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

- Ascaris
- Paragonimus
- Taenia
Broad (Medical) Classification of Parasites

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

* Fungi, not protozoa

https://www.cdc.gov/dpdx/
Broad (Medical) Classification of Parasites

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

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

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

http://neuroradiologyteachingfiles.com/bfa.html
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*

- **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 Acanthamoebal Balamuthia

- Cysts
- Trophozoite
- Mitosis

1. Cysts
2. Trophozoite
3. Mitosis
4. Amebae (cysts and trophozoites) can enter humans in various ways
5. Through the eye
6. Through nasal passages to the lower respiratory tract
7. Through ulcerated or broken skin

- CDC

Balantium in brain tissue, H&E stain

1. Results in severe keratitis of the eye.
2. Results in granulomatous amebic encephalitis (GAE) and/or disseminated disease in individuals with compromised immune systems.
3. Results granulomatous amebic encephalitis (GAE), disseminated disease, or skin lesions in individuals with compromised immune systems.
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

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

- **Eggs or gravid proglottids in feces and passed into environment.**
- **Embryonated eggs ingested by human host.**
- **Oncospheres hatch, penetrate intestinal wall, and circulate to musculature.**
- **Embryonated eggs and/or gravid proglottids ingested by normal intermediate host (swine).**
- **Humans acquire intestinal tapeworm infection via consumption of cysticerci in meat.**
- **Cysticerci develop in any organ, most commonly in subcutaneous tissues, brain, and eyes.**

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
Angiostrongylus
tasis

• 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
    ▪ Dissemination of cutaneous
  » Visceral (kala-azar)
    ▪ Fever, weight loss, hepatosplenomegaly
    ▪ Anemia
    ▪ Thrombocytopenia
    ▪ Leukopenia

• Different species w/ different clinical manifestations

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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)

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Trichinellosis

- Caused by nematode, *Trichinella*

- Acquired: ingestion of undercooked meat containing encysted larvae

- Geographically dispersed:
  - Worldwide with bias towards
    - Europe
    - N. America

[Image of the CDC diagram related to Trichinellosis]
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

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

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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-appeared-blind}

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

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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

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

1. Unembryonated eggs
2. Embryonated eggs
3. Miracidia hatch and penetrate snail
4. Sporocysts Rediae Cercariae
5. Cercariae invade the crustacean and encyst into metacercariae.
6. Humans ingest inadequately cooked or pickled crustaceans containing metacercariae.
7. Exocyst in duodenum
8. Adults in cystic cavities in lungs lay eggs which are excreted in sputum. Alternately eggs are swallowed and passed with stool.

= Infective Stage
= Diagnostic Stage
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

Diagram showing the life cycle of *Echinococcus granulosus*.
Echinococcosis

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

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

1. **Embryonated eggs passed in feces.**
2. **Eggs ingested by the snail intermediate host.**
3. **Free-swimming cercariae encyst in the skin or flesh of freshwater fish.**
4. **Metacercariae in flesh or skin of fresh water fish are ingested by the definitive host.**
5. **Excret in duodenum**
6. **Adults in biliary duct of definitive host.**

**Additional Notes:**
- Egg in wet mount of stool
- Clonorchis sinensis is a liver fluke that infects humans and can cause clonorchiasis, a parasitic disease.
- The life cycle involves a snail intermediate host and freshwater fish as paratenic hosts.
Clonorchiasis/Opisthorchiasi

• 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
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

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

Gastrointestinal and biliary tract microsporidiosis:
E. bieneusi
E. intestinalis

Ocular microsporidiosis:
Encephalitozoon spp. (E. cuniculi, E. hellem, E. intestinalis)
Vittaforma corneae
Anncaiiia algerae

Disseminated microsporidiosis:
E. hellem
E. cuniculi
E. intestinalis
Trachipleistophora anthropopthera
Trachipleistophora hominis
Tubulinoosema 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 (♂)
A nonprofit enterprise of the University of Utah and its Department of Pathology