Protozoal Infections of the GIT

Parasitic kingdom include three phyla, protozoa, metazoa (helminths) and arthropods

- Protozoa is a phylum consisting of unicellular parasites that are divided into 4 classes according to their locomotion and the presence sexual reproduction in their life cycle.
- Protozoa classes are:

1. Rhizopoda, move by pseudopodia (crawling motion زحف); replicate asexually by binary division
2. Flagellates, move by flagella; replicate asexually.
3. Ciliates, move by cilia; replicate asexually.
4. Sporozoa, move by gliding as they don't possess an organ of locomotion, they are the only class that replicate sexually (they can also reproduce asexually), and they are obligate intracellular pathogens

❖Entamoeba histolytica

✓ The causative agent of amoebiasis. ✓ It belongs to Rhizopoda class; they multiply asexually by binary division.

❖Giardia Lamblia

✓ The causative agent of giardiasis. ✓ It belongs to flagellates class; they multiply asexually by binary division.

❖Cryptosporidium

✓ The causative agent of cryptosporidiosis. ✓ It belongs to Sporozoa class and coccidia subclass, they multiply sexually.

All the diseases that are caused by these protozoa share the fecal-oral route of disease transmission by ingestion of the infective stage

1.Entamoeba histolytica

Third most important parasitic infection in the humen according to mortality

✓ Common protozoal diseases show more prevalence in developing countries, as lower standards of sanitation and hygiene there contribute to more spread of infections.

✓

❖Disease: Amoebiasis or amoebic dysentery (الزحار الامي بي) .

Dysentery: characterized by bloody diarrhea containing mucus, with the presence of WBC & RBC in the stool

✓ Compared with bacterial infections, protozoal infections are insidious and progress slowly, while bacterial infections are rapid and acute. Protozoa are not known for their toxic-related pathogenesis unlike the toxicity associated with bacterial endotoxins.

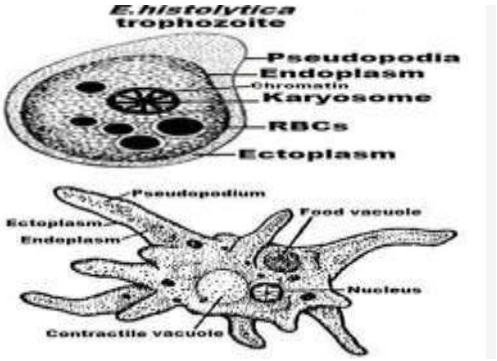
❖Habitat: Large intestine (caecum, colonic flexures and sigmoidorectal region). They prefer to stay at these sites that show low peristaltic movements and fecal stasis, ulcers caused by amoeba are commonly found there

❖Definitive host (DH): Man

❖Reservoir host (RH): Man, Dogs, pigs, rats and monkeys.

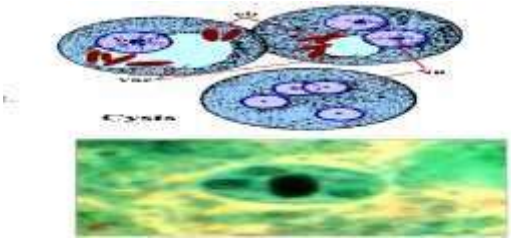
✓ Man is also the main reservoir host, as 90% of infected people are asymptomatic carriers (also called cyst passers). These patients don't develop symptoms, as Entamoeba histolytica colonize their large intestine lumen without invading the mucosa and the submucosa, carriers with poor personal hygiene working as a food handlers could cause outbreaks of amoebiasis

Morphological characters :



1.Trophozoite stage (vegetative form or tissue form):

- ✓ It is the active, motile, and feeding form.
- ✓ Entamoeba histolytica has an ectoplasm and a granular endoplasm. They both contribute to the formation of pseudopods for crawling. The endoplasm contains a central nucleus that has a central nucleolus (or karyosome) surrounded by a ring of fine chromatin; this nucleus morphology is called cartwheel appearance.
- ✓ The endoplasm also shows glycogen granules and engulfed RBCs; the presence of RBCs inside the endoplasm is a pathognomonic sign of Entamoeba histolytica trophozoites, as this distinguishes them from other commensal species that are part of the microbiome of the gut such as Entamoeba coli, Entamoeba dispar and Entamoeba moshkovskii, which lack the ability to phagocytose RBCs.
- ✓ They are normally found rounded as in the first picture; the second picture draws pseudopodia as an illustration of their motility .



2. Cyst stage (Luminal form):

✓ The Cyst stage represents the quiescent phase of the protozoal life cycle. During this stage, protozoa encyst themselves to survive the harsh conditions environmentally and acidic state in the stomach.

✓ These cysts may be either:

A) Immature cyst:

✓ Immature cysts are either uninucleate or binucleated, whereas mature cysts are quadrinucleated, containing four nuclei per cyst.

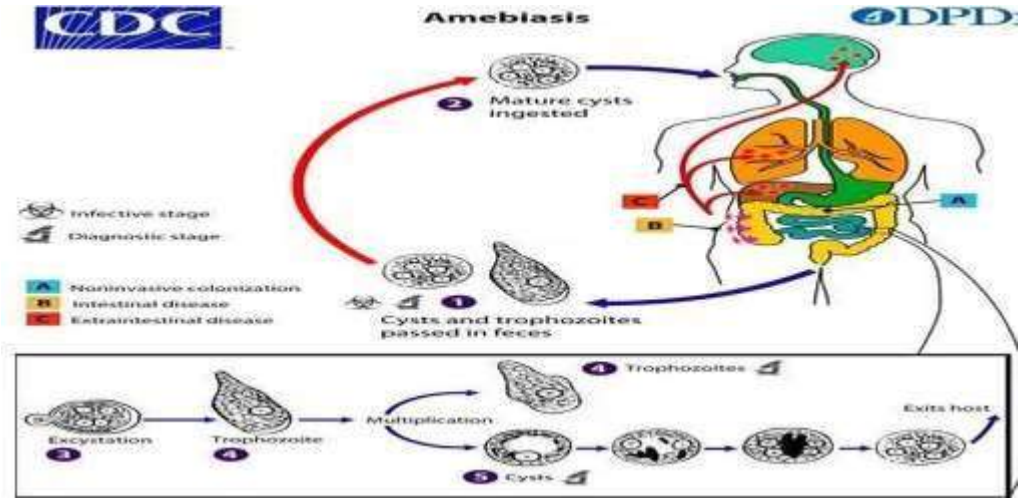
✓ Exposure to immature cysts does not result in infection, as they lack the ability to establish a new infection in the host.

B) Mature cyst (quadrinucleate cyst).

✓ The mature cyst is the only form that can continue the cycle of infection. This quadrinucleate cyst must undergo two successive mitotic divisions to produce eight trophozoites.

✓ The nucleus shows a cigar-shaped morphology; it has a central karyosome with chromatoid bars (or chromatoid bodies).

Life cycle of Entamoeba histolytica :



✓ The INFECTIVE stage of Entamoeba histolytica is the mature quadrinucleate cyst . After ingesting these cysts by contaminated food or water, they travel through the GI tract surviving the acidity of the stomach until they reach the small intestine, where each cyst excysts in the small intestine, releasing eight trophozoites.

✓ After excystation, the trophozoites may remain confined to the lumen of the large intestine and re-encyst, a condition known of asymptomatic carriers or cyst passers (this is the case in 90% of infected people).

✓ Trophozoites may invade the mucosa and submucosa of the intestinal tract, causing acute (fever ,abdominal pain and mesentry) or chronic(if not treated or prolong symptom) amoebic dysentery. In severe cases, complete penetration of all the layers of the large intestine and the erosion of blood vessels there will lead to perforation and haemorrhage, this can progress to extraintestinal amoebiasis by direct or hematogenous spread, typically starting with the right lobe of the liver, as it is close to the right colonic flexure (direct rout), and potentially spreading to the lungs, brain, or the skin area above the large intestine.

✓ The DIAGNOSTIC stage could be the mature or the immature cyst as well as the trophozoites (as patients with acute amoebic dysentery have frequent bowel movements; these trophozoites didn't have the time to encyst themselves). Modes of infection:

1. Contaminated water and food (e.g. green vegetables) or hands with human stool containing mature cysts.
2. Handling food by infected food handlers as cookers and waiters.
3. Flies and cockroaches that carry the cysts from feces to exposed food.
4. Autoinfection (faeco-oral or hand to mouth infection).

✓ Occurs when a person contaminates their own hands or surroundings with feces containing infective cysts and then ingests them through hand-to-mouth contact. In this case, it is external autoinfection, which is different from internal autoinfection that will be discussed with cryptosporidium infections.

5. Homosexual transmission.

✓ Can also occur during anal-oral sexual practices, especially in men who have sex with men (MSM)

CLINICAL PICTURES OF INTESTINAL AMOEBIASIS

1-Asymptomatic infection Most common, trophozoites remain in the intestinal lumen feeding on nutrients as a commensal without tissue invasion (Asymptomatic patient As a known healthy carrier and cyst passers).

2-Symptomatic infection

a) Acute amoebic dysentery Presented with fever, abdominal pain, tenderness, tenesmus and frequent motions of loose stool containing mucus, blood, cysts and trophozoites.

b) Chronic infection Occurs if acute dysentery is not properly treated. With low grade fever, recurrent episodes of diarrhea that alternates with constipation. Only cysts are found in stool.

3 - Complications

- Hemorrhage due to erosion of large blood vessels.
- Intestinal perforation ➪ peritonitis.
- Appendicitis.

✓ If located near the ileocecal junction.

- Amoeboma (Amoebic granuloma) around the ulcer ➪ stricture of affected area.

✓ It should be distinguished from intestinal tumors.

- ✦ The trophozoites of E.histolytica invade the mucosa and submucosa of the large intestine by secreting lytic enzymes
- ✦ amoebic ulcers. The ulcer is inverted flask-shaped with deeply undermined edges containing cytolyzed cells, mucus and trophozoites.
- ✦ The most common sites of amoebic ulcers are caecum, colonic flexures and sigmoidorectal regions due to decrease peristalsis &slow colonic flow at these sites that help invasion.

EXTRA-INTESTINAL AMOEBIASIS

Due to invasion of the blood vessels by the trophozoites in the intestinal ulcer and reach the blood to spread to different organs as: A-Liver

- ✓ Most common site
- ✓ Amoebic liver abscess amoebic hepatitis.
- ✓ The contents of the abscess is described as "anchovy paste" colored golden-brown
- ✓ Affect commonly right lobe either due to spread via *portal vein or *extension from perforating ulcer in right colonic flexure or *hematogenously.
- ✓ Clinical picture: Fever ,Hepatomegaly ,Right hypochondriac pain ,Jaundice

B-Lungs or diffuse

- ✓ Lung abscess ➔ pneumonitis

✓ Chest pain

✓ Cough

✓ Fever

✓ Amoebic lung abscess usually occur in the lower part of the right lung due to *direct spread from the liver lesions through the diaphragm or very rarely trophozoites may reach the lung via *blood.

C-Brain

✓ Brain abscess ➔ meningoencephalitis (fatal).

D-Skin

✓ Cutaneous amoebiasis (Amoebiasis cutis)

E-Urogenital Amebiasis

LABORATORY DIAGNOSIS

I) Intestinal Amoebiasis

A) Direct

Macroscopic:

✓ Offensive loose stool mixed with mucus and blood. Microscopic:

✓ Stool examination: Reveals either trophozoites (in loose stool) or cysts (in formed stool) by direct smear, iodine stained & culture.

✓ RBCs and WBCs can also be seen by microscopy.

✓ Sigmoidoscopy: To see the ulcer or the trophozoites in aspirate or biopsy of the ulcer.

✓ X-ray after barium enema: to see the ulcer, deformities or stricture.

B) Indirect

Serological tests:

- ✦ CFT (Complement Fixation Test)
- ✦ IHAT (Indirect Hemagglutination Test)
- ✦ IFAT (Indirect Fluorescent Antibody Test)

- ✦ ELISA (Enzyme-Linked Immunosorbent Assay), Such as ELISA for PLDH2 (parasite lactate dehydrogenase 2), which is only present in E.histolytica (differentiates it from other commensal species).
- ✦ GDPT (gel-diffusion precipitin test)

N.B. These serological tests are positive only in invasive intestinal amoebiasis (dysentery) but negative in asymptomatic carriers (most common).

II) Extra-Intestinal Amoebiasis:

Depends on the organ involved

A) Direct

- ✓ X-ray:

  In liver → space occupying lesion.

  In lung → pleuritis with elevation of the diaphragm.
- ✓ Ultrasonography, CT scan & MRI: For liver abscess.
- ✓ Aspiration of abscess content: For liver abscess to detect trophozoites. Hepatomegaly can also be detected.

B) Indirect

- ✓ Serological tests: As intestinal amoebiasis. They are positive and can persist for years.
- ✓ Molecular by PCR.
- ✓ Blood examination: Leucocytosis.
- ✓ Liver function tests: Increased in amoebic liver abscess

Treatment:

A) Asymptomatic intestinal carrier ➡

Luminal amoebicides

Paromomycin ,Diloxanide furoate , Iodoquinol

Cyst passer :found cyst in their stool

we give them drug to avoid incedience

Flagyl cannot be used for this group because it doesn't reach cysticidal levels in the lumen. In other words, it cannot kill the cysts in the lumen of the gut of those cyst-passers.

B) Intestinal Amoebiasis ➡ Tissue amoebicides

Metronidazole (Flagyl) or tinidazole is the drug of choice

C) Extra-Intestinal Amoebiasis ⇒ Tissue & Luminal amoebicides

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.

✓ E. histolytica cysts can be viable in the environment for at least 3 weeks.

✓ Amoebic cysts are not killed with low doses of chlorine or iodine, and if the concentration is increased to a cysticidal level, it will not be safe for human use.

✓ Bringing water to a boil ensures the absence of amoeba (also works with Giardia and Cryptosporidia); filtration also can be used

Giardia duodenalis & Giardia lamblia :

Pathogenesis is in the small intestine (duodenum and jejunum), unlike E. histolytica (large intestine).

✓ Common cause of intestinal infection worldwide.

✓Cause the giardiasis in Canada is also known as beaver fever (misleading name).

✓ Flagellated and reproduce by binary fission.

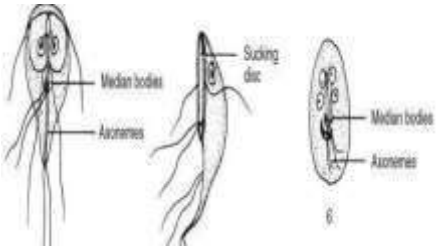
✓ Both the trophozoite and the cyst are included in the life cycle.

✓ Found most commonly in the crypts in the duodenum.

✓ It doesn't invade (no bloody diarrhea), but instead it can cause steatorrhea, yet most cases are either asymptomatic or mild.

✓ Part of the differential diagnoses of both infantile (EPEC) and traveler's (ETEC) diarrheae.

Important features of the trophozoite:



✓ Pair of nuclei.

✓ Ventral (sucking) discs اللي هم زي النضارات → used for attachment.

✓ Axoneme (axostyle) → causes the falling leaf pathognomonic motility under microscopy.

✓ Heart-shaped.

✓ 4 pairs of flagellae.

✓ Under the microscope, the trophozoite's paired nuclei resemble eyes, contributing to its 'face-like' appearance.

The quadrinucleated cyst is the infective stage just like E. histolytica.

Epidemiology:

✓ Transmission of G. lamblia occurs by ingestion of viable cysts by fecal oral route same as entamoeba histolytica but here more clustering of cases (family member, mental institutions and dycare center(

✓ It is more associated with contaminated water sources.

✓ High incidence of giardiasis occurs in patients with immune deficiency syndromes, as well as cannabis smokers or people suffering from malnutrition or over crowdedness.

✓ The incubation period ranges from approximately 1-2 weeks and

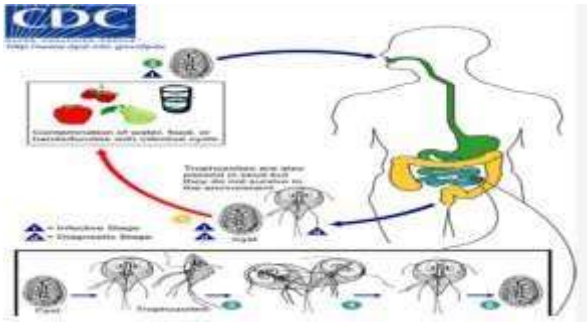
infectious dose is 10 Clinically Pathogenesis :

is by attachment to duodenum or jejunum by their ventral discs, causing mild irritation so it cause diarrhea and because of attachment causing mal absorption of fat and proteins and some vitamins, such as vit A, vit B12 & folic acid (steatorrhea).

➢Asymptomatic Infection (treatment not recommended)

➢Symptomatic:

- Diarrhea usually watery: profuse watery diarrhea that later becomes greasy foul smelling and may float (steatorrhea).
- Abdominal cramps, bloating, malaise, weight loss,Mal absorption.
- Vomiting and tenesmus are not common.

Life Cycle: 

✓ Ingestion of quadrinucleate cyst (infective Stage).

✓ Excystation is in the small intestine, forming 2 trophozoites per cyst.

✓ It encysts when it reaches the large intestine.

✓ The diagnostic stage can be both cysts and trophozoites depending on the severity of the diarrhea, just like amoebic dysentery

Lab Diagnosis:

- Routine Methods:- Stool analysis: cysts and sometimes trophozoites.
- Antigen Detection:

✓ Immuno chromatographic enzyme immunoassay for GSP65 – giardia specific protein 65 (kilo-Dalton).

✓ The string test (enterotest) can be used. The patient swallows a gelatinous capsule connected to a string that is attached in their mouth, and after the capsule dissolves after 4-5 hours, the string is retracted, and trophozoites can be detected if present.

✓ Serology can be used to screening and epidemiology.

Treatment: Metronidazole or tinidazole.

Cryptosporidium spp

Cause cryptosporidiosis disease

- 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 (crypts) of the small intestine and develop into merozoites then oocyst.

In addition to the transmission discussed in amoebiasis and giardiasis, cryptosporidiosis in known to contaminate recreational water sources.

In the small intestines, oocysts, inside which there are sporocyst, which in turn enclose sporoblasts, finally form merozoites (type I and type II meronts).

Internal autoinfection is a well-known feature of Cryptosporidia. It occurs when sexual reproduction, initiated by type II meronts, leads to the formation of zygotes that develop into oocysts finally into thin-walled oocysts, which remain inside the host and allow the parasite to complete its life cycle without leaving the body. On the other hand, type I meronts asexually reproduction, form thick-walled oocysts which is the infective stage that can withstand environmental conditions.

Clinically:

➢Abdominal pain and vomiting

✓ Cryptosporidiosis is typically asymptomatic or with mild transient diarrhea in immunocompetent individuals, however in immunocompromised individuals (specifically AIDS & cancer) , it can cause severe debilitating intractable diarrhea.

Diagnosis:

Oocyst in stool using modified acid-fast stain (also called Kinyoun technique). It is used for nocardia and the coccidia subfamily: cryptosporidium, cyclospora & isospora.

- The gold standard in the US is the direct fluorescence antibody test from a stool sample.

Treatment:

➢ Usually, self limited with Oral or intravenous rehydration.

➢ Nitazoxanide is used for immunocompetent individuals.

✓ Nitazoxanide and other antiparasitic agents can be tried for immunocompromised patients, but the efficacy is not well proven , HAART is vital for HIV patients.