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In this lecture we will discuss some of the parasitic infections of the GIT, 3 protozoal, and 4 helminthic. Please concentrate on these 3 most important features of each parasite: **Infective stage, diagnostic stage, and route of transmission**.

Protozoal (Unicellular) Infections

1. <u>Entamoeba Hystolitica</u>: The causative agent of Amoebiasis and one of the causative agents of dysentery (intestinal inflammation with **bloody diarrhea**). Amoebiasis has several clinical presentations which will be discussed in detail later. Its definitive host is humans while its reservoir is other animals (dogs, pigs, rats, monkeys).

Definitive host: the host where <u>maturation</u> or <u>sexual reproduction</u> of the parasite takes place.

Transmission is by the feco-oral route. Infection is mainly by contaminated water, but other modes of infection include contaminated food, autoinfection (hand to mouth), and homosexual activity. The preferred habitat is the flexures of the large intestine because fecal stasis in these regions helps in invasion. These flexures include the cecal, hepatic, splenic, and sigmoidal flexures.

- Morphology: has two stages:
 - Cyst: This is the infective and diagnostic form of *E. hystolitica* and can survive outside a host and withstand harsh environmental conditions. An *E. hystolitica* cyst can have more than one nucleus, but only the form with four nuclei is the mature and infective form of the cyst. Cysts with less than four nuclei mature outside the body when there is a drop in both temperature and moisture.
 - Trophozoite (vegetative form): can be viable outside the host for several minutes only. This is the mature and invasive form (→ bloody diarrhea) of *E. hystolitica*. Trophozoites have a nucleus, cytoplasm, an endoplasm (granulated) and an ectoplasm (clear). Trophozoites use pseudopodia for locomotion. Trophozoites encyst (transform into cysts) in the large intestine before leaving the body through the anal canal.

The presence of RBC's in the endoplasm is diagnostic of invasion.



- Life Cycle:
 - Ingestion of the mature cyst.
 - Excystation: the cyst transforms into one 4-nucleied trophozoite. This trophozoite then divides three times to produce four 1nucleied trophozoites. Each trophozoite then divides into two to produce <u>8 trophozoites</u> total from each cyst.
 - Migration of trophozoites into the large intestine.
 - Multiplication (asexual) by binary fission.



- Invasion into mucosa might occur, if not, the trophozoite encyst and exit the body through the anal canal.
- Pathogenesis: might <u>invade into the mucosa, then submucosa</u> and reach the blood circulation → spread to other organs, mainly the liver, or less commonly the lung or meninges of the brain, or very rarely into the skin (*amoebiasis cutis*).
- Clinical outcomes: Intestinal and extraintestinal:
 - Intestinal:
 - <u>Asymptomatic</u> (cyst passers): constitute the majority of those infected with *E. hystolitica*. Trophozoites remain in the intestinal lumen feeding on nutrients as a commensal *without* tissue invasion.
 - <u>Acute</u> amoebic dysentery: fever, abdominal pain, tenderness, and loose stool containing mucus, blood and trophozoites (only in acute can you find trophozoites in stool!).
 - <u>Chronic</u> infection: occurs if acute dysentery is not properly treated. Presents with low fever and recurrent episodes of diarrhea alternating with constipation. **Only cysts are found in stool**.
 - Complications:
 - Haemorrhage: due to the invasion.
 - Intestinal perforation \rightarrow peritonitis.
 - Toxic megacolon.
 - Flask-shaped ulcers.

- Extraintestinal: Due to invasion of the blood vessels by the trophozoites in the intestinal ulcer → reach the blood → spread to different organs as mentioned above like the liver (right lobe most mainly), lung (through the daiphragm), and brain, where they cause the formation of abscesses. Rarely reaches the skin.
- Diagnosis of intestinal amoebiasis:
 - Direct:
 - Macroscopic appearance of stool: loose stool with mucus and blood.
 - Microscopic:
 - Finding the characteristic cyst (or trophozoite in acute dysentery only) by a direct smear with iodine stain.
 - Sigmoidoscopy
 - X-ray with barium enema to observe ulcers or other features.
 - Indirect: Serology (only when there is invasion so uselees in asymptomatic carriers).
- Treatment:
 - Metronidazole (Flagyl): is the first drug of choice for serious anaerobic bacterial and parasitic infections. Works by inhibiting their nucleic acid synthesis.
 - *Paromomycin*: more commonly used with asymptomatic carriers. Works by inhibiting protein synthesis.
- Prevention: avoid drinking water that might be contaminated. **Boiling** the water ensures the abscense of *E. hystolitica*. Be careful! The amount of chlorine in municipality water and swimming pools is not enough to kill of the *E. hystolitica* in it.
- 2. <u>Giardia Duodenalis</u>: the causative agent of Giardiasis, also called *Beaver fever* especially in Canada but is argued if the reservoir for this parasite is zoonotic or if the disease causes **fever** in the first place. Giardiasis can be asymptomatic or present with watery diarrhea and **steatorrhea** depending on the strength of the infected individual.

Steatorrhea: foul smelling greasy stool.

Transmission is by the feco-oral route, mainly indirectly through contaminated water or food (direct modes of infection include homosexual activity). The habitat of *G. duodenalis* is the duodenum and jejunum. **Infective dose is less than 10**, so is considered very infective. *G. duodenalis* affects all age groups but are more common in immunocompromised individuals, elderly, and children.

- Morphology: has two stages: (mostly same as *E. hystolitica*, differences are in dark blue)
 - Cyst: this is the infective and diagnostic form of *G. duodenalis* and can survive outside a host and withstand harsh environmental conditions. A *G. duodenalis* cyst has two nuclei in the immature form and four in the mature and infective form of the cyst.
 - o Trophozoite (vegetative form): can be viable outside the host for several minutes only. This is the mature form of *G. duodenalis*. Trophozoites have two nuclei with central parabasal bodies, giving the appearance of a face wearing spectacles (glasses) as well as four pairs of flagella giving the appearance of whiskers. Trophozoites use flagella for locomotion. Trophozoites encyst (transform into cysts) in the large intestine before leaving the body through the anal canal. Trophozoites DO NOT invade, they only colonize and attack to intestinal villi by a large concave sucking disk on the ventral surface → no bloody diarrhea.



- Life cycle: also very similar to *E. hystolitica*, differences are in dark blue.
 - Ingestion of the mature cyst.
 - Excystation: the 4-nucleid cyst divides to produce two 2-nucleied trophozoites.
 - Migration of trophozoites into the large intestine.
 - Multiplication (asexual) by binary fission.





• Trophozoite encyst and exit the body through the anal canal. NO INVASION.

- Clinical outcomes: usually asymptomatic and self-limited. Can cause steatorrhea and other common signs and symptoms of infection (malaise, abdominal pain, etc.).
- Diagnosis: same as *E. hystolitica*:
 - Stool analysis: find cysts (or trophozoites too but only in acute).
 - Serology, but this is method uncommon.
- Treatment: *Metronidazole* (5-7 days) or *Tinidazole* (single dose).

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3. <u>Cryptosporidium</u>: '*Crypto-*' comes from how this parasite's habitat is the crypts of the intestine. '*-sproridium*' is because this parasite is a sporozoid.

Sporozoids: alternate during their life cycle between sexual and asexual reproduction.

This infection is insignificant and may present with self-limited diarrhea in immunocompetent individuals, but is a **very important infection in immunocompromised individuals like HIV patients**. In these patients, cryptosporidia cause severe intractable diarrhea that doesn't stop until treated with abX.

Transmission is by the feco-oral route and the incubation period is about 2 weeks (direct person to person transmission is likely to occur because they leave as oocyst).

Unlike Giardia and Entamoeba, the **infective and diagnostic stage of cryptosporidia is the oocyst**.

- Diagnosis: find the **<u>oocyst</u>** in stool using a modified acid fast stain.
- Treatment: usually electrolyte balancing and rehydration, but *Nitazoxanide* must be used for immunocompromised individuals like HIV patients.

Helminths

- <u>Ascaris Lumbricoides</u>: a nematode and the causative agent of Ascariasis. EGGS TAKE TIME (2-3 weeks in soil) TO MATURE AND BECOME INFECTIVE. Nematodes have separate sexes and a limited lifespan; *A. lumbricoides* live for 2 years in the body. **Transmission is by the feco-oral route by ingestion of fertilized mature eggs.** Diseases transmitted feco-orally are always endemic in areas with poor sanitation.
 - Morphology and Life Cycle: *A. lumbricoides* have 3 stages:
 - Eggs: laid and fertilized in the intestines and passed in the feces. THEY ARE NOT INFECTIVE YET. Eggs become infective after about 2-3 weeks in the soil and are infectious for several months. Note the mamillated (bumpy) surface, this feature is used diagnostically.



 \circ Larvae: if infective eggs are ingested, the larvae hatch in the duodenum (1 egg \rightarrow 1 larva). Larvae take 2-3 months to mature, but if they stayed in the intestines, peristaltic movement would shed them away before they have the chance to mature and lay eggs, so they developed a unique cycle to avoid the intestines until they matured.

After the larvae hatch, they penetrate through the mucosa, migrate in the circulatory system, **lodge in lung** capillaries, penetrate the alveoli, and migrate from the bronchioles to the trachea and pharynx. Then the larvae are swallowed and thus returned to the intestine to mature into adults. This cycle takes about 2-3 months and has important clinical outcomes discussed below. • Adults: After mating, females can release 200,000 eggs per day (may or may not be fertilized), which are passed in the faeces. Females are larger than males.



- Clinical outcomes: most cases are asymptomatic, but if the infection dose was high, the resulting adult worms can cause mechanical obstruction and malabsorption in the bowel and/or growth impairment in children. Larvae in the lungs can cause a hypersensitivity rxn → high eosinophilia → Löeffler syndrome (coughing).
- Diagnosis:

◦Look for **mamillated** eggs by microscopy using a direct smear.

oAdult worm may also be identified in feces.

•Only larvae may be found in sputum (lung aspirate).

Note: Diagnostic stage are immature non-infective eggs while infective stage is mature eggs.

 Treatment: oral Albendazole 400mg STAT (usually single dose). STAT means immediately after diagnosis.

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- Enterobius Vermicularis (Pinworm): EGGS ARE IMMEDIATELY INFECTIOUS AFTER HATCHING. Females are larger than males and have a slender-pointed posterior end that males don't have. Adult worms inhabit the caecum.
 - Transmission is by the feco-oral route by ingestion of eggs. Since eggs are immediately infectious, autoinfection is possible, with fomites (towels,

bedsheets, etc.) increasing the chance of transmission between individuals or reinfection of the same individual, especially in children (by scratching then putting their fingers in their mouth). It was found that retro-infection is also possible, but the percentage of its occurrence is yet to be researched.

Retro-infection occurs if gravid (carrying eggs) females that exit through the anal canal at night to lay their eggs on the perianal area directly reenter through the anus or if the eggs that were just laid reentered through the anus too.

- Clinical outcomes: typically asymptomatic but the most common complaints are **perianal pruritus** (itching) and sleeping disturbances especially in children.
- Life cycle: eggs hatch in the intestines and mature in the colon. Females migrate at night to lay their eggs around the perianla area.

• Diagnosis: Scotch-tape test, with identification of the flat-sided clear-shelled egg.

Adult eggs can be seen too but rarely.

* Please concentrate on the differences in the eggs between different helminths.

• Treatment: *Albendazole*

Echinicoccus Granulosus: the causative agent of *hydatid cysts*. The definitive host is the dog, but humans typically become accidental hosts when infected. Since humans are not the definitive host, humans are considered a dead-end to the organism's life cycle since it is unable to multiply or mature. This leads to the formation of hydatid cysts. Eggs are the infective stage.

A 14-cm hydatid cyst from a splenectomised patient.





Group of hydatid cysts.





- Life cycle: dogs pass the eggs in stool, if the eggs are ingested by a human, they hatch in the small intestine and the larvae then penetrate the mucosa and reach the blood circulation (like *A. lumbricoids*). The larvae migrate to other organs mainly the liver. Since they can't mature, they encyst in a fluid filled sack (hydatid cyst). The characteristic feature of these cysts is that they can grow up to 7 cm per year.
- Treatment: Surgery + *Albendazole*. Extreme care must be taken when removing the cyst. If the cyst ruptures, the highly immunogenic hydatid fluid can lead to anaphylactic shock.
- 4. <u>Schistosoma Haematobuim, Mansoni, & Japonicum</u>: the causative agents of Schistosomiasis (Balharzia), which is an endemic disease in Egypt. *S. haematobium* is related to urinary disease while *S. mansoni* and *S. japonicum* are related to GIT disease.
 - Life cycle: eggs laid in the intestine are excreted in feces and hatch outside the body in fresh water → ciliated miracidium is liberated. The miracidia then enter their intermediate host, a species of freshwater snail, in which it multiplies → large numbers of tailed cercariae are then liberated into the water. Ceracriae are the infectious stage. Cercariae penetrate human skin and migrate through the lung and the liver to reach portal venous system.

Therefore, transmission is through the skin, not feco-oral!



• Pathogenesis:

The most significant pathology is associated with the schistosome eggs, not the adult worms. Adults worms inhabit the veins of the urinary/GI system. Female schistosomes can lay hundreds or thousands of eggs per day within the venous system. Eggs circulate in the blood and lodge in the liver (*S. mansoni* and *S. japonicum*) or urinary bladder (*S. haematobium*). A granulomatous reaction surrounds the eggs and leads to fibrosis of the liver with *S mansoni* and *S japonicum*.

- Diagnosis: detection of eggs in stool (for *S. mansoni* and *S. japonicum*) or urine (*S. haematobium*). Each species of egg has a characteristic spine.
- Treatment: *Praziquantel*

