

Section 1 Infectious Diseases

Chapter 1

Amoebiasis

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DEFINITION

Amoebiasis is an infection caused by *Entamoeba histolytica* with or without symptoms (WHO 1969). Synonyms include entamoebiasis, amoebiosis, amoebic dysentery or bloody flux. *Entamoeba dispar* is a harmless commensal, which is indistinguishable from *E. histolytica*. The other members of the group infecting humans are *E. moshkovskii*, *E. hartmannii*, *E. gingivalis*, *Endolimax nana* and *Iodamoeba butschlii*.

HISTORY

The earliest records of bloody mucous diarrhea were found in Bhrigu Samhita (1000 BC). Assyrian and Babylonian texts (600 BC) also made a mention. Subsequently, division between amoebic and bacterial infection was made. The relationship between dysentery and liver involvement was noticed in 200 AD. Around 16th century, amoebiasis became worldwide due to the rapid growth of trade and settlements. Accurate description of invasive and noninvasive forms of amoebiasis was made by James Annersley in 19th century. Fredrich Losch (1875) discovered amoeba in St Petersburg (Russia). Emile Brumpt (1925) suggested existence of two types of parasites, the invasive (*E. histolytica*) and noninvasive (*E. dispar*). WHO (1997) gave clear guidelines for distinguishing both the species.

EPIDEMIOLOGY

Amoebiasis occurs worldwide, but is mostly seen in tropical and developing countries, which have bad sanitary and hygienic practices. Ten percent of world's population is estimated to be infected by the parasite (4% in USA) with an estimated annual mortality of 40,000-70,000. However, 90% of those infected are asymptomatic, 1% may develop invasive/extraintestinal amoebiasis. Spread is mostly through fecal-oral route, by ingestion of cysts and also through contaminated vegetables fertilized by feces and foods and water handled by unclean hands. Fomites and flies also have a role in the transmission. Autoinfection through improper cleaning of hands is also reported. It is uncommon in children below the age of 5 years. HIV infection peculiarly does not aggravate the illness.

TAXONOMY

Unicellular eukaryote-protista of Schaudin is reclassified by Cavalier Smith (1998). *E. histolytica* belongs to the kingdom of protozoa, subkingdom of neozoa, infrakingdom of sarcomastigota, phylum amoebzoa, and subphylum conosa. *E. histolytica* is found to

be having 8,197 genes, a genome of 20.6 MB size containing six isoenzymes, which help in the lysis of tissues, digestion of food material, intraluminal cellular debris and bacteria and in its penetration. Trophozoite is 20-40 μ in size, moves with the help of pseudopodia, formed by the flow of ectoplasm followed by the endoplasm, changing its shape. Hence, the name of Proteus is given simulating the Greek God. It has a single nucleus, food/contractile vacuole, an excretory vacuole called uroid and rudimentary mitochondria. It is also found to move at a surprising speed of 5 mm/sec (Figure 1).

PATHOGENESIS AND PATHOLOGY

Note: Theoretically, ingestion of even one viable cyst can cause infection. Trophozoites are digested and destroyed by the gastric acid, hence, cannot cause infection even though they are ingested (Flow chart 1).

The cyst divides into four initially, which divide again into eight daughter amoebae after an incubation period of 1-4 weeks, which may, however, be from few days to a year. These grow and mature into adult amoebae in about 7-10 days and stay as boarders in the large intestine, mainly the cecum and the sigmoid, feeding on intraluminal cellular debris and the bacteria. The infection is usually asymptomatic. Under unfavorable conditions and as the liquid stool becomes solid during its passage down the colon, the vegetative forms become cysts and are passed in the feces. Most individuals are asymptomatic cyst shredders.

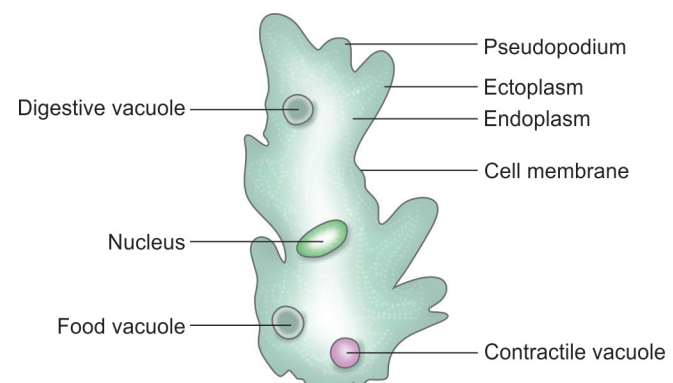
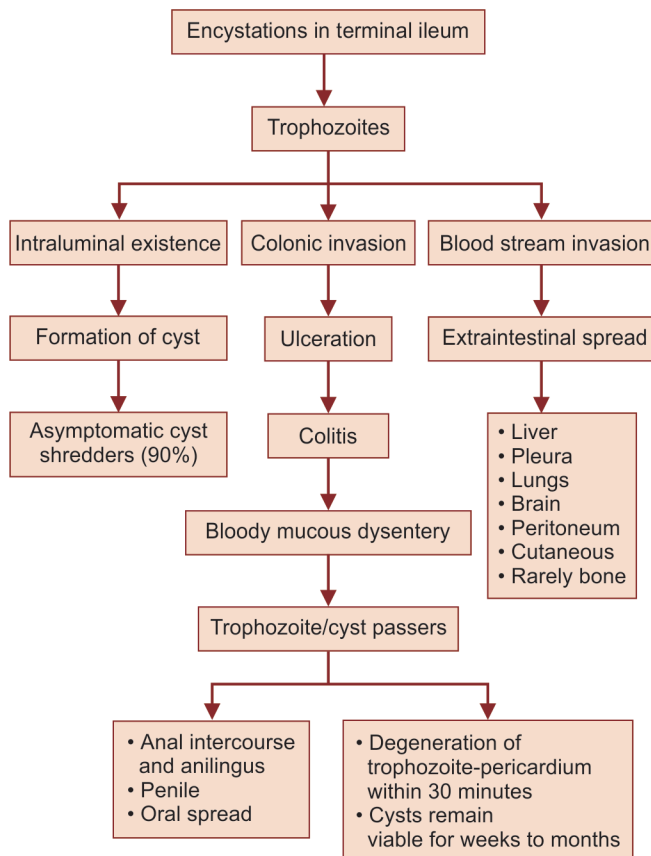


Figure 1: Structure of an amoeba

Flow chart 1: Ingestion of mature cysts (oral)



However, depending on the genetic and immune enzymatic profile and the parasite's ability to produce proteolytic enzymes, enabling resistance to complement-mediated lysis, the trophozoite becomes virulent and starts invading the intestinal mucosa. The trophozoites enhance the mucous secretion, alter its composition and deplete goblet cells of mucin, thereby making epithelial surfaces more vulnerable to invasion. Following depression of the mucous blanket, trophozoites attach to the cells of interglandular epithelium (Gal/GalNAc adherence lectin), and with the aid of proteolytic enzymes that degrade elastin, collagen and fibronectin (especially cysteine proteinase, phospholipase and hemolysin), they invade the colonic epithelium by disruption of the extracellular matrix. Although there is evidence to suggest that *E. histolytica* can induce apoptosis of host cells, cell damage is primarily contact dependent. The first sign of colonic aggression may be manifested as nonspecific thickening of the mucosa or by pin-head size micronodules visible by sigmoidoscopy. Peptide-mediated lysosome enzymes released by the lysed polymorphonuclear leukocytes and monocytes contribute to the destruction of host tissue and extend the lesion. The microulcers coalesce extending the lesion further, undermining other areas of the colonic mucosa. With continued expansion, trophozoites invade the submucosa and spread out laterally, creating the classical flask-shaped amoebic ulcers. Histopathology shows necrotic areas and vascular congestion. There is, however, little inflammation in contrast to the extension of the lesion. The amoebae may be found on the surface of the ulcers. Bacterial infection causes deficiency of blood supply leading to necrosis, hemorrhage, gangrene and subsequent perforation. Vascular invasion results in systemic spread. Once

inside the portal vasculature, amoebae are resistant to complement-mediated lysis. Right lobe of the liver is commonly involved, since blood draining the cecum, through a hypothetical laminar flow in portal vein, preferentially goes there. Left lobe involvement is fraught with the danger of pericardial involvement and sudden tamponade. Occasionally, small multiple abscesses occur mimicking bacterial abscesses.

E. histolytica has the capacity to destroy almost all tissues of the human body, the intestinal mucosa, liver and to lesser extent the brain, skin, cartilage and even bone. The virulence factors, though not known with certainty, include adhesion molecules, proteases, hemolysins, contact-dependent cytolysis, apart from its phagocytic activity.

CLINICAL MANIFESTATIONS

Most often, clinical manifestations are insidious and intermittent, commencing as abdominal discomfort, bloating, irregular bowel habits, intermittent dysentery with or without blood/mucous, tenesmus with bloody mucoid diarrhea, constitutional symptoms, abdominal tenderness, toxic megacolon, and finally symptoms and signs of peritonitis secondary to perforation.

Extraintestinal manifestations are primarily those of hepatic involvement. These include fever, pain in right lower chest, which may be related to respiration, appetite disturbances, breathlessness, cough with or without expectoration and breathlessness, occasionally mild jaundice, rarely convulsions.

COMPLICATIONS

These are secondary to severe toxemia, perforation of the bowel, toxic megacolon, rupture of the hepatic abscess into pleura, lung, peritoneum, pericardium, skin and subcutaneous tissue. Extraintestinal spread metastasizing in the brain and bones is uncommon. Formation of a granuloma in the bowel wall mimicking a malignant growth, the amoeboma, is also not common. Rarely, a large hepatic abscess producing obstructive jaundice can occur. Fever, leukocytosis with elevated polymorphs, rise in hepatic enzymes and serum bilirubin are the accompaniments of the complications.

DIAGNOSIS

High degree of suspicion in endemic areas is a prerequisite. Fresh liquid stool examination showing hematophagous trophozoites with Charcot-Leyden crystals is characteristic. Stool examination, preferably for three consecutive days is advocated. Presence of only cysts in asymptomatic individuals is not diagnostic, since the cysts of *E. dispar*, which is noninvasive and harmless are indistinguishable from those of invasive *E. histolytica*. Sigmoidoscopic scrapings of ulcers showing hematophagous trophozoites are diagnostic. So also is the finding of amoebae from the walls of hepatic abscess.

Ultrasound (USG) scan of the abdomen helps in the delineation of hepatic abscesses. X-ray of the chest helps in the detection of spread to the pleura, lung or pericardium. X-ray of the abdomen is useful for the diagnosis of peritonitis and toxic megacolon. Computed tomography/magnetic resonance imaging help in the diagnosis of intracranial spread of amoebiasis.

Conditions to be kept in the mind are different types of *E. coli* and the *Shigella* enteric infections in acute presentation and tuberculosis in subacute or chronic presentation.

Antibody detection at the end of 1 week of invasive amoebiasis, indirect hemagglutination assay (IHA) and enzyme-linked immunosorbent assay (ELISA) are diagnostic.

Polymerase chain reaction (PCR) in advanced centers is confirmatory.

TREATMENT

Asymptomatic cyst shredders, need/should not be treated—WHO guidelines.

Combination therapy with luminal and tissue amoebicides is highly recommended.

Introduction of nitroimidazole derivatives has revolutionized the treatment of amoebiasis. Usage of cardiotoxic emetine and the relatively less toxic dehydroemetine are now of historical interest. Though metronidazole and other derivatives are highly toxic to the vegetative forms and to a lesser extent the cysts, a course of luminal amoebicides is recommended for complete cure.

Tissue Amoebicides

- *Metronidazole*: 500 mg IV 8th hourly. For 7–10 days for extraintestinal amoebiasis.
400 mg thrice daily orally for 7–10 days (40–60 mg/kg body weight in children)
- *Tinidazole*: 2 g as single dose for 2–3 days.
300 mg twice daily orally for 7 days (50–60 mg/kg body weight in children)
- *Ornidazole*: 1.5 g once daily for 3 days.
500 mg twice daily orally for 7–10 days (40 mg/kg body weight in children)
- *Secnidazole*: 2 g as single dose
- *Nitazoxanide*: 500 mg twice daily for 3 days (age > 12 years), 200 mg twice daily for 3 days (4–11 years) or 100 mg. Twice daily (1–3 years)
- *Chloroquine*: 300 mg twice daily followed by 300 mg daily for 21 days as an adjunct to metronidazole.

Luminal Amoebicides

These are recommended to prevent relapses following the course of tissue amoebicides:

- *Diloxanide furoate*: 500 mg thrice daily for 10 days (20 mg/kg body weight in children)
- *Quinodochlor*: 500 mg twice daily for 10 days
- *Iodochlorhydroxyquin*: 500 mg twice daily for 10 days
- *Paromomycin*: 30 mg/kg body weight thrice daily for 7 days (25 mg/kg body weight in children).

DRAINAGE

Surgical drainage of hepatic abscess is not mandatory, though some authorities advocate to speed up the recovery process and to bring down the systemic manifestations. This is restricted to large abscess with imminent danger of rupture and to those in the left lobe of liver and on the undersurface of liver. Closure of the cavity takes weeks to months. Rupture in to pleura needs to be drained. Rupture in to the pericardial cavity needs emergency drainage in view of the danger of cardiac tamponade.

PREVENTION

- Public education about personal hygiene, especially the sanitary disposal of feces.
- Education of food handlers about proper food and equipment handling and hygiene.
- Advise infected individuals to avoid food preparation.
- Educate about risk of sexual practices that permit fecal-oral contact.
- Test private water supplies for the presence of parasitic contamination.
- Advise infected individuals against using public swimming pools. Contaminated water can be a source of transmission of enteric pathogens.

POINTS TO REMEMBER

- Flies may act as vectors in transferring cyst-laden feces on to eatables.
- Cysts remain viable for several days to months depending on the temperature and moisture of the external atmosphere.
- Cysts may survive up to 45 minutes in the fecal material lodged under the finger nails.
- Cysts are killed only by boiling water for 10 minutes and not by routine chlorination.
- Sand filters are useful.

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