

AMOEBIĆ DYSENTERY

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PHARMACOLOGY-II

AMOEBIĆ DYSENTRY

Introduction:

Amoebiasis, also known as amoebic dysentery, is an infection with the intestinal protozoa *Entamoeba histolytica*. It may also cause systemic manifestation.

- About 90% of infections are asymptomatic
- Remaining 10% produce a spectrum of clinical syndromes
- Ranging from asymptomatic to dysentery to abscesses of liver or other organs.
- Protozoal infection initially involves colon, liver, lungs.

Background:

- Amoebiasis is the third leading parasitic cause of death worldwide.
- worldwide in distribution
- India, China, Africa, South America
- 2-60% prevalence
- 100,000 deaths/yr
- 500 million infections
- 50 million cases

Causative agent

❑ *Entamoeba histolytica*

The genus *Entamoeba* contains many species, some of which (ie, *E. histolytica*, *Entamoeba dispar*, *Entamoeba moshkovskii*, *Entamoeba bangladeshi*, *Entamoeba polecki*, *Entamoeba coli*, and *Entamoeba hartmanni*) can reside in the human interstitial lumen. Of these, *E. histolytica* is the only one definitely associated with disease,

- Prevalent in unsanitary areas
- Common in warm climate
- Acquired by swallowing

Cysts survive a few days outside the body.

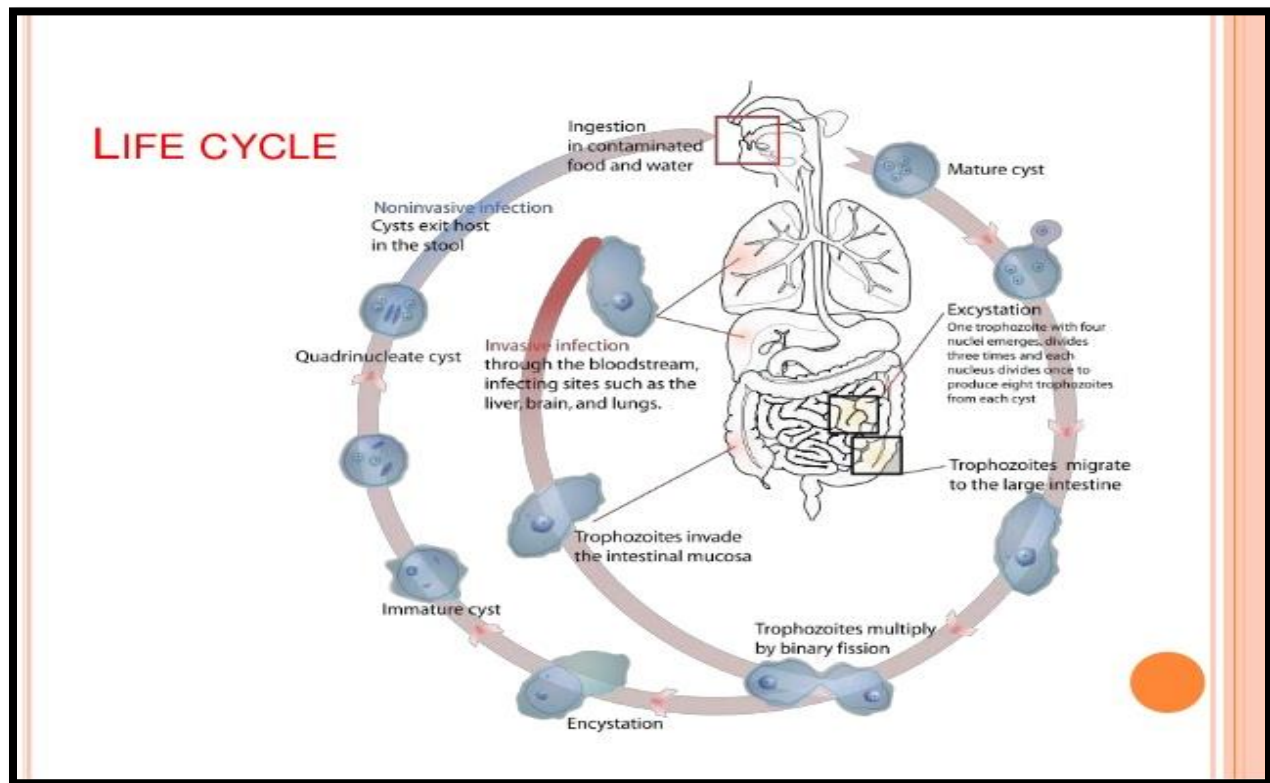
Life Cycle

■ Infection by *Entamoeba histolytica*:

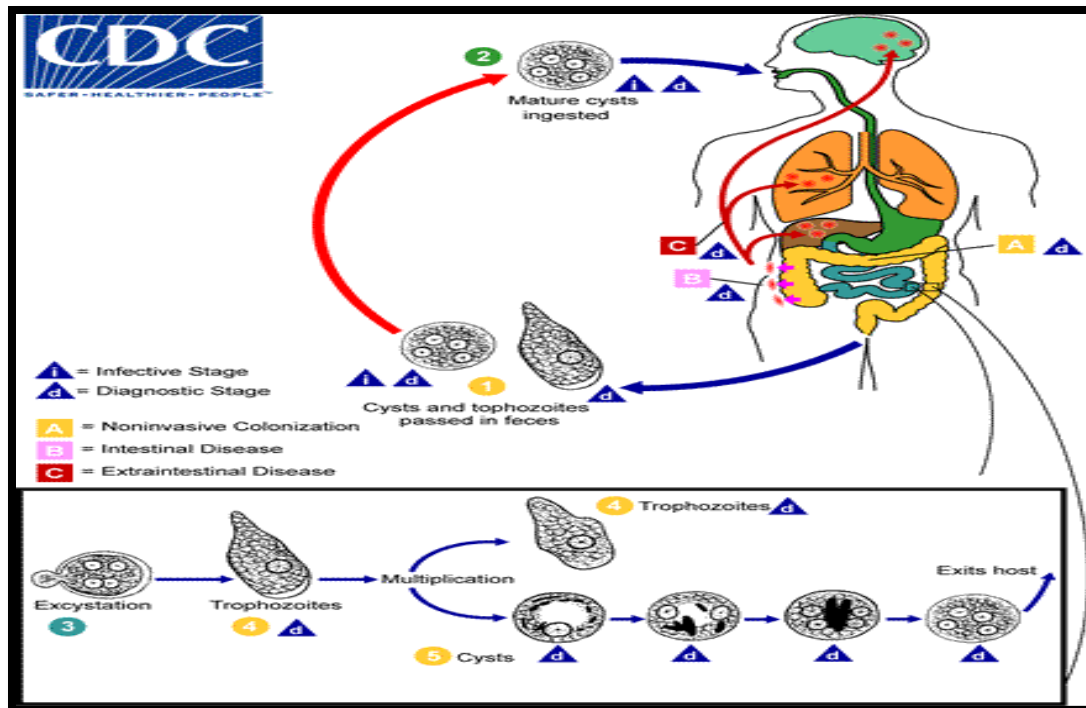
1. Occurs by ingestion of mature cysts in fecally contaminated food, water, or hands.
2. Excystation occurs in the small intestine and
3. Trophozoites are released, which migrate to the large intestine.
4. Trophozoites multiply by binary fission and produce cysts, which are passed in the feces. Because of the protection conferred by their walls, the cysts can survive days to weeks in the external environment and are responsible for transmission. (Trophozoites can also be passed in diarrheal stools, but are rapidly destroyed once outside the body, and if ingested would not survive exposure to the gastric environment.)

- In many cases, the trophozoites remain confined to the intestinal lumen (**A: non-invasive infection**) of individuals who are asymptomatic carriers, passing cysts in their stool.
- In some patients the trophozoites invade the intestinal mucosa (**B: intestinal disease**), or,
- Pass through the bloodstream, extraintestinal sites such as the liver, brain, and lungs (**C: extra-intestinal disease**), with resultant pathologic manifestations.

The invasive and noninvasive forms represent two separate species, respectively *E. histolytica* and *E. dispar*, however not all persons infected with *E. histolytica* will have invasive disease. These two species are morphologically indistinguishable.



- The parasite has 2 forms:
 - a motile form, called the trophozoite, and
 - a cyst form
- The trophozoite of *E. histolytica* inhabits the large intestine to produce lesions of amebic colitis.
 - Invasion of the colonic mucosa leads to dissemination of the organism to extracolonic sites, predominantly the liver.
- Cysts passed in the feces can survive in moist environmental conditions for weeks to months. Upon ingestion of fecally contaminated food or water, the cysts travel to the small intestine, where the trophozoites are released.
- In 90% of patients, the trophozoites re-encyst and produce asymptomatic infection, which usually spontaneously resolves within 12 months.
- In the remaining 10% of patients who are infected, the parasite causes symptomatic amebiasis.
 - Under unfavorable conditions, the trophozoite reverts to the cyst form, and the life cycle is repeated.
- *Entamoeba dispar* is a nonpathogenic protozoon morphologically identical to *E. histolytica*.
- These 2 species of *Entamoeba* can be distinguished by the monoclonal antibodies.
 - Specific and sensitive means to detect *E. histolytica* in stool are now available and include antigen detection and polymerase chain reaction (PCR).



Infections due to *E histolytica*:

Intestinal disease

- Asymptomatic infection
- Symptomatic noninvasive infection
- Acute proctocolitis (inflammation of the rectum and colon)
- Fulminant colitis (coming on suddenly with great severity) with perforation
- Toxic megacolon (dilated colon)
- Chronic nondysenteric colitis
- Ameboma (an inflamed, tumor like, spreading nodule)
- Perianal ulceration.

Extraintestinal disease

- Liver abscess
- Pleuropulmonary disease
- Peritonitis – Pericarditis
- Brain abscess
- Genitourinary disease

Transmission

- 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.
- Infection is spread through ingestion of the cyst form of the parasite, a semi-dormant and hardy structure found in feces. Any non-encysted amoebae, or *trophozoites*, die quickly after leaving the body but may also be present in stool: these are rarely the source of new infections. Since amoebiasis is transmitted through contaminated food and water.

Pathophysiology

- Amoebiasis results from tissue destruction induced by the *E. histolytica* parasite. *E. histolytica* causes tissue damage by three main events:
 - direct host cell killing,
 - inflammation, and
 - parasite invasion.

Pathogenesis:

- *E. histolytica* possess a potent repertoire of -adhesins, proeinases and pore forming proteins and other molecules that enable them to lyse cells and tissue.
- These mol. Induce cellular necrosis and apoptosis
- Resist both innate and adaptive immunity
- *E. histolytica* trophozoites adhere to the colonic mucosal epithelial cells leads to disruption
- Adherence is mediated by a family of surface lectin molecules capable of binding to galactose and Nacetylgalactosamine residues.
- *E. histolytica* can lyse host cells upon contact through a family of amphipathic peptides called amoebopores
- *E. histolytica* posses a large family of cysteine proteinases that are capable of lysing the extracellular matrix between the cells and cleaving host defense molecules (complement and antibodies)
- An extracellular cysteine kinase causes proteolytic destruction of the tissue, producing flask-shaped ulcers
- The ultimate effect of all these amebic virulence factors on the human colon is the production of small ulcers that have heaped borders and contains focal areas of epithelial cell loss.
- The intervening mucosa is normal
- *E. histolytica* trophozoites can then invade laterally through the submucosal layer, creating the classic flask shaped ulcers that appear on pathologic examination as narrow-necked lesions broaden the submucosal region
- *E. histolytica* trophozoites found at the margin between dead and the live tissues

Why immunity do not able to respond?

- Cell-mediated immunity is important in limiting the disease and preventing recurrences.
- Production of lymphocytes, including interferon- γ (IFN- γ), which activates the killing of *E. histolytica* trophozoites by the macrophages. This killing depends on contact, oxidative pathways, nonoxidative pathways, and nitric oxide (NO).
- Lymphokines, such as tumor necrosis factor- α (TNF- α), are capable of activating the amebicidal activity of neutrophils.
- During acute invasive amebiasis, T-lymphocyte response to *E. histolytica* antigens is depressed by a parasite-induced serum factor.
- Serum antibodies in patients with amebic liver abscess develop in 7 days and persist for as long as 10 years.
- *E. dispar* infections do not elicit antibody response
- Mucosal immunoglobulin A (IgA) response to *E. histolytica* occurs during invasive amebiasis.

- However, no evidence suggests that invasive amebiasis is increased in incidence or severity in patients with IgA deficiency.

Diagnosis

- Demonstration of E.histolytica or cyst in the stool or colonic mucosa of pts with diarrhea.
- Microscopy & culture test
- Antigen detection based ELISAs that can specifically identify E.histolytica in the stool probably represent the best choice in the endemic areast
- PCR assay for DNA in the stool samples is currently the most sensitive and specific method for identification but used as research and epidemiological tool.
- Diagnosis of amebic liver abscess is based on the detection of one or more space occupying lesions in the liver by Ultrasound and CT scan and a positive serology
- Amebic liver abscess are classically described as single, large and located in right lobe of liver
- When a pt. with space ahs a occupying lesion in the liver, a positive serology is highly sensitive(>94%) and highly specific(>95%) for the diagnosis of the liver abscess

➤ Laboratory studies:

Samples (Light microscopy:

I. Stool (3 consecutive samples)

II. Biopsy material from the ulcers (colonoscopy or sigmoidoscopy)

III. Aspirate from liver abscess

IV. Serum

V. Pleural fluid

VI. Pericardial fluid VII.Sputum

➤ Serology

Antibody detection

• ELISA

• IHA

• IFA

Copro-antigen detection by ELISA is another recent and very useful method.

➤ Antigen detection

- Coagglutination

- ELISA

➤ For amoebic liver abscess and other metastatic lesions.

I.Radiological examination

II. Radio isotope tracing of liver

III. Ultrasonography of upper abdomen

IV. CT and MRI abdomen

Complications and manifestation

➤ Two types- Intestinal and Extra Intestinal

- Most patients harboring Entamoeba species are asymptomatic, but individuals with E.histolytica can develop disease.
- Severe dysentery with 10-12 small volume, blood and mucus containing stools may develop

- **Amoebic colitis:** generally appear 2-6 weeks after ingestion of the cyst of parasite
- Abdominal cramp to severe pain • Fever, vomiting, anorexia • Mucus in stool, dysentery
- Flask shaped ulcer in intestine.



- **Fulminant colitis:**
 - <0.5%
 - Severely ill with high fever
 - Intestinal bleeding, perforation
 - Paralytic illness
 - CFR-40%



- **Amoeboma:**
 - Pseudotumoral lesion
 - Necrosis, edema and inflammatory thickening of mucosa and submucosa of intestinal wall
 - 1% of cases
 - Palpable mass with trophozoites • Always coexists with ulceration
 - Single, rarely multiple in different parts of colon, on skin at site of amoebic liver aspiration.



- **Metastatic lesions in liver:**
- Amoebic liver abscess(ALA)- Most common extra-intestinal presentation
- The parasite reaches liver via portal system
- • Occurs within 5 months of dysentery in 95% of cases
- • But concomitant active diarrhea is seen in less than a third of cases
- • Pain and point tenderness over right hypochondrium and fever
- • Jaundice rare, pleural effusion is common
- Rupture is the most dreaded complication of ALA.
- • It may spread to pleura, lungs, peritoneum, pericardium or open outside through the anterior abdominal wall.

