



GIS

MICROBIOLOGY

8



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ÿ In this sheet we will discuss parasitic infections of the GIT.

> Three protozoal (unicellular) infections:

1. *Entamoeba histolytica*.
2. *Giardia lamblia*.
3. *Cryptosporidium parvum*

> Four helminthic (multicellular) infections:

1. *Ascaris lumbricoides*.
2. *Enterobius vermicularis*.
3. *Echinococcus granulosus*.
4. *Schistosomia mansoni*.

o But before getting through the details of each infection, let's revise some important definitions:

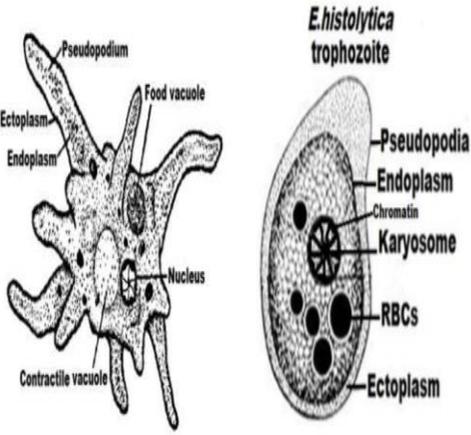
- ⊗ Infective stage (IS): The stage in the life cycle of a parasite in which it can initiate infection to its host.
- ⊗ Diagnostic stage (DS): The stage at which the parasite leaves the host, e.g. through excretion together with the stool, urine, or sputum.
- ⊗ Definitive host (DH): An organism which supports the **adult (mature)** or **sexually reproductive** form of a parasite.
- ⊗ Intermediate host (IH): An organism that supports the **immature (larval)** or **non-reproductive** forms of a parasite.
- ⊗ Reservoir host (RH): An animal (or species) that is infected by a parasite, and which serves as a source of infection for humans or another species.
- ⊗ Dysentery is an intestinal inflammation, primarily of the colon. It can lead to mild or severe stomach cramps and severe diarrhea with mucus or blood in the feces.

ÿ *Entamoeba histolytica*:

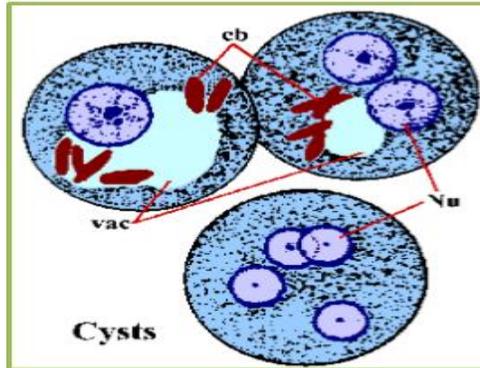
- > **Amebiasis** or **amoebic dysentery** is a disease caused by the parasite *Entamoeba histolytica*. It can affect anyone, although it is more common in people who live in tropical areas with poor sanitary conditions.
- > **(DH)**: Humans.
- > **R.H**: Dogs, pigs, rats and monkeys.

- > **Habitat:** Large intestine (caecum, colonic flexures and sigmoidorectal region).
- > **Mode of infection:** Amoebiasis is usually transmitted by the **fecal-oral route**, but it can also be transmitted indirectly through contact with dirty hands or objects as well as by anal-oral contact.
 1. Contaminated water, food (ex. green vegetables), or drinks or hands contaminated with human stool containing mature cysts.
 2. Handling food by infected food handlers such as cooks and waiters.
 3. Flies and cockroaches that carry the cysts from feces to exposed food.
 4. Autoinfection (feco-oral or hand to mouth infection).
 5. Homosexual transmission (transmissible pathogen in men who have sex with men (**MSM**)).

⊗ Morphological Characters:

<p>Trophozoite Stage (Vegetative form or tissue form):</p> 	<ul style="list-style-type: none"> > Active, motile, feeding form. > Mature and invasive form - (bloody diarrhea)-of <i>E. histolytica</i>. > Trophozoites have: <ol style="list-style-type: none"> 1. Nucleus. 2. Cytoplasm. 3. Granulated endoplasm. 4. Clear ectoplasm. 5. Pseudopodia for locomotion. > The presence of ingested RBCs within the trophozoite is diagnostic for <i>E. histolytica</i>.
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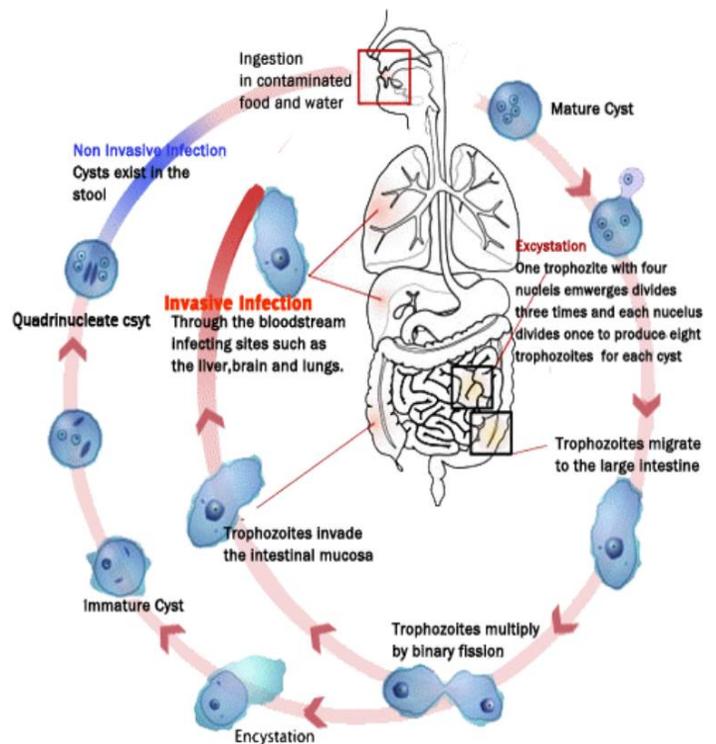
Cyst Stage (Luminal form):



- › Both infective and diagnostic stage.
- › Can survive and withstand harsh environmental conditions outside of the host (resistant form).
- › Only Mature (Quadrinuclate) cyst is infective.

† Life Cycle:

1. Ingestion of mature cyst.
2. Excystation (in the small intestine): Every mature cyst gives off four “uninucleate” trophozoites, each of which divide-by binary fission-into two separate trophozoites, producing a total of 8 trophozoites.
 - › 1 cyst → 8 trophozoites.
3. Trophozoites migrate to the large intestine.
4. Trophozoites multiply by binary fission.
5. Trophozoites invade the intestinal mucosa, (invasion is the main virulence factor of the amoeba responsible for “inflammatory or bloody diarrhea).”



6. Invasion does not necessarily take place. Without invasion, trophozoites encyst and pass through feces.

‡ Important Notes:

- › Both stages (cysts and trophozoites) are passed in the feces, but only cysts can withstand the external environment. Trophozoites passed in the stool are rapidly destroyed once outside the body. However, trophozoites can be detected in rapidly analyzed acute diarrheal samples.
- › Both cysts and trophozoites (if viable) are considered the “diagnostic stage.”
- › Only cysts are responsible for transmission, or the “infective stage.” If trophozoites were ingested, they would not survive exposure to the gastric acidic environment.

‡ Clinical Pictures:

In many cases, the trophozoites remain confined to the intestinal lumen (**noninvasive infection**) of individuals who are asymptomatic carriers, passing cysts in their stool. In some patients, the trophozoites invade the intestinal mucosa (**intestinal disease**), or, through the bloodstream, extraintestinal sites such as the liver, brain, and lungs (**extraintestinal disease**), with resultant pathologic manifestations like liver abscess.

- › E. histolytica rarely spreads to the skin causing **amoebiasis cutis**.

‡ Extra-intestinal Amoebiasis:

- › Due to invasion of the blood vessels of the intestine by trophozoites, they reach the blood → spread to different organs as:
- › Liver: Amoebic liver abscess or diffuse amoebic hepatitis.
- › Commonly affects the right lobe either due to spread via the portal vein or extension from a perforating ulcer in the right colonic flexure.
- › CP: Includes fever, hepatomegaly and pain in right hypochondrium.
- › Underlined statements are present in the slides but were not mentioned by the doctor.
- › Lung abscess, brain abscess...

Intestinal Amoebiasis

Asymptomatic Infection

-Most common and trophozoites remain in the intestinal lumen feeding on nutrients as a commensal without tissue invasion.

(Asymptomatic patients are known as **healthy carriers and cyst passers**).

Symptomatic infection

Acute Amoebic Dysentery

Presents with fever, abdominal pain, tenderness, tenesmus and frequent motions of loose stool containing mucus, blood, **trophozoites and cysts**.

Chronic Infection

Occurs if acute dysentery is not properly treated. Presents with low grade fever and recurrent episodes of diarrhea that alternate with constipation.

- **Only cysts are found in stool.**

Complications:

-Haemorrhage due to erosion of large blood vessels.

- Intestinal perforation → peritonitis.
- Appendicitis.
- Amoeboma (Amoebic granuloma) around the ulcer. → Stricture of affected area.

With heavy infection and lowering of host immunity:

The trophozoites of *E. histolytica* invade the mucosa and submucosa of the large intestine by secreting lytic enzymes → Amoebic ulcer.

The ulcer is **flask-shaped** with deeply undermined edges containing cytolysed cells, mucus and trophozoites.



The most common sites of amoebic ulcers are the caecum, colonic flexures and sigmoidorectal regions due to decrease peristalsis & slow colonic flow at these sites that help invasion.

† Laboratory Diagnosis of Intestinal Amoebiasis:

⊗ Direct:

- Macroscopic: Offensive loose stool mixed with mucus and blood.
- Microscopic:
 - An ova and parasite (O&P exam) is a microscopic evaluation of a stool sample that is used to look for parasites that may infect the digestive tract. The parasites and their eggs (ova) are shed from the lower digestive tract into the stool.
 - 1. Stool examination: Reveals either trophozoites (in loose stool) or cysts (in formed stool) by direct smear, iodine stain & culture.
 - 2. Sigmoidoscopy: To see the ulcer or the trophozoites in an aspirate or biopsy of the ulcer.
 - 3. X-ray after barium enema: To see the ulcer, deformities or stricture.

⊗ Indirect:

- Serological test: Antigen detection.
- Asymptomatic infections do not show a serum anti-amoebic antibody response. Only symptomatic **invasive intestinal** infections show a systemic immune response.

† Treatment:

- Metronidazole is the drug of choice, ideal for treating all forms of amoebiasis.

Asymptomatic intestinal carrier Luminal amoebicides	Intestinal amoebiasis Tissue amoebicides	Extra-intestinal amoebiasis Tissue & luminal amoebicides
Paromomycin or Diloxanide furoate. (Although flagyl can be used as well)	Metronidazole (Flagyl) or tinidazole is the drug of choice	Metronidazole (Flagyl) + Paromomycin or Diloxanide furoate

† Prevention:

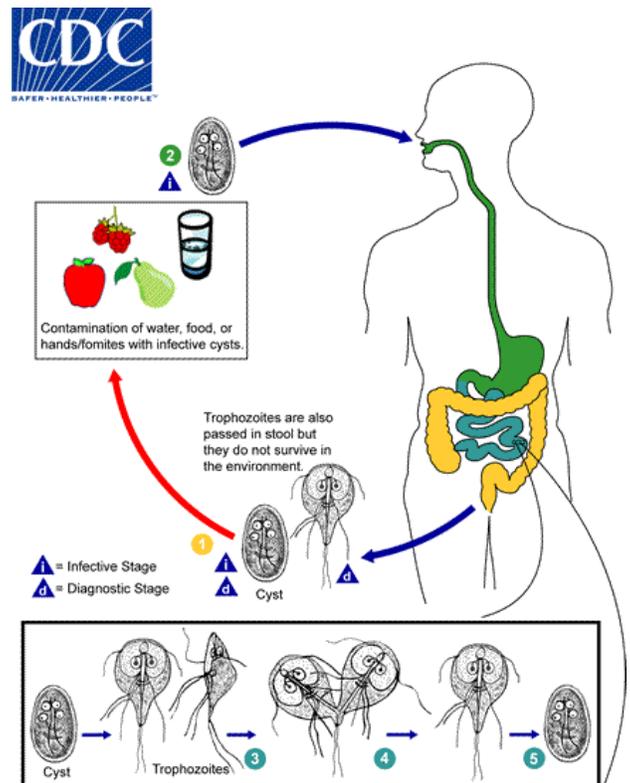
- › Amoebic infection is prevented by eradicating fecal contamination of food and water.
- › **Water is a prime source of infection** and therefore the most contaminated foods are vegetables such as lettuce.
- › Amoebic cysts are not killed with low doses of chlorine or iodine (present in municipal water and swimming pools).
- › **Bringing water to a boil ensures the absence of amoeba.**

† Giardia: (also known as *Giardia intestinalis*, *Giardia lamblia*, or *Giardia duodenalis*)

- › The causative agent of **Giardiasis**, found most commonly in the crypts of the duodenum.
- › Known as “**beaver fever**” in Canada because beavers are considered a zoonotic reservoir for Giardia. It is debated if the disease causes fever.
- › Giardia may not have any symptoms. These asymptomatic individuals can still pass the disease on to others, again “cyst passers.”

† Life Cycle:

1. Infection occurs by the **ingestion of cysts** in contaminated water, food, or by the **fecal-oral route**.
2. In the small intestine, **excystation** releases trophozoites (each cyst produces **two** trophozoites).
3. Trophozoites multiply by binary fission. They can be free or attached by a **ventral sucking disk**.
1 cyst → 4 trophozoites.
4. **Encystation** of trophozoites: Cyst formation takes place as the organisms move down through the jejunum after exposure to biliary secretions.



> Both cysts and trophozoites can be found in the feces (**diagnostic stage DS**).

> The cyst is the stage found most commonly in nondiarrheal feces. Both cysts and trophozoites can be found in diarrheal feces.

> Cysts are infectious when passed in the stool (**infective stage IS**).

> Giardia **trophozoites** have two nuclei, giving the characteristic **monkey face appearance** or an **old man appearance** (wearing spectacles (glasses)).

> **4 pairs of flagella** are responsible for locomotion and give the appearance of whiskers.

> Trophozoites **DO NOT invade (no dysentery)**.

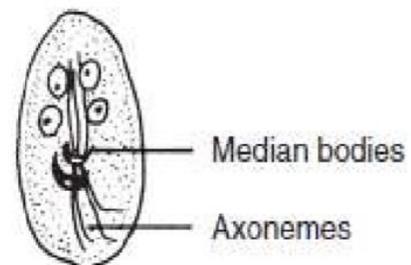
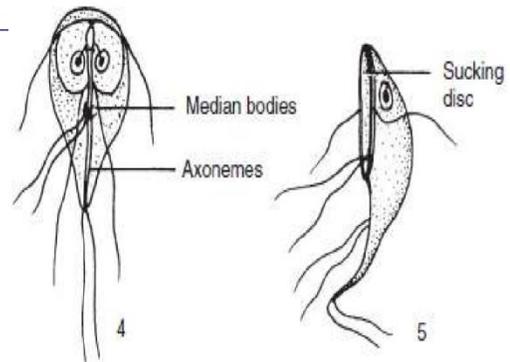
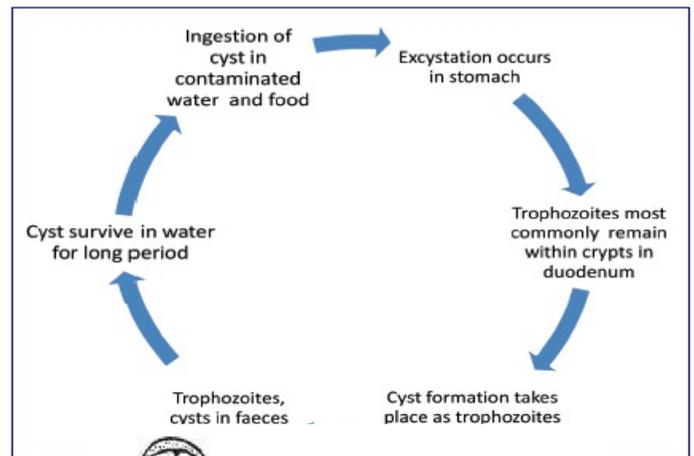
The ventral sucking disk attaches to the epithelium of the host villi causing fatty, **foul-smelling, greasy diarrhea (steatorrhea)**.

> **Steatorrhea** → malabsorption.

> **Cyst**: The infective and diagnostic form of G. duodenalis. Cysts are hardy and can withstand harsh environmental conditions. A G. duodenalis cyst has two nuclei in the immature form and **four in the mature, infective** form of the cyst.

> High incidence of giardiasis occurs in patients with **immunodeficiency syndromes** (G. duodenalis affects all age groups but is more common in immunocompromised individuals, elderly, and children (day-care centers)).

> The incubation period ranges from approximately 1-2 weeks and the infectious **dose is 10** (low infectious dose).



ÿ Clinically:

✿ Asymptomatic Infection: (treatment not recommended).

✿ Symptomatic:

1. Diarrhea is usually watery: profuse watery diarrhea that later becomes greasy, foul smelling, and may float (steatorrhea).
2. Abdominal cramps, bloating, malaise, weight loss.
3. Malabsorption and weight loss.
4. Vomiting and tenesmus are not common.

ÿ Lab Diagnosis:

✿ Routine Methods:

Stool analysis (O&P) test: cysts and sometimes trophozoites.

✿ Antigen Detection:

Sensitive and specific in detecting *G. lamblia* in fecal specimens.

ÿ Treatment: **Metronidazole** or tinidazole.

ÿ Cryptosporidium sp.

- › Name origin: **crypto**, because it inhabits the intestinal crypts.
- › **Spora:** because this parasite is a sporozoan.
- › **Sporozoans:** Parasites that have an alternation of sexual and asexual stages in their life cycle.
- › Intracellular enteric parasites that infect epithelial cells of the stomach, intestine, and biliary ducts.
- › *C. parvum* (mammals, including humans) and *C. hominis* (primarily humans).
- › Infections begin with ingestion of viable **oocysts**. Each oocyst releases four sporozoites, which invade the epithelial cells and develop into merozoites then oocysts. (called oocyst because it reproduces sexually).

ÿ Clinically:

- › Some people with Crypto will have no symptoms at all. Symptoms usually last about 1 to 2 weeks in people with healthy immune systems. People with weakened immune systems may develop serious, chronic, and sometimes fatal illness (intractable diarrhea).
- › **Copious Diarrhea:** These patients may have 3-17 liters of stool per day.

- › Abdominal pain and vomiting.
- › Transmission is by the feco-oral route.
- › The infective and diagnostic stage of cryptosporidia is the **oocyst**.

ÿ Diagnosis: Oocyst in stool using **modified acid-fast stain**.

ÿ Treatment:

- › Usually self-limited with oral or intravenous rehydration.
- › Nitazoxanide is used for immunocompromised individuals e.g HIV patients.

Helminths

ÿ ASCARIS LUMBRICOIDES:

- › Nematode and the causative agent of **Ascariasis**.
- › Nematodes have separate sexes and short life-span. Lumbricoides live for 2 years in the body and die even without treatment.

ÿ Morphology:

- › Male adult worm measures 15-20 cm in length.
- › Female adult worm measures 20-40 cm in length.
- › The posterior end of male adult worm is curved- (known as copulatory spicules, which are needle-like mating structures found only in males)-while the end of the female adult worm is straight.

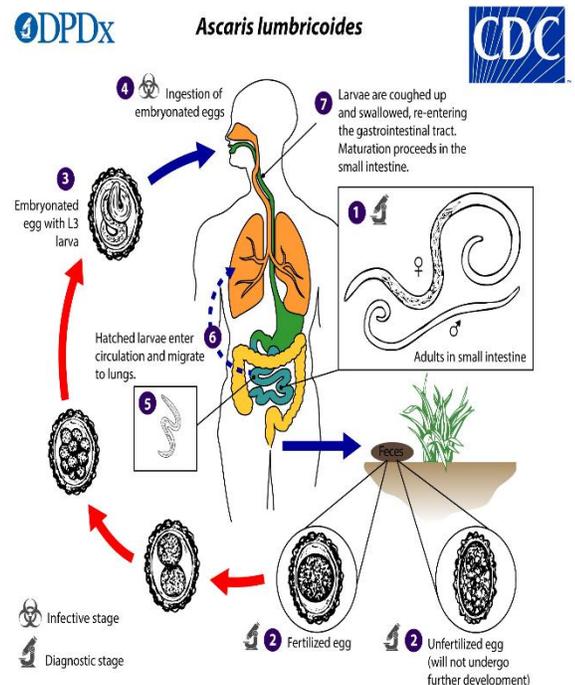
ÿ Mode of Transmission

- › Fecal–oral transmission by ingestion of fertilized, mature eggs. Diseases transmitted feco-orally are always endemic in areas with poor sanitation.
- › Reinfection is possible.



† Life cycle:

1. Infective (**embryonated**) eggs are swallowed.
2. The larvae hatch, invade the intestinal mucosa, and are carried via the portal and then systemic circulation to the **lungs**.
3. The larvae mature further in the lungs, penetrate the alveolar walls, ascend the bronchial tree to the throat, and are swallowed.
4. Upon reaching the small intestine, they develop into **adult worms**.
5. **Adult worms** live in the lumen of the small intestine. A female may produce approximately 200,000 eggs per day, which are passed with the feces.
6. Unfertilized eggs may be ingested but are not infective. Eggs become infective after about 2-3 weeks in the **soil (soil-transmitted helminths)**.



⊗ Important notes:

- > Infective stage (IS): Embryonated eggs with characteristic **mamillated (bumpy) surface**. This feature is beneficial in the diagnosis of ascariasis.
- > Diagnostic stage (DS): Immature non-infective eggs.
- > Ascaris eggs are capable of survival within harsh environmental conditions, including dry or freezing temperatures.
- > The pulmonary route is beneficial because if larvae stay 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 mature.



ÿ Pathogenesis and Spectrum of Disease:

- › People infected with Ascaris often show no symptoms. Heavy infections can cause intestinal blockage (mechanical obstruction) and impair growth in children.
- › Children and young adolescents have higher infection rate.
- › Symptoms:
 - Pulmonary symptoms occur during migration (**Loeffler's syndrome**: respiratory symptoms, infiltrates and eosinophilia).
 - Larvae in the lungs can cause a hypersensitivity rxn → eosinophilia → Loeffler syndrome (coughing and difficulty in breathing).
 - GI manifestations: Malnutrition, anemia, malabsorption, steatorrhea and intestinal obstruction, biliary obstruction and jaundice.

ÿ Diagnosis:

- › Microscopic examination (looking for eggs).
- › Direct smear (stool mixed with saline) identifies both fertilized and infertile eggs.
- › The adult worm may also be identified in feces.
- › Larvae may be found in sputum or gastric aspirates.

ÿ Treatment:

- › Oral **Albendazole** 400mg STAT (usually single dose).
 - › STAT means 'immediately'.
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ÿ ENTEROBIUS VERMICULARIS (pinworm):

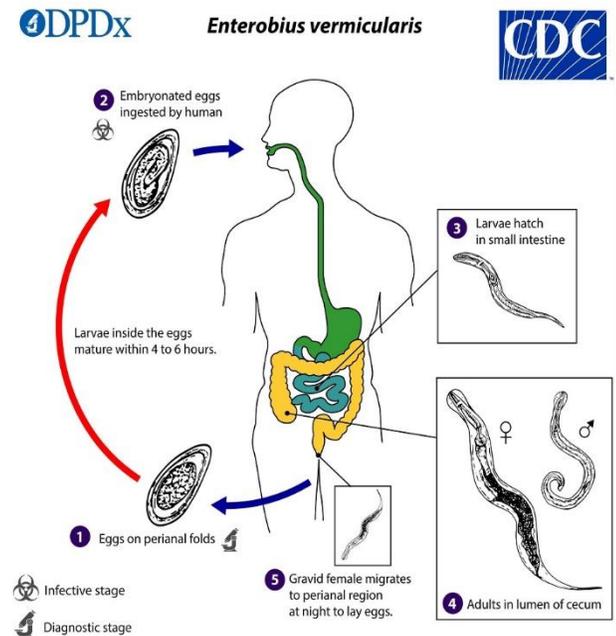
- › Pinworm infection is caused by a roundworm called Enterobius vermicularis. Although pinworm infection can affect all people, it most commonly occurs among children.
- › Small, thin and white worm.
- › Distributed worldwide and commonly identified in group settings of children ages 5 to 14 years.

- > The female worm measures 8 to 13 mm long with a pointed “pin” shaped tail (lays 11000 ova and live for a month).
- > The males measure only 2 to 5 mm in length, die following fertilization, and may be passed in feces.
- > **Habitat:** Large intestine (caecum).



☪ Life Cycle:

1. Infection occurs via self-inoculation (transferring eggs to the mouth with hands that have scratched the perianal area) or through exposure to eggs in the environment (e.g. contaminated surfaces, clothes, etc.)
2. Following ingestion of infective eggs, the larvae hatch in the small intestine and the adults establish themselves in the colon, usually in the cecum.
3. Gravid (adult females) migrate nocturnally (at night) outside the anus and oviposit (lay eggs) on the skin of the perianal area.



- > Eggs are immediately infectious because they embryonate within hours.
- > No pulmonary route.

☪ Mode of transmission:

- > Fecal-oral or inhalation (autoinfection).
- > Sexual transmission has been reported.
- > Direct transmission occurs from an infected host to another.
- > Infections are associated with institutional crowding and families.
- > **Retro-infection**, or the migration of newly hatched larvae from the anal skin back into the rectum, may occur but the frequency with which this happens is unknown.
- > **Infective stage (IS):** Mature, embryonated eggs.
- > **Diagnostic stage (DS):** Immature eggs on the perianal fold.

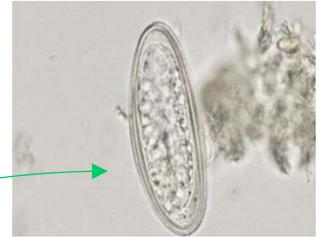
ÿ Clinically:

- › Enterobiasis is frequently asymptomatic. The most typical symptom is **perianal pruritus**, especially at night.
- › The parasite may migrate to other nearby tissues, causing appendicitis, oophoritis, and ulcerative bowel lesions.

ÿ Diagnosis: Typically by microscopic identification of the characteristic flat-sided ovum.

- › The method that is used for diagnosis of pinworm is the cellophane (**Scotch**) tape test.

ÿ Treatment: **Albendazole** 400 mg stat repeated after two weeks.



ÿ Hydatid Cysts (Echinococcus granulosus):

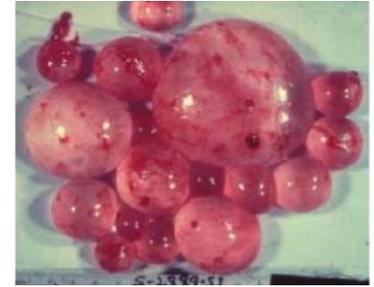
- › Human echinococcosis is caused by the **larval stages** of cestodes (tapeworms, Echinococcus).
- › Echinococcus is the smallest of all tapeworms (3 to 9 mm long).
- › E. granulosus is a tapeworm found in the small intestine of the **definitive host (DH): canines (dogs)**.
- › Eggs are ingested by the **intermediate hosts (IH)**, which include a variety of mammals including sheep, cattle and **humans**.

ÿ Life Cycle:

1. The adult Echinococcus granulosus resides in the small intestine of the definitive host (dogs), which releases eggs that are passed in the feces and are immediately infectious.
2. After ingestion by the intermediate host (humans), eggs hatch in the small intestine and release larvae that penetrate the intestinal wall and migrate through the circulatory system into various organs, especially the liver and lungs.
3. Humans are considered dead-end hosts since the life cycle of the organism is unable to continue in a human host leading to **hydatid cysts**.

✿ Clinically:

- Hydatid disease in humans is potentially dangerous depending on the size and location of the cyst.
- The majority occur in the liver and lungs and are usually asymptomatic.
- Some cysts may remain undetected for many years until they grow large enough to affect other organs.
- The characteristic feature of these cysts is that they can grow up to 7 cm per year.



Ÿ Diagnosis: Incidentally by radiology, serology.

Ÿ Treatment: **Surgery** (the most effective treatment to remove the cyst and can lead to a complete cure), **albendazole**.

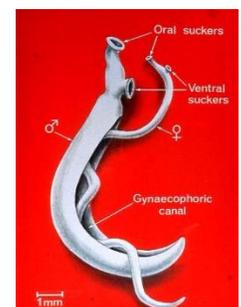
Extreme care must be taken when removing the cyst. If the cyst ruptures, the highly immunogenic hydatid fluid can lead to anaphylactic shock.

Ÿ SCHISTOSOMIASIS:

- Schistosomiasis (Bilharziasis) is caused by some species of blood trematodes (flukes). The three main species infecting humans are:
- ***Schistosoma haematobium*** discovered by Theodor Bilharz in Cairo in 1861 (mainly UTS).
- ***S. japonicum* and *S. mansoni* (mainly GIT).**
- It is estimated that more than 200 million people are infected all over the world and about 500-600 million are exposed to infection.

Ÿ Morphology:

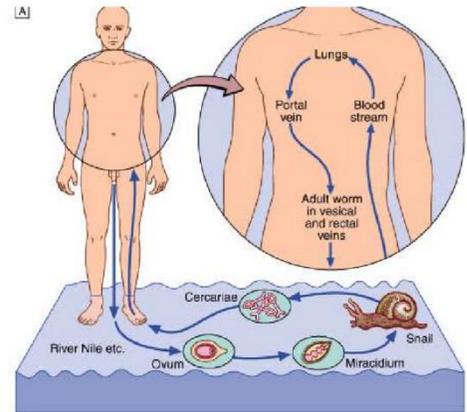
- The adult male & female have an oral sucker surrounding the mouth anteriorly & ventrally. It uses the sucker on the ventral surface to attach itself to the wall of the vessel in which it lives.
- The male worm is flat, leaf-like, and folded to form the gynacophoric canal.



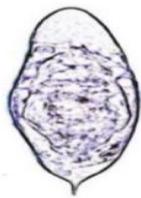
- > The adult female worm resides within the adult male worm's gynacophoric canal.

Ÿ Life Cycle:

1. The ovum is passed in the feces of infected individuals and gains access to fresh water where the ciliated **miracidium** inside it is liberated.
2. It enters its **intermediate host**, a species of freshwater **snail**, in which it multiplies.
3. Large numbers of tailed cercariae are then liberated into the water.
4. Infectious cercariae **penetrate human skin** and migrate through the lung and the liver to reach the **portal venous system**.
 - > Adult worms inhabit the portal venous system.
 - > *S. japonicum* is more frequently found in the superior mesenteric veins draining the small intestine, while *S. mansoni* occurs more often in the inferior mesenteric veins draining the large intestine.
 - > *S. haematobium* most often inhabits veins of the bladder.
 - > The most significant pathology is associated with the schistosome **eggs**, not the adult worms. The females deposit eggs in the small venules of the portal system. Production of eggs causes a **granulomatous reaction and sclerosis** in the portal venous system to eggs deposited in tissues. This may lead to portal hypertension, esophageal varices, HSM and liver failure.



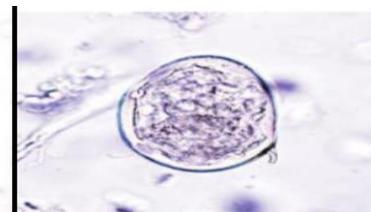
Ÿ **Diagnosis:** Detection of eggs in stool (for *S. mansoni* and *S. japonicum*) or urine (*S. haematobium*).



haematobium
Terminal spine



Mansoni
Lateral spine



Japonicum
curved rudimentary spine

- › Doctor Nader said that each species of eggs has a characteristic spine but he did not go through the details of each spine. They are added for the sake of clarity.

† Treatment: Praziquantel.

Quiz

1. A group of 6 college students undertake to climb Mt. Rainier outside Seattle on their spring break. They pack food and camping provisions except for water, which they obtain from the many fresh water mountain streams that arise at the summit. The adventure takes a little over a week to accomplish, and all return safely in good spirits to their classes the following week. Within the first week after their return, 5 of the 6 students report to the infirmary with profuse diarrhea and tenesmus. Each affected student experiences weakness and weight loss, and stool samples submitted to the lab are yellow, greasy, and foul smelling. What attribute of this parasite imparts its pathogenicity?
 - A) Lytic enzymes.
 - B) Flagella.
 - C) Ventral sucking disk.
 - D) Encystment.
 - E) Toxic metabolites.
2. After one-week vacationing in Mexico, a 14-year-old girl presents with abdominal pain, nausea, bloody diarrhea, and fever. Stool specimens are collected and sent to the laboratory for bacteriologic and parasitologic examination. Bacterial cultures are negative for intestinal pathogens. The laboratory report reveals organisms with red blood cells inside them. The most likely causal agent is:
 - A) *Cryptosporidium parvum*.
 - B) *Entamoeba histolytica*.
 - C) *Giardia lamblia*.
 - D) *Toxoplasma gondii*.
 - E) *Shigella dysenteriae*.

3. A three-year-old girl presents to her pediatrician with intense perianal itching. Her mother explains that the child has also been extremely irritable during the day and has not been sleeping well at night. Eggs with a flattened side were identified by the laboratory technician from a piece of scotch tape brought in by the parent. Infection with which of the following organisms is most likely?
- A) *Ascaris Lumbricoides*.
 - B) *Echinococcus granulosus*.
 - C) *Entamoeba histolytica*.
 - D) *Enterobius vermicularis*.
 - E) *Trichuris trichiura*.

⊗ Answers:

- 1. (C)
- 2. (B)
- 3. (D)

Good luck ♥