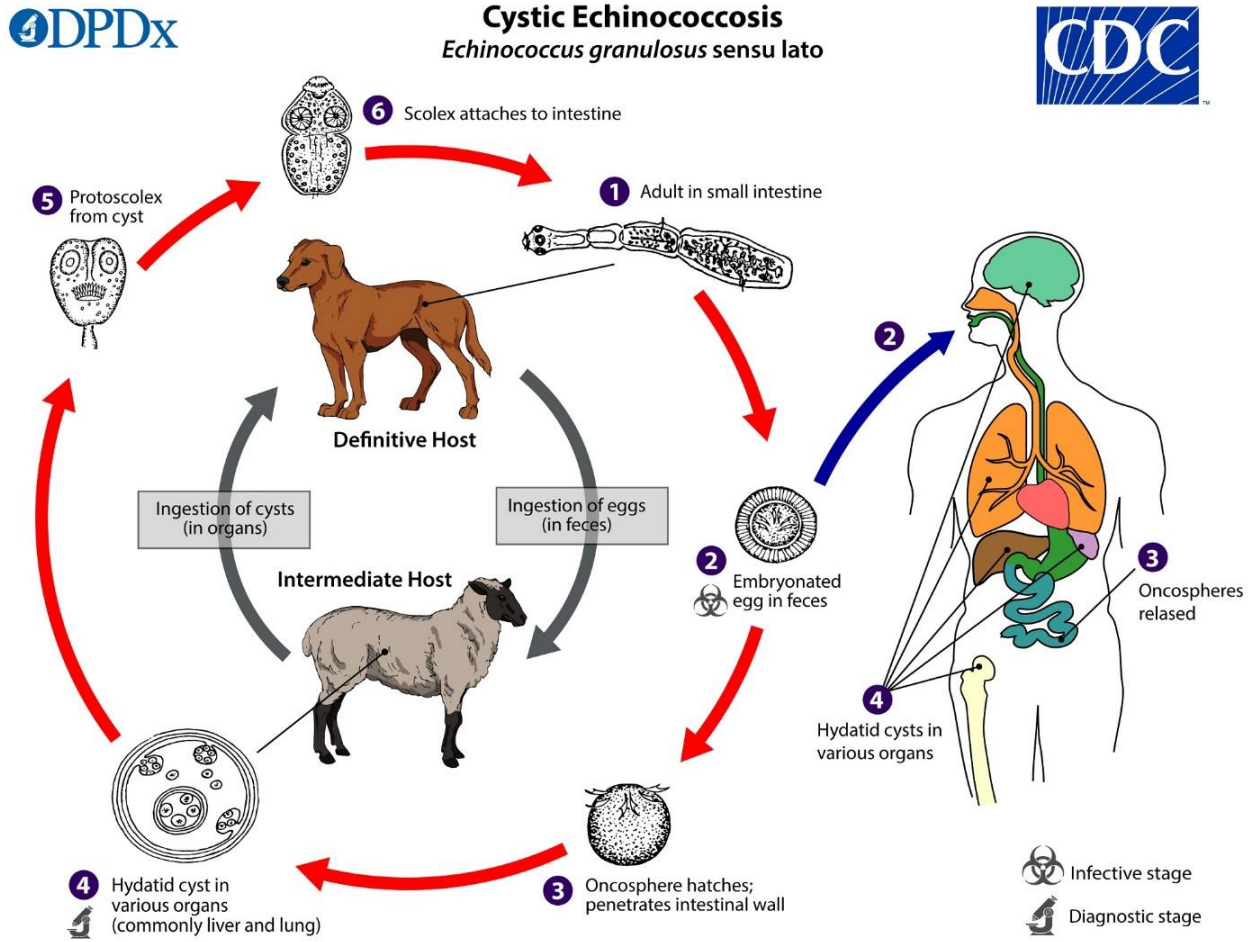
Echinococcosis

- Caused by cestodes in the genus *Echinococcus*.
  - » *Echinococcus granulosus* (complex) – cystic echinococcosis
  - » *Echinococcus multilocularis* - alveolar echinococcosis
- Infection caused by the ingestion of tapeworm eggs in food and fomites contaminated with dog feces.
- Parasites cannot mature in human host (humans are dead-end hosts)
- Symptoms:
  - » Cystic: dependent on size, number, and location of cysts (hepatic, pulmonary most common)
    - Cyst rupture: anaphylaxis, urticarial, eosinophilia
  - » Alveolar: slow-growing, destructive tumor; abdominal pain and biliary obstruction (high case fatality rate untreated).

Life Cycle of *Echinococcus granulosus*



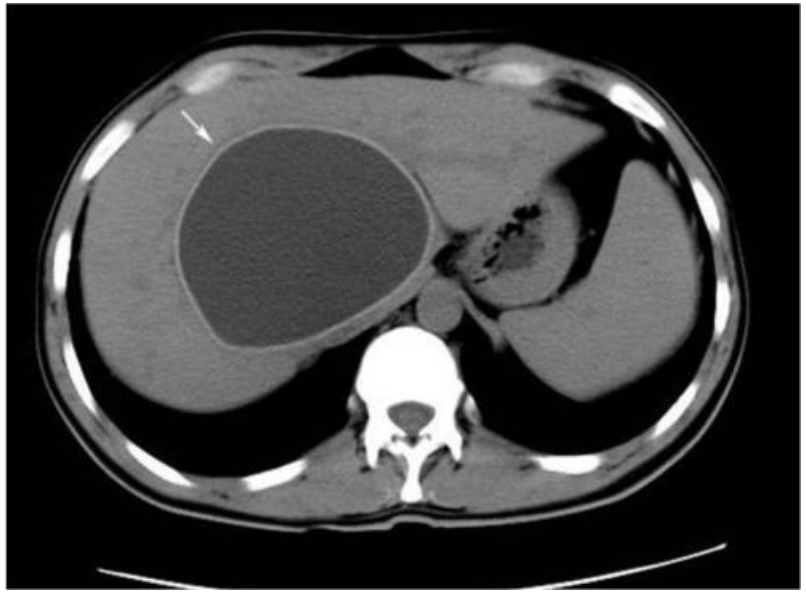
Protoscoleces in ‘hydatid sand’ in liver aspirate



Echinococcosis

- Diagnosis
  - » Imaging (CT, MRI)
  - » Antibody detection
  - » Morphology (e.g. hydatid sand in aspirates)

- Treatment:
  - » Albdendazole (praziquantel preoperative)
  - » Surgical removal of cyst (as indicated)
  - » PAIR (percutaneous aspiration, injection, reaspiration)
  - » Nothing (as indicated)

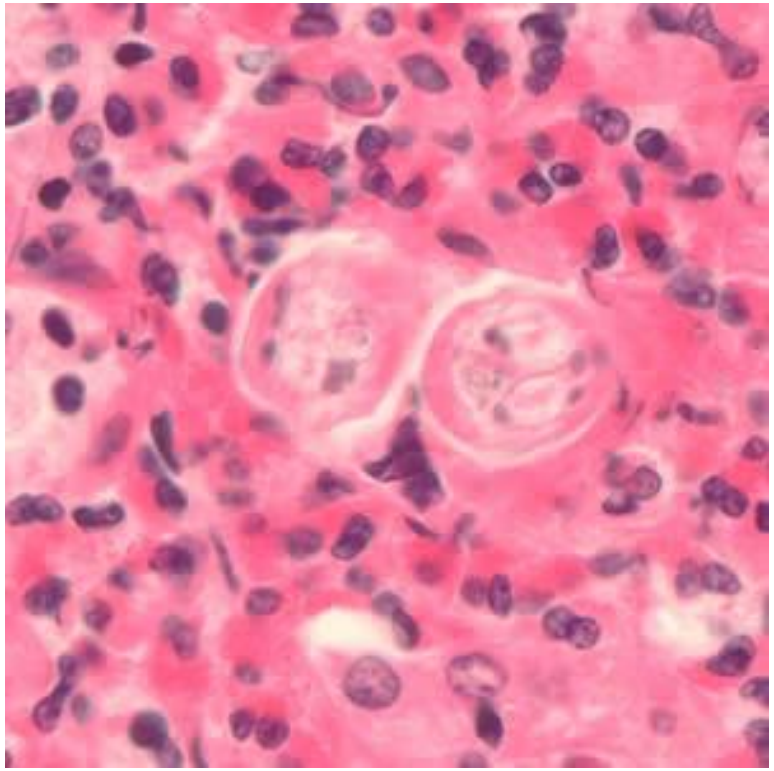


CT image of hepatic hydatid cyst

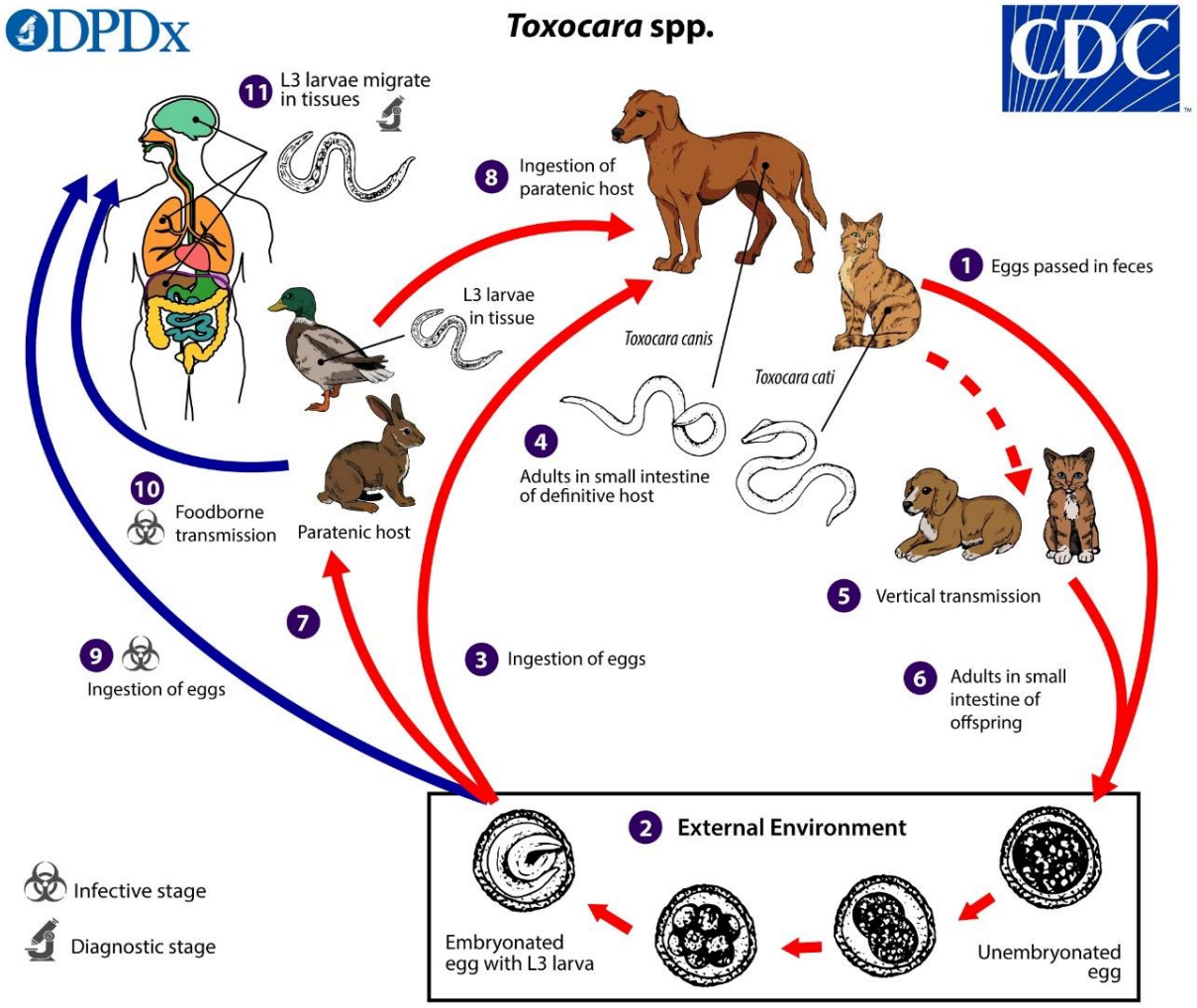
Visceral Larval Migrans

- Caused by larvae of nematodes of animals:
  - » *Toxocara canis* & *T. cati* (dogs and cats)
  - » *Baylisascaris procyonis* (raccoons) [predilection for CNS]
- Humans ingest fully-embryonated eggs
  - » Soil, food, & on fomites contaminated with feces of natural definitive host or eating paratenic hosts.
- Humans are dead-end hosts
- Symptoms: fever, myalgia, weight loss, cough, rashes, hepatosplenomegaly, hypereosinophilia
  - » Eosinophilic meningoencephalitis uncommon
  - » Ocular – uveitis, retinitis, endophthalmitis

Life Cycle of *Toxocara* spp.



Cross sections of larvae in liver biopsy



Visceral Larval Migrans

- Diagnosis: antibody detection

- Treatment:
  - » Visceral: albendazole or mebendazole with steroids
  - » Ocular: albendazole or mebendazole with topical steroids

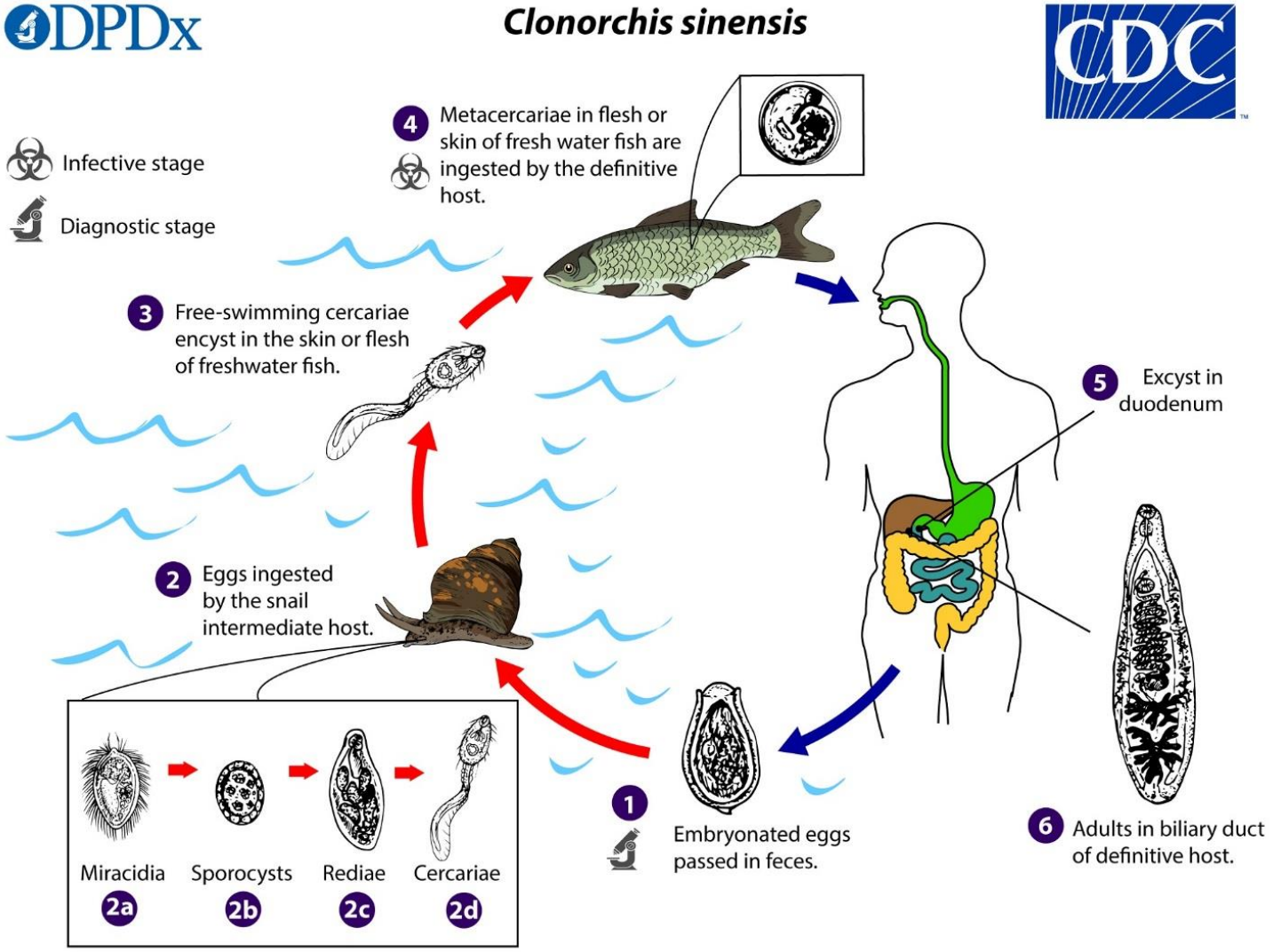
Clonorchiasis/Opisthorchiasis

- Caused by liver flukes *Opisthorchis viverrini*, *O. felineus,* and *Clonorchis sinensis* (Chinese liver fluke).
  - » *Clonorchis*: parts of Asia incl. China, Japan, Korea, Taiwan, & Vietnam.
  - » *Opisthorchis viverrini*: mainly in NE Thailand & Laos
  - » *O. felineus:* Eastern Europe and Russia.
- Infection: ingestion of raw or undercooked fish containing metacercariae.

'*koi* ' – raw fish dish eaten in Laos and Thailand

Life Cycle of *Clonorchis sinensis*

Egg in wet mount of stool



Clonorchiasis/Opisthorchiasis

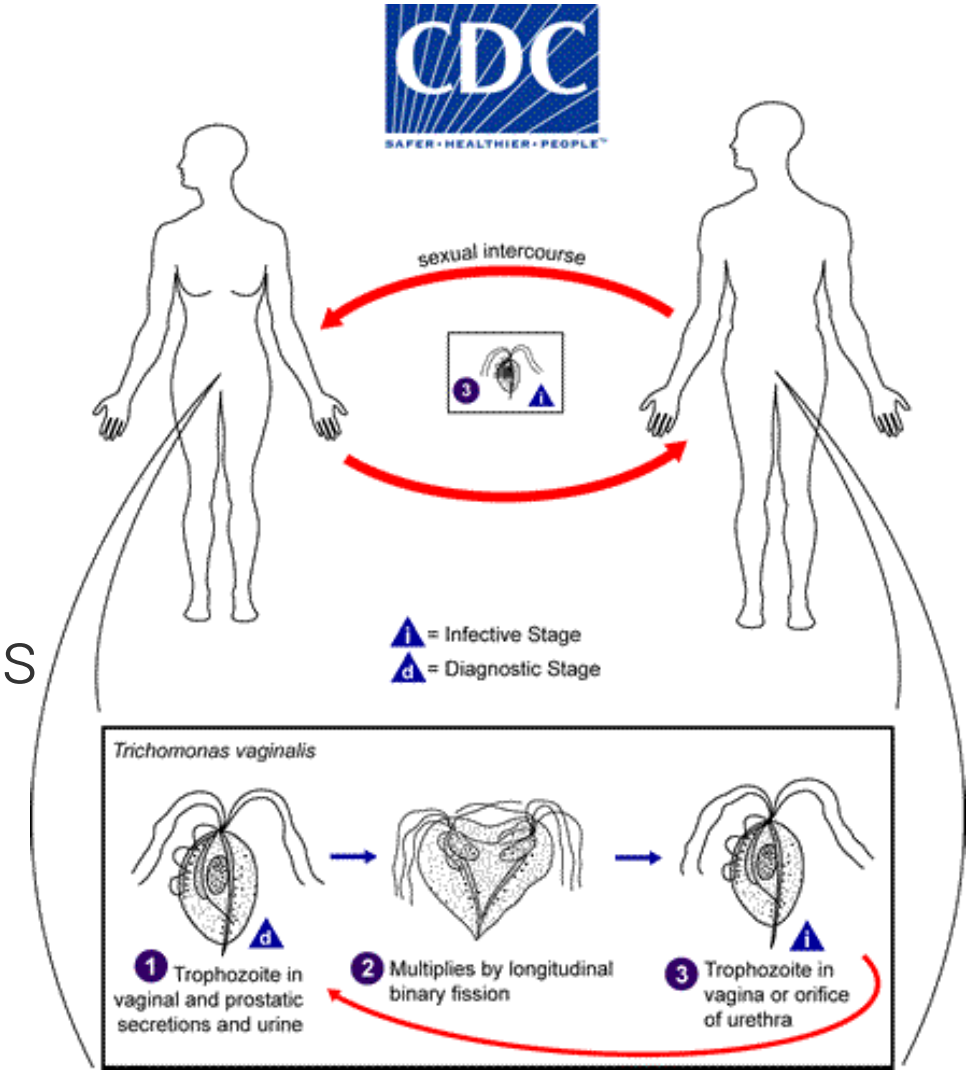
- Symptoms related to worm burden
  - » Inflammation, intermittent obstruction of biliary ducts; abdominal pain (RUQ)
  - » Toxicity (metabolic products of worms), secondary bacterial infections
  - » Leading cause of cholangiocarcinoma; also cholangitis, cholecystitis, pancreatitis.
- Diagnosis: detection of eggs in feces.
- Treatment: praziquantel

Parasites of Genitourinary tract

https://www.cdc.gov/dpdx/

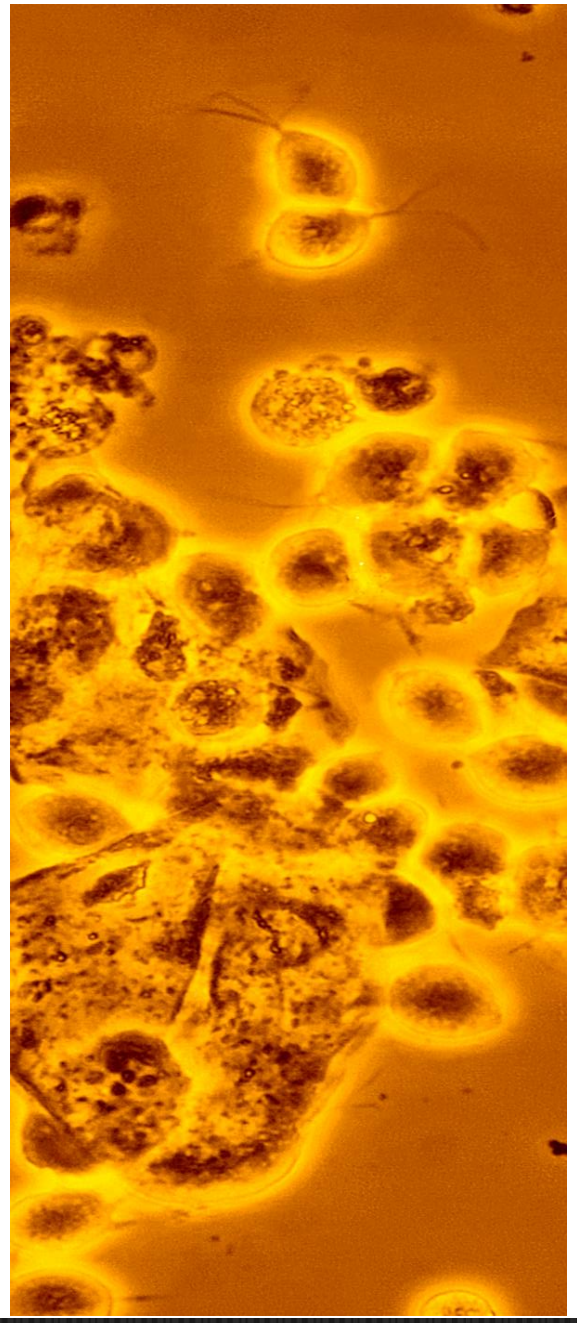
Trichomoniasis

- Caused by the protozoa *Trichomonis vaginalis*
- Acquired by direct sexual contact with infected human
- Worldwide distribution
  - » Increased prevalence among populations w/multiple sexual partners



Trichomoniasis

- Symptoms:
  - » Women: vaginitis w/purulent discharge
    - Can lead to adverse pregnancy outcomes
    - Rarely cervical lesions, abdominal pain, dysuria
  - » Men: Typically asymptomatic
    - Rarely urethritis, prostatitis, epididymitis
- Diagnosis:
  - » NAAT testing (preferred clinically)
  - » Wet mount exam (obsolescence)
- Treatment: single dose metronidazole

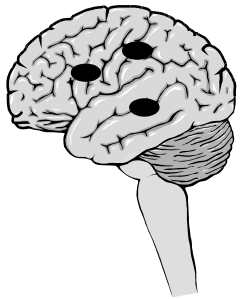


Microsporidia

- Obligate intracellular *fungal* parasites of most animal phyla
  - » Thought to be ingested
- Most-commonly seen in immunocompromised patients.
  - » May disseminate
- Numerous species are known to be involved in human infections
- Treatment: Albendazole (for most species)

Human Microsporidiosis

CNS microsporidiosis:



E. cuniculi

E. intestinalis

Trachipleistophora anthropopthera

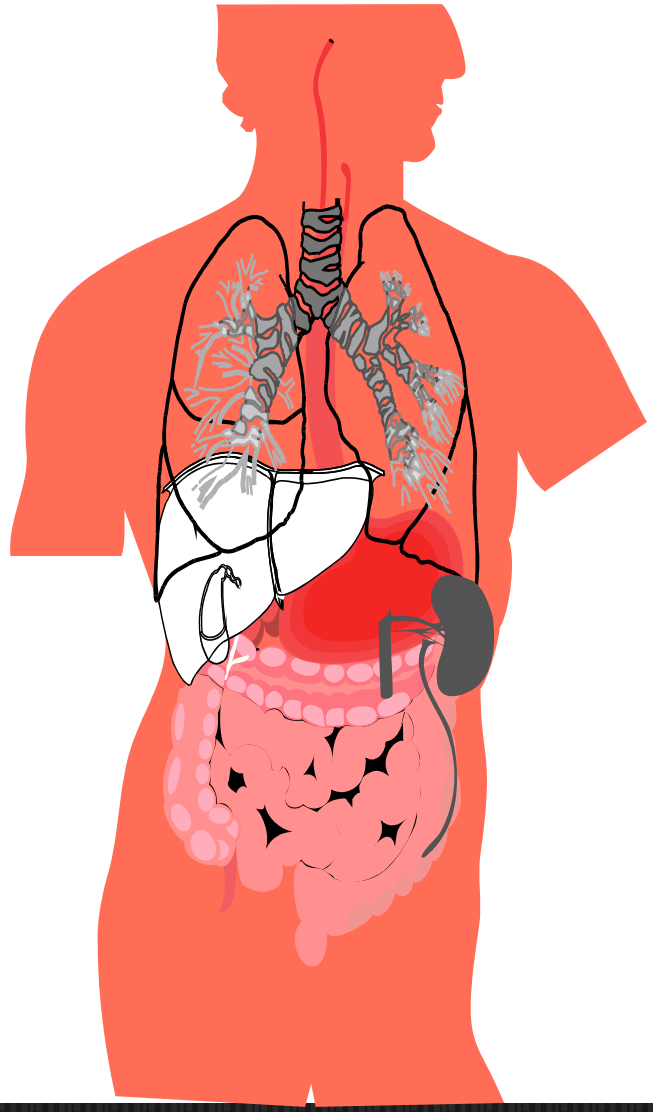
Skin lesions

Anncaliia algerae

Gastrointestinal and biliary tract microsporidiosis:

E. bieneusi

E. intestinalis

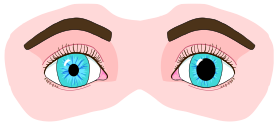


Ocular microsporidiosis:

Encephalitozoon spp. *(E. cuniculi, E. hellem, E. intestinalis)*

Vittaforma corneae

Anncaliia algerae



Disseminated microsporidiosis:

E. hellem

E. cuniculi

E. intestinalis

Trachipleistophora anthropopthera

Trachipleistophora hominis

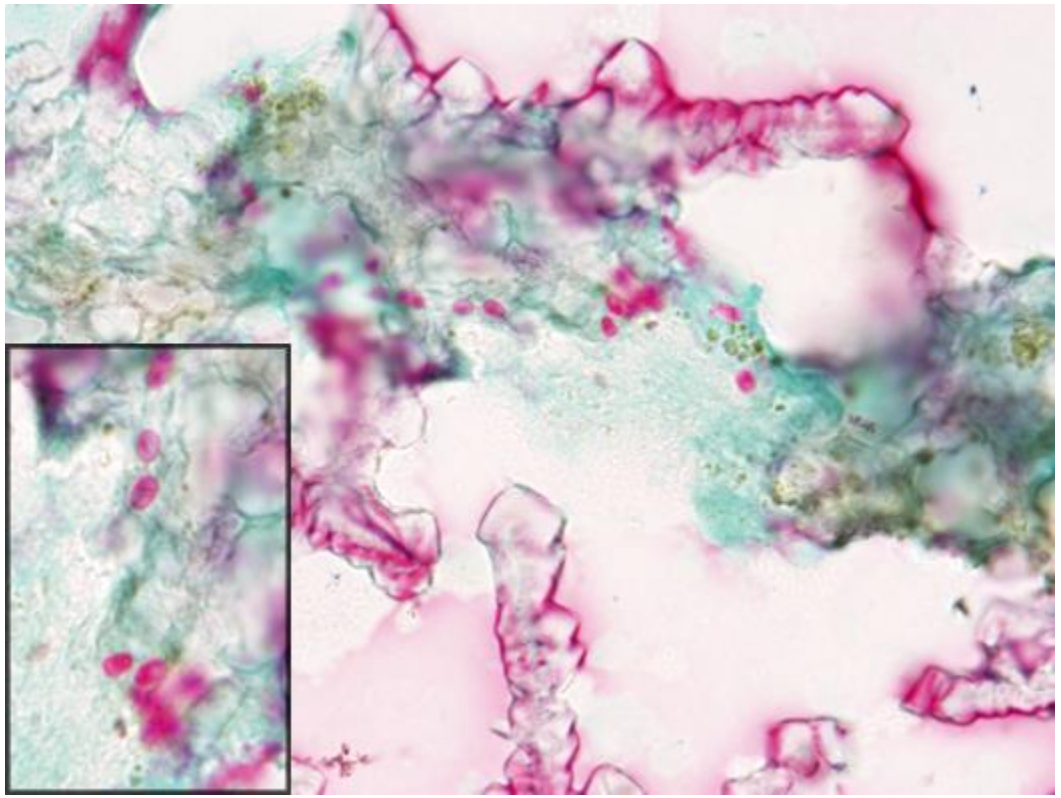
Tubulinosema acridophagus

Microsporidiosis - Diagnosis

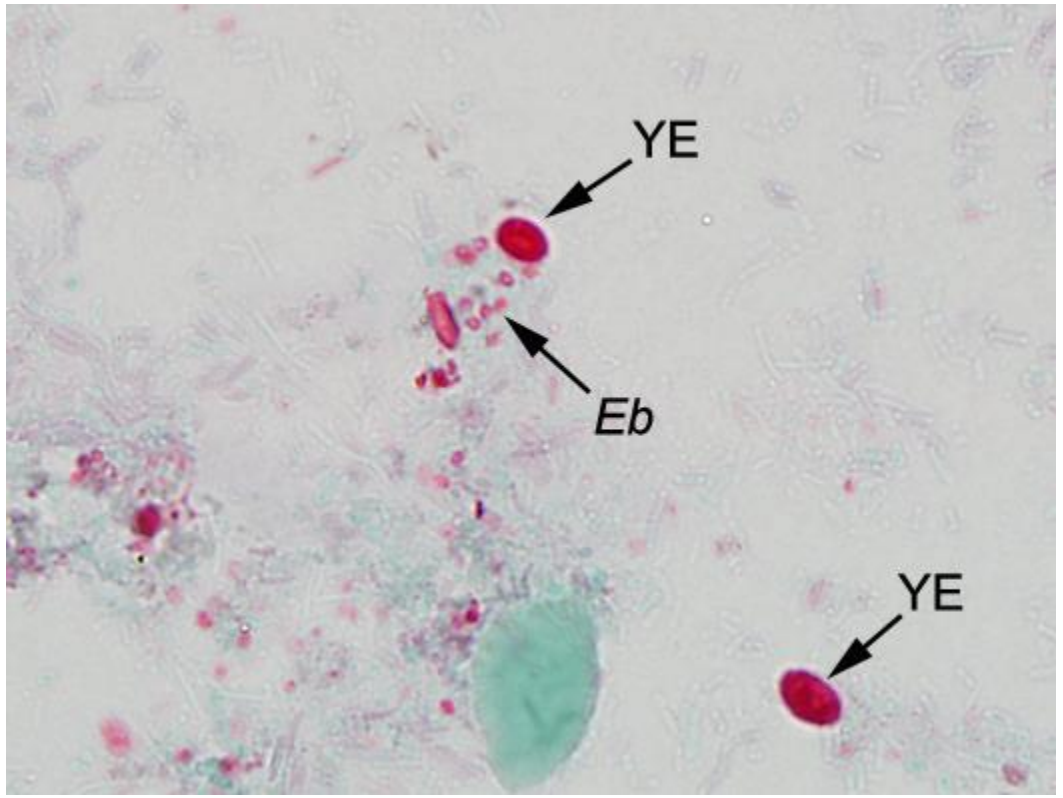
- Not readily detected by traditional stool O&P
  - » Very small & do not retaining trichrome stain
  - » Require special stains

- PCR and DNA sequencing typically used for species-level identification
  - » PCR not practical for routine screening.

Microsporidia stained with Modified trichrome



BAL



Stool

Key Points

- *Toxoplasma* – cats, congenital infections, & immunocompromised hosts
- *Angiostrongylus* – eosinophilic meningitis
- *Cysticercosis* – Caused by the pork tapeworm but not acquired from eating pork! Brain lesions
- *Naegleria* – Diving into fresh warm water, rapidly fatal meningoencephalitis
- *Acanthamoeba* – brain and cornea infections, often fatal

Key Points

- *Leishmania* – disfiguring lesions, severe visceral form (*kala azar*)
- *Trichinella* – undercooked pork/bear, larvae in muscles
- *Onchocerca* – River Blindness, subcutaneous nodules
- *Paragonimus* – Iron fillings → hemoptysis, raw crustaceans
- *Echinococcus* – liver cysts, sheep dog exposures
- *Chlonorchis* – cholangiocarcinoma, raw fish
- *Trichomonas* – Vaginitis w/discharge (♀), asymptomatic (♂)

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