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Popular Article

Amoebiasis: A long lasting Zoonotic threat to mankind

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Introduction

Amoebiasis is caused by the parasite Entamoeba histolytica that is a pathogenic intestinal protozoan transmitted through water and food. This parasite is the only species of its genus that can cause mild irritation, injury, inflammation in the walls of the colon and cecum. Although it is more common in people who live in tropical areas with poor sanitary conditions still it can affect anyone. Few cases around 4-10% showed parasites invading other organs, especially the liver, lungs, kidneys, and brain. Based on the location of the infection, amoebiasis is divided into two types namely intestinal amoebiasis and extraintestinal amoebiasis.

Taxonomy (Junaidi et al; 2020)

Entamoeba histolytica originate from the Sarcomastigophora phylum, the Lobosea class, the Endamoebidae family, the Amoebida order and the genus Entamoeba

Causal Agent

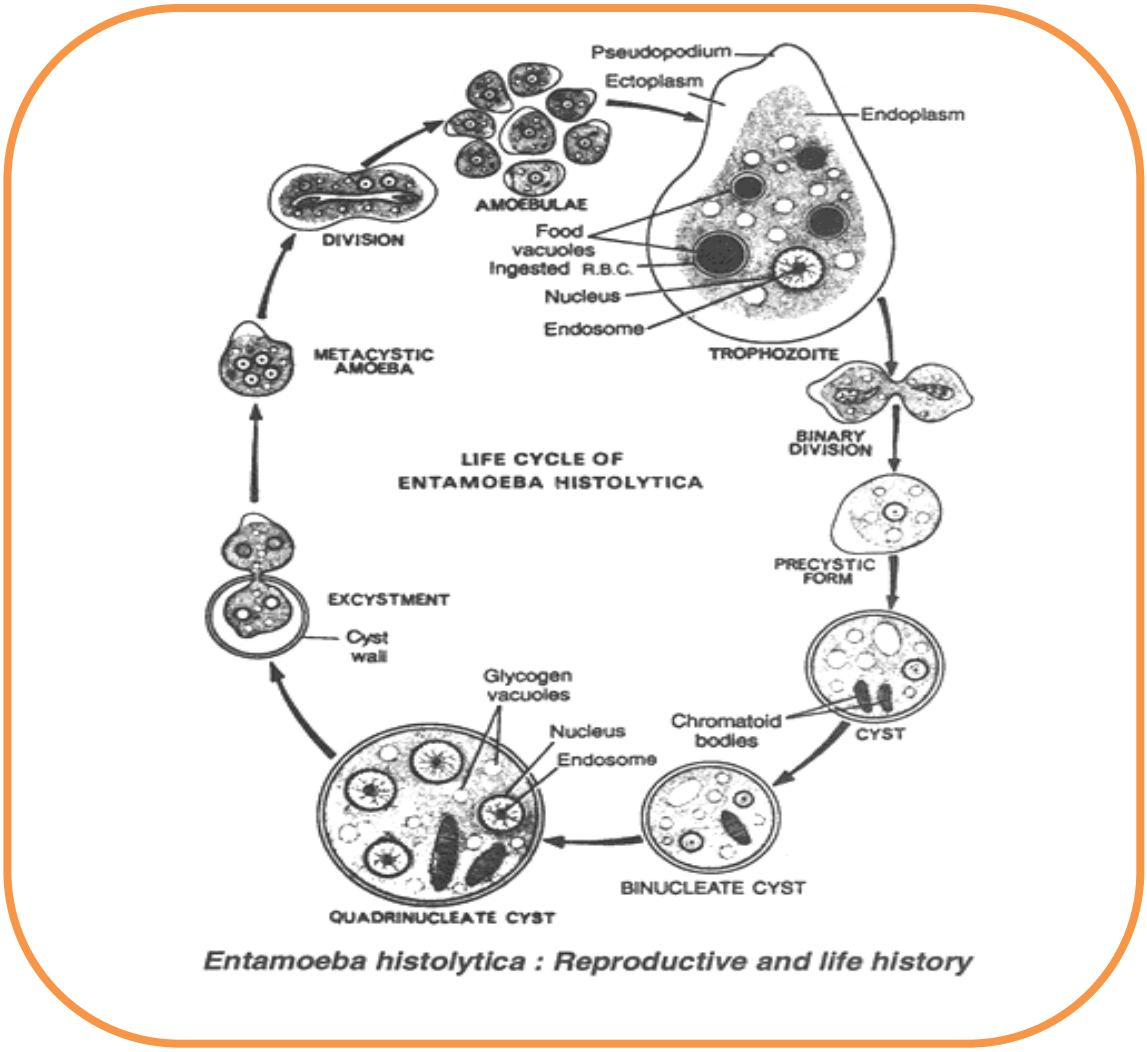
Several protozoan species in the genus Entamoeba colonize humans, but not all of them are associated with disease. Entamoeba histolytica is well recognized as a pathogenic amoeba, associated with intestinal and extraintestinal infections.

Epidemiology (Cope & Ali, 2019)

Amoebiasis is distributed worldwide, particularly in the tropics, most commonly in areas of poor sanitation. Long-term travelers (duration >6 months) are significantly more likely to be affected by E. histolytica infection than short-term travelers (duration <1 month). Recent immigrants and refugees from endemic areas are also at risk. Outbreaks among men who have sex with men have been reported. People at higher risk for severe disease are those who are pregnant, immunocompromised, or receiving corticosteroids; associations with diabetes and alcohol use have also been reported.

Life Cycle (Junaidi *et al;* 2020)

The life cycle of E. histolytica includes trophozoite stages, precystes, cysts, metacysts, and metacystic tropoozoites (Figure 1). Stage E. histolytica transition is strongly influenced by factors of food availability and environmental stress. 1) Cyst with 4 nuclei (metacyst) from contaminated food or drinking water (A-C). 2-4) once in the small intestine, the cytoplasm and nucleus are divided into 8 small amoebulae (metacystic to trophozoites). 5, 6) adult trophozoites (minuta form) reproduce by binary fission 7) non-nucleated cysts (precursors) containing large chromatoid objects and glycogen vacuoles. 8) Cyst with 2 nuclei and body chromatoid. 9) Metacyst is excreted with the patient's stool and transmits another host. 10- 11) Some forms of minuta can grow into histolytic (magna) forms, penetrate the intestinal wall and through the bloodstream, to other organs such as the liver, lungs, and brain (11 ac), parasites cause abscesses (amoebomae). Live amoebas are only found at the edge of this ameboma.



Entamoeba histolytica : Reproductive and life history

Transmission (Junaidi *et al;* 2020)

Three important pathways that contribute to the spread and spread of E. histolytica are 1) person to person transmission; 2) water and foodborne transmission and 3) borne transmission vector. Other factors that can also increase the risk of disease transmission are malnutrition, poverty, low education, population density, inadequate water supply, and poor sanitation. Risk factors that are associated with increased disease severity and mortality include young age, pregnancy, malignancy, malnutrition, alcoholism, and corticosteroid use. Fruits and vegetables that are eaten raw and are not peeled, washed properly also act as medium for entry of various parasites into the digestive system. Parasitic cysts do not die by water chlorination and detergents. However, washing with detergent and running water can dissolve attached parasites. Cysts can also be damaged with 5% acetic acid or low heating for 15 minutes.

Immune Response

Various host immune mechanisms educed in response to amoebiasis to clear or prevent infection. Interferon gamma (IFN-Ɣ) provides protection from amoebiasis. It has been seen those children with higher IFN-Ɣ had a significantly lower incidence of future *E. histolytica* diarrhea and protection from amoebiasis by acquired immunity from antibodies against the amebic antigens like Gal/GalNAc lectin and *Eh*MIF. Another cytokine produced during infection is interleukin-8 (IL-8), a potent neutrophil chemoattractant, which increases the neutrophils infiltration in the intestinal tract as the first cells of an innate immune response against amoebic invasion. Even though the immune response is normally protective sometimes it may produce undesirable effects if the amount of immune response is excessive.

Pathology (Harries, 1982)

If the intestinal environment is favorable and the variety of E. *histolytica* is pathogenic, invasion of the mucosa occurs. The amoebae having lysosomal enzymes shows cytopathogenic effect in addition with their active pseudopodic movement which helps them to penetrate intact mucosa. At the submucosa, lateral spread takes place by a process of lysis and necrosis of cells. There is no inflammatory reaction around these initial lesions, which produce **flask-shaped ulcers** and are seen on the mucosal surface as slightly raised areas with central yellow pits often surrounded by petechial hemorrhages. This mode of invasion causes the edges of these ulcers to be undermined, which becomes more obvious as they enlarge. The ulcers tend to be diamond-shaped. In the majority of cases the intervening mucosa is unaffected and the visible lesions are distinct, unlike the convergent changes in bacillary dysentery and ulcerative colitis. Repeated

invasion of the colon by *E. histolytica* followed by secondary infection may leads to formation of granuloma formation called as the ameboma

Clinical Manifestations (Kantor *et al.;* 2018)

Intestinal Amoebiasis

Approximately 19% of *Entamoeba* infections are asymptomatic. Amoebic colitis generally has a subacute onset, with symptoms ranging from mild diarrhea to severe dysentery, abdominal pain and watery or bloody diarrhea. Rare but serious complications such as toxic megacolon, fulminant necrotizing colitis, and fistulizing perianal ulcerations can also occur, particularly when diagnosis and treatment is not done timely. Patients shows signs of toxemia, with fever, bloody diarrhea and peritoneal irritation.

Ameboma formation is another uncommon manifestation that is seen in amebic colitis. It causes pain and swelling in the right iliac fossa with symptoms of bowel obstruction. Macroscopically, amebomas look like a mass (or multiple masses) typically localized in the cecum or ascending colon and consist of localized hyperplastic granulation tissue. Ameboma formation is generally associated with untreated or partially treated amoebic colitis. Its appearance sometimes may resemble lymphoma, neoplasm, tuberculosis, abscess, or inflammatory bowel disease. Thus, colonoscopy and histopathological examination of the biopsied material helps in differentially diagnosing the actual lesions and excluding the others.

Extra Intestinal Invasive Amoebiasis

Liver

Amebic liver abscess (ALA) is the most common extra intestinal manifestation of amoebiasis. Patients show chronic symptoms like diarrhea, weight loss and abdominal pain. Dysentery is most common symptom seen in 40% of affected patients. Leukocytosis, transaminitis and elevated alkaline phosphatase on laboratory evaluation are usually recorded and imaging shows abscess, mainly on the right hepatic lobe. Amoebic abscesses are usually solitary but sometimes multiple abscesses can also occur (described in previous literature). Anemia and hypoalbuminemia is commonly recorded in ALA in comparison to pyogenic abscesses.

Lungs

Lungs are the second most common extra intestinal organ affected. Pulmonary amoebiasis usually occurs by direct extension of an ALA but can also occur by direct

hematogenous spread from intestinal lesions or by lymphatic spread. The right lower or middle lobe of the lung is most commonly affected. Patients present with fever, hemoptysis, right upper quadrant pain, and referred pain to the right shoulder or intrascapular region. **Patients characteristically present with "anchovy sauce-like" like pus or sputum.** The presence of bile in these secretions indicates liver origin.

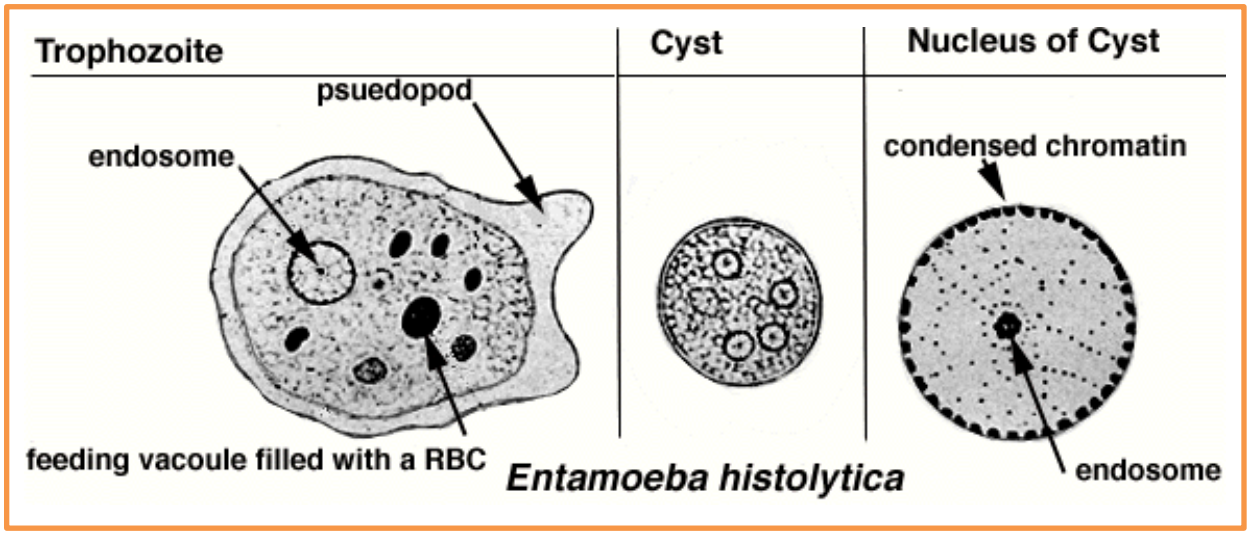
Differential Diagnosis

Symptoms are mainly nonspecific and the differential diagnosis is broad. Infectious causes that need to be excluded include shigella, salmonella, campylobacter, and enteroinvasive and enterohemorrhagic *Escherichia coli* . Noninfectious causes include inflammatory bowel disease, intestinal tuberculosis, diverticulitis, and ischemic colitis (Kantor *et al.;* 2018).

Diagnosis

Various diagnostic tools exist for the diagnosis of *E. histolytica* including microscopy, serology, antigen detection, molecular techniques, and colonoscopy with histological examination. Identification of cysts or trophozoites in stool cannot accurately identify the disease caused by *E. histolytica*, because it is morphologically indistinguishable from *E. dispar* and *E. moshkovskii* which are considered nonpathological species.

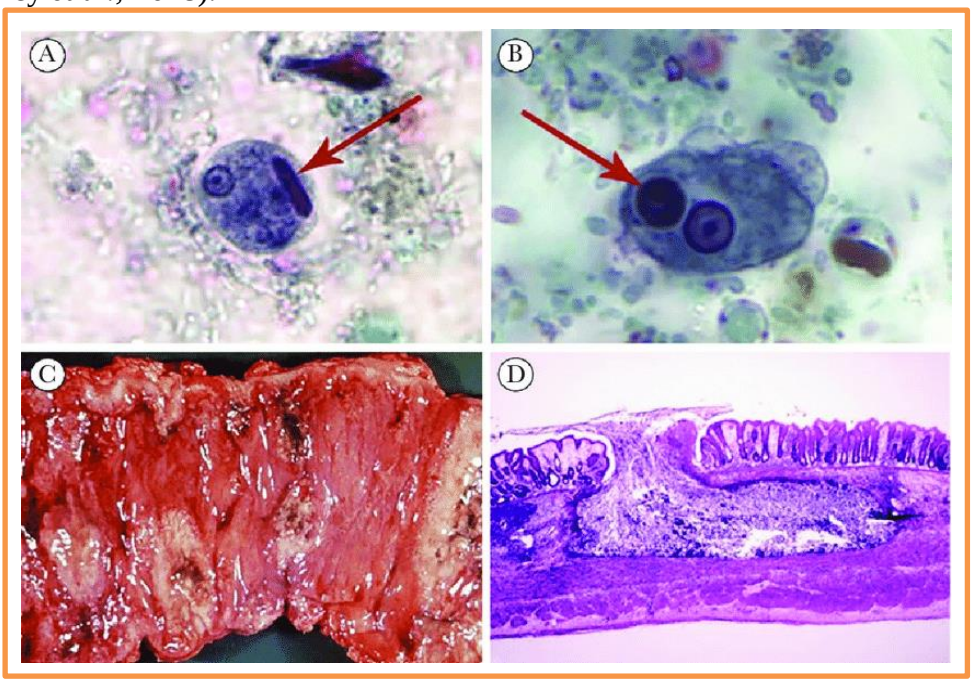
Stool Microscopy Cysts and trophozoites can be visualized with evidence of hemophagocytosis. Fresh stools increase the recovery of both trophozoites and cysts and can be prepared as either wet mounts or stained preparations. **Mature cysts have 4 nuclei measuring about 12–15 µm in diameter. Trophozoites have a single nucleus and are slightly larger, measuring about 15–20 µm.**



The identification of *E. histolytica*-specific nucleic acids **by PCR** is fast, precise and efficient in diagnosing both intestinal and extra intestinal disease. It has high sensitivity and specificity but due to lack of standardization and high cost, it is not available widely for diagnostic testing. **Stool and serum antigen detection assays** are sensitive, specific (differentiating between strains), and easy to perform and can possibly diagnose early infection. Antigen detection can also be done using **radioimmunoassay, ELISA or immunofluorescence.**

To diagnose amoebiasis, direct visualization of the colon can be done by colonoscopy specially when nonspecific gastrointestinal symptoms are present and diagnosis becomes difficult. It also helps in excluding other disease, mainly neoplasms. **The most common findings are "flask-like" ulcerations or erosions typically present in the cecum,** followed by the rectum, ascending colon, sigmoid colon and, rarely, the transverse and descending colon.

Currently the best diagnostic approach for diagnosis is combination of serological testing with PCR or antigen detection. Combined technique usage increases the specificity and sensitivity for the diagnosis of *E. histolytica* infection. Further, these method allows clinicians to distinguish acute infection from chronic or previously treated infection (Kantor *et al.;* 2018 & Shirley *et al.;* 2018).



Treatment & Prevention

The amoebicidal agents include metronidazole and tinidazole, which are both nitroimidazole agents. There is no vaccine to prevent amoebiasis. Therefore, focus of primary

preventative efforts remains attention to hand hygiene, food and water safety and avoidance of fecal–oral exposure, including sexual practices. Before travel to endemic areas such as Asia, Mexico, South America, and sub-Saharan Africa, patients should be advised about food safety to prevent enteric illness. Patients, should also be advised to avoid sexual practices that may lead to fecal–oral transmission.

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