AMOEBA

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Introduction

- Are simple protozoans with no fixed shape & have a cytoplasm bounded by a membrane and differentiated into an outer ectoplasm and inner endoplasm.
- Movement and engulfment of food by phagocytosis occur by pseudopodia formed by thrusting out cytoplasm.
- Reproduction occurs by fission and budding.
- Cyst is formed in unfavorable conditions and is usually the infective form for vertebrate host (e.g. Entamoeba histolytica).

- Amoebae are classified as either free-living or intestinal amoebae.
- The free-living amoebae occasionally act as human pathogens causing meningoencephalitis and other infections, e.g. Naegleria and Acanthamoeba.
- The parasitic amoebae inhabit the alimentary canal.

Classification of Amoebae

Intestinal amoebae

- Entamoeba histolytica
- Entamoeba dispar
- Entamoeba coli
- Entamoeba gingivalis
- Entamoeba polecki
- Endolimax nana

Note: All intestinal amoebae are non pathogenic, except Entamoeba histolytica

Free-living amoebae

- Naegleria fowleri
- Acanthamoeba spp
- Balamuthia mandrillaris

Note: All free-living amoebae are opportunistic pathogens

Entamoeba Histolytica

- The parasite was discovered & demonstrated in dysentery feces of a patient in St. Petersburg in Russia by Lösch in 1875.
- In 1891 the pathogenesis of intestinal & hepatic amoebiasis was established('amoebic dysentery' and 'amoebic liver abscess‘) by Councilman and Lafleur .
- E. histolytica strains can be classified into at least 22 strains of which only 9 are invasive and the rest are noninvasive commensals.
- The pathogenic & nonpathogenic strains though morphologically identical may represent 2 distinct species—the pathogenic strains being E. histolytica & the nonpathogenic strains reclassified as E. dispar.
- Trophozoites of E. dispar contain bacteria, but no RBCs.

Epidemiology

- Prevalent worldwide although much more common in the tropics.
- It has been found wherever sanitation is poor.
- Reported to affect about 10% of world population of which 50% of people in developing countries may be infected with the parasite.
- Majority of infected humans (80–99%) are asymptomatic.
- 50,000 deaths occur annually mostly in the tropical belt of Asia, Africa & Latin America.
- It is the third leading parasitic cause of mortality, after malaria & schistosomiasis.

Immunity

- Infection with invasive strains leads to both humoral & cellular Immune responses.
- Serological response is not seen in infection with non-invasive strains.
- Antibodies can be demonstrated within a week of invasive infection.
- Infection confers some degree of protection as evidenced by the very low frequency of recurrence of invasive colitis and liver abscess in endemic areas.
- Course & severity of amoebiasis does not seem to be affected by human immunodeficiency virus (HIV) infection.

Morphology

- E. histolytica occurs in 3 forms.

1. Trophozoite
2. Precyst
3. Cyst

Trophozoite- is the growing stage of the parasite & the only **FORM** present in tissues.

-It is large, irregular in shape & actively motile in freshly-passed dysenteric stool.

-Tend to be smaller in convalescents & carriers

- Trophozoites in acute dysenteric stools often contain phagocytosed erythrocytes a feature diagnostic of Entamoeba histolytica .
- Phagocytosed red cells are not found in any other commensal intestinal amoebae.
- Infection is not transmitted by trophozoites as they are rapidly destroyed in stomach hence cannot initiate infection even if live trophozoites from freshly-passed stools are ingested.
- Trophozoites can survive only up to 5 hours at 37°C & are killed by drying, heat, & chemical sterilization.

Precystic Stage

- Trophozoites undergo encystment in the intestinal lumen. Encystment does not occur in the tissues nor in feces outside the body
- Before encystment, the trophozoite extrudes its food vacuoles and becomes round or oval. This leads to the precystic stage of the parasite.
- It contains a large glycogen vacuole and two chromatid bars.
- It then secretes a highly retractile cyst wall around it and becomes cyst.

Cystic Stage

- Is highly resistant to gastric juice & unfavorable environmental conditions.
- It begins as an early cyst with a single nucleus, a glycogen mass & 1–4 chromatoid bodies.
- As the cyst matures, the other structures disappear and the nucleus undergoes 2 successive mitotic divisions to form 4 nuclei.
- The mature cyst is thus quadrinucleate.

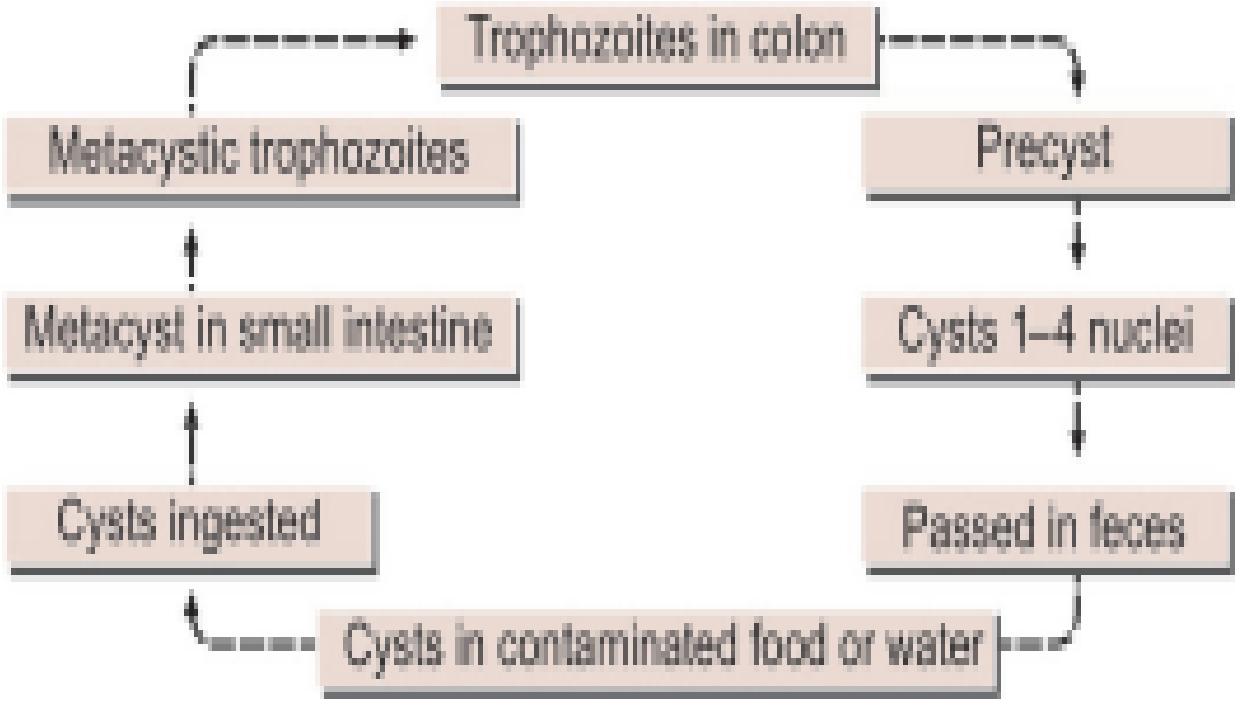
Life Cycle

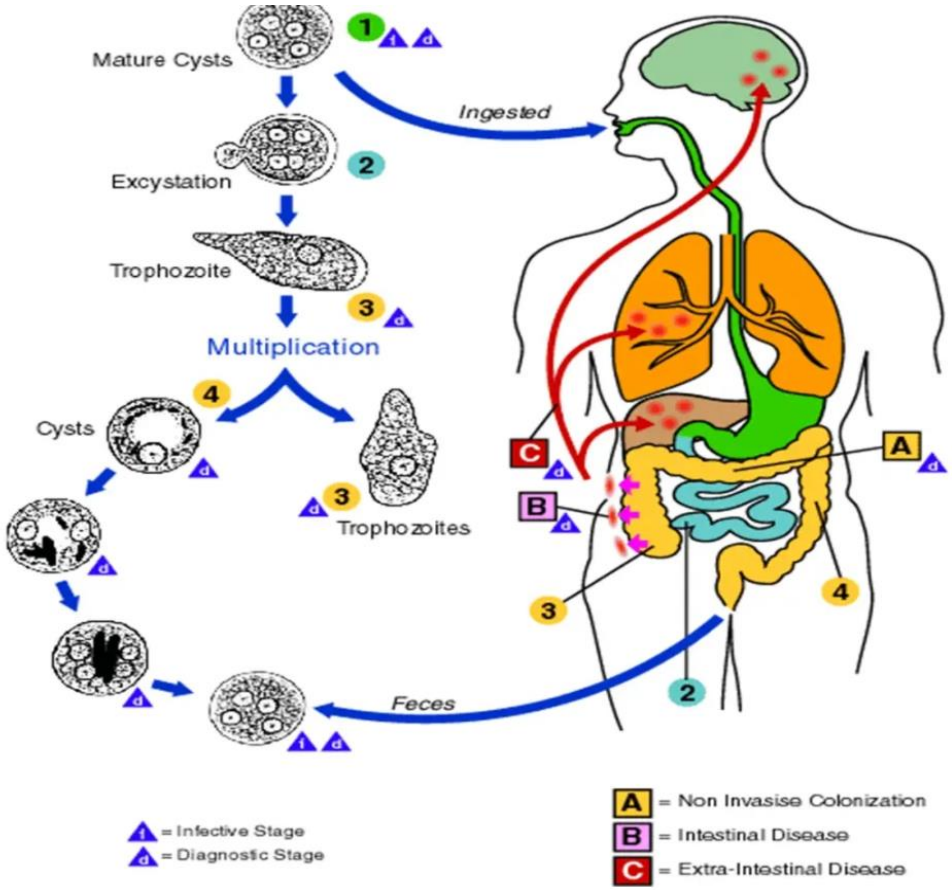
- E. histolytica passes its life cycle in a single host-man
- Mode of transmission is the fecal oral route where man acquires infection by ingestion of food & water contaminated with cysts.
- Infective form is the mature quadrinucleate cyst passed in feces of convalescents and carriers.
- The cysts can remain viable under moist conditions for about 10 days.
- When ingested the cyst passes through the stomach undamaged until the terminal ileum or caecum where excystation occur due to the alkaline environment.

- Excystation leads to release of a quadrinucleate amoeba called the metacyst.
- The metacyst nuclei immediately undergo division to form 8 nuclei each of which gets surrounded by its own cytoplasm to form 8 small amoebulae or metacystic trophozoites.
- The metacystic trophozoites colonise the submucosal tissue of caecum & colon in the glandular crypts and grow by binary fission.
- Some metacystic trophozoites develop into precystic forms & cysts which are passed in feces to repeat the cycle.

- In most of the cases, E. histolytica remains as a commensal in the large intestine without causing any ill effects.
- Such persons become carriers or asymptomatic cyst passers and are responsible for maintenance and spread of infection in the community.
- It may however be activated leading to clinical disease.
- Such latency and reactivation are the characteristics of amoebiasis.

Schematic summary of Life cycle




Mature Cysts
1
Ingested
Excystation
2
Trophozoite
3
Multiplication
4
Cysts
3
Trophozoites
C
A
B
3
4
2
Feces
= Infective Stage
= Diagnostic Stage
A = Non Invasise Colonization
B = Intestinal Disease
C = Extra-Intestinal Disease

Pathogenesis & Clinical Features

- E. histolytica causes two forms of the disease ,intestinal & extra-intestinal amoebiasis.

- Incubation period is highly variable with an average ranges of 4 days to 4 months.

- Amoebiasis can present in different forms & degree of severity, depending on the organ affected & the extent of damage caused.

Intestinal Amoebiasis

- Is characterized by multiple flask shaped ulcers confined to the colon-caecum, sigmoid & rectum.
- The intervening mucous membrane btn the ulcers remains healthy although ulcers may coalesce to form large necrotic lesions covered with brownish slough.
- This happens only in about 10% of cases of infection with the remaining 90% being asymptomatic.
- Ulcers are caused by penetration of the mucosa by trophozoites facilitated by their motility & the tissue lytic enzyme histolysin which damages the mucosal epithelium.
- Other parasite virulence factors include Amoebic lectin, cystine proteinase which inactivates complement factor C3 and ionophore.

- Host factors affecting the course of infection are stress, malnutrition, alcoholism, corticosteroid therapy, bacterial flora & immunodeficiency.

- Glycoproteins in colonic mucus blocks attachment of trophozoites to epithelial cells hence changes in the nature & quality of colonic mucus may influence virulence.

- Tumor-like masses of granulation tissue called **amoeboma** form on the intestinal wall from a chronic ulcer.

- The amoeba penetrates to submucosal layer & multiplies rapidly, causing lytic necrosis thus forming an abscess which then breaks down to form an ulcer.

- Occasionally, the ulcers may involve the muscular & serosa layer of the colon causing perforation & peritonitis.

- Superficial lesions generally heal without scarring, deep ulcers form scars which may lead to strictures, partial obstruction & thickening of the gut wall.

Clinical Features of Intestinal Amoebiasis

- The clinical course is characterized by prolonged latency, relapses intermissions or short breaks btn episodes.
- Typical manifestation of intestinal amoebiasis is amoebic dysentery although quite often, only diarrhea or vague abdominal symptoms may occur.
- Compared to bacillary dysentery, amoebic dysentery is usually gradual in onset with abdominal tenderness which is less & localized.

- The patient is usually afebrile & nontoxic however in fulminant colitis where there is confluent ulceration & necrosis of colon the patient is febrile and toxic.
- Chronic involvement of the caecum causes a condition simulating appendicitis.
- Charcot-Leyden crystals are often present & E.histolytica trophozoites can be seen containing ingested erythrocytes.

Extra intestinal Amoebiasis
Hepatic Amoebiasis

- Involvement of the liver is the most common extra intestinal complication of amoebiasis.

- Usually there is no hx of amoebic dysentery in 50% of cases & about 2–10% of the infected suffer from hepatic complications.
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- Amoebic hepatitis from probable repeated invasion by amoebae from an active colonic infection/toxic substances occur.

- Liver damage is due to the inflammatory response to trophozoites (lysosomal enzymes and cytokines).
- Liver abscesses usually in the upper right lobe may occur in 5–10% of persons with intestinal amoebiasis.
- It consists of central necrotic tissue & normal periphery liver tissue with invading amoeba.
- They may be multiple or solitary with jaundice only occurring in multiple lesions or when pressing on the biliary tract.

Pulmonary Amoebiasis

- Most often follows extension of hepatic abscess through the diaphragm .
- Rarely primary amoebiasis of the lung may occur by direct hematogenous spread from the colon bypassing the liver.
- The lower part of the right lung is usually affected.
- Hepato-bronchial fistula usually results with expectoration of chocolate brown sputum.
- The patient presents with severe pleuritic chest pain, dyspnea & non-productive cough.

Metastatic Amoebiasis

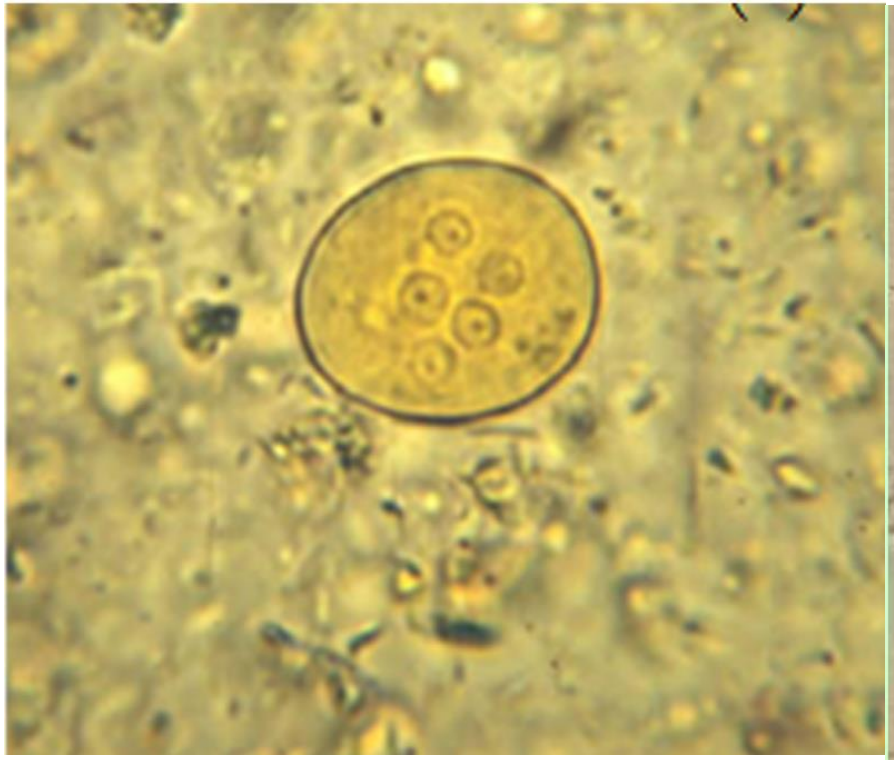
- Involvement of distant organs occur by hematogenous spread & via lymphatics.
- Hence abscesses in the kidney, brain, spleen & adrenals have been noticed.
- Spread to brain leads to severe destruction of brain tissue and is fatal.
- Other areas affected are the skin (Cutaneous Amoebiasis) & Genitourinary Amoebiasis(where the prepuce& glans are affected).
- Penile amoebiasis is acquired through anal intercourse
- The destructive ulcerative lesions resemble carcinoma.

Laboratory Diagnosis

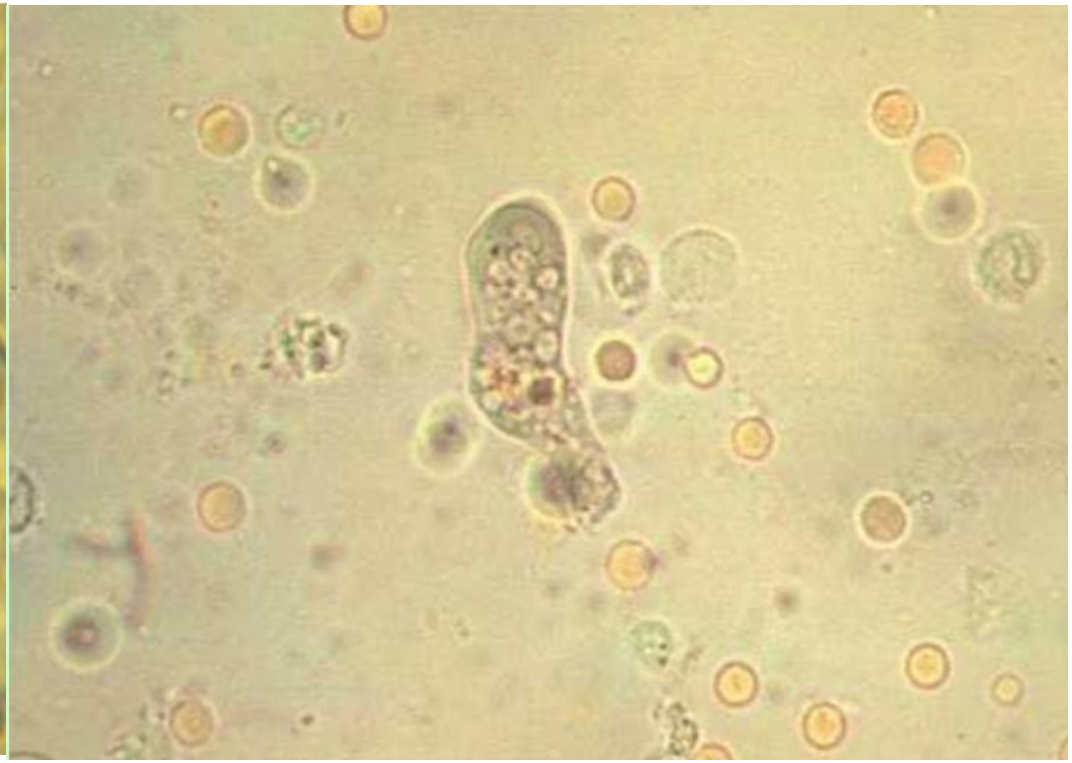
Microscopy

- Definitive diagnosis depends on microscopic demonstration of actively motile trophozoites in freshly-passed stool.
- Presence of ingested RBCs identifies E. histolytica.
- Iodine-stained preparation is needed to demonstrate cysts or dead trophozoites.
- Macroscopic features include brownish black foul-smelling stool intermingled with blood & mucus.

A cyst of Entamoeba histolytica



A trophozoite of Entamoeba histolytica showing ingested red blood cells



Stool Culture

- Stool culture is a sensitive method in diagnosing chronic & asymptomatic intestinal amoebiasis.

Sero-diagnosis

- Serological tests become positive only in invasive amoebiasis.
- Tests done include IHA,Latex agglutination test & ELISA.
- lHA & LA are highly sensitive but often give false-positive results as they remain positive for several years even after successful treatment.

Diagnosis of Extra-intestinal Amoebiasis

- Can be done by microscopic examination of the liver biopsy & also pus aspirate from the abscess may demonstrate trophozoite.
- Radiological examination is useful e.g the diagnosis of amoebic liver abscess is based on the detection (generally by USG or CT) of space occupying lesions in the liver & a positive serologic test for antibodies against E. histolytica antigens.

Treatment

- Three classes of drugs are used in the treatment of amoebiasis.

1. Luminal amoebicides: These include Iodoquinol, paromomycin, & tetracycline which act in the intestinal lumen but not in tissues.

   Note: Metronidazole & tinidazole act on both sites but non of them reach high levels in the gut lumen hence patients with amoebic colitis or amoebic liver abscess should also receive a luminal agent.

2. Tissue amoebicides: Are effective in systemic infections but less effective in the intestine. Examples include emetine, chloroquine, etc.
3. Luminal & tissue amoebicides: Metronidazole and related compounds like tinidazole and ornidazole act on both sites and are the drug of choice for treating amoebic colitis and amoebic liver abscess.

Prevention

- Preventive measures are like those of other fecal-oral infections. These are :

1. Improved sanitation to prevent water/food contamination from human excreta.
2. Health education & improved personal habits helps in control.
3. Detection & treatment of carriers and their exclusion from food handling occupations will help in limiting the spread of infection.