Entamoeba histolytica :

Geographical distribution:

Entamoeba histolytica has been found in all populations throughout the world where search has been conducted. It is more prevalent in the tropics and subtropics than the cooler climates.

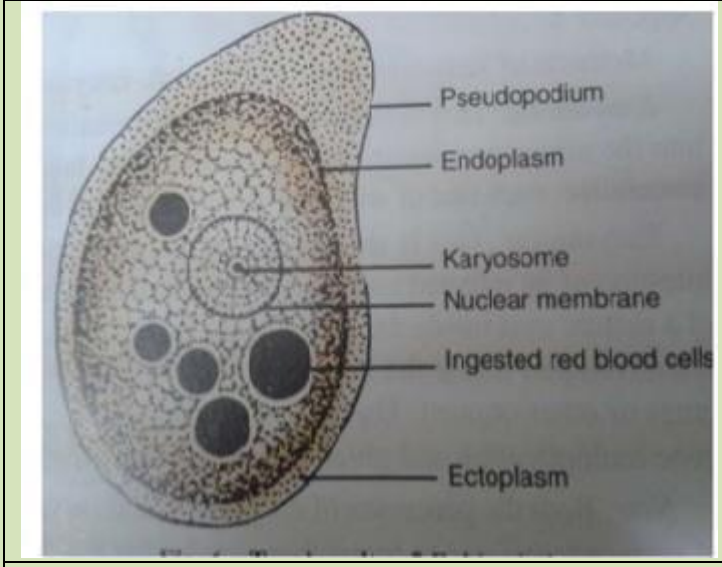
Habitats:

Trophozoites of *Entamoeba histolytica* live in the mucous and sub mucous layers of large intestine.

Morphology:

S.no.	Character	
1.	Size (μ)	12 to 60
2.	Ratio of nuclear material to cytoplasm	1:10 to 1:12
3.	Nuclear morphology	Round, vesicular with a central karyosome and peripheral chromatin
4.	Ingested material	RBC
5.	Cytoplasm	Uniform, finely granular
6.	Trichrome staining characteristics	Green cytoplasm dark red nucleus

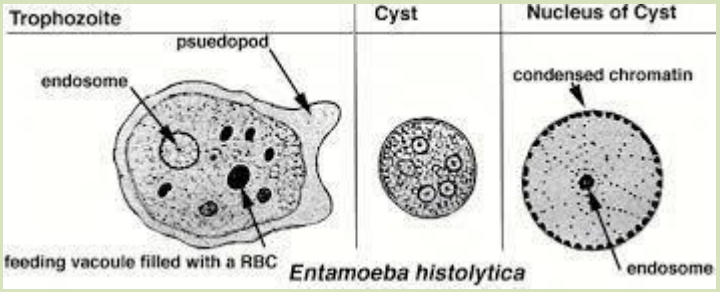
The organism takes the following forms: **a)**
Trophozoite:



a) Trophozoite:

- Under the microscope the living parasite on warm stage exhibit remarkable locomotion. It exhibit slow gliding movements. Movement results from long fingerlike pseudopodial extensions of ectoplasm into which the endoplasm flows. The pseudopodia are composed of hyaline ectoplasm. It is 15 to 30 μ in size.

- Cytoplasm is divisible into an outer, clear, translucent ectoplasm and inner granular endoplasm which has the nucleus. Cytoplasm may contain erythrocytes, white blood cells and tissue debris.
- Nucleus is 4 μ spherical in shape and placed eccentrically. It has well-defined nuclear membrane, inner line of which is lined with uniform and closely packed fine granules of chromatin. Karyosome is centrally placed which is slightly larger granule. This morphological appearance of the nucleus is characteristic of all species of *Entameoba* and therefore it is important from the diagnostic point of view. The trophozoite causes acute amebic dysentery and tissue amebiasis.



b) Pre-cystic forms:

- It is colorless, round or oval, smaller than trophozoite but larger than cyst about 10 μ to 20 μ, endoplasm free from RBC, etc. with sluggish pseudopodial activity.
- They have a blunt pseudopodium.
- Characters of nucleus remain intact.

c) Cystic stage:

- Cysts are encountered only in the lumen of intestine under unsuitable conditions.
- The cysts are round or oval in outline, refractile and pearly white in color.
- Cyst begins as a uninucleated body but divides by binary fission and develops into binucleated and quadrinucleated structure.
- The cyst is 6 to 15 μ with clear and hyaline cytoplasm containing oblong bars with rounded ends called chromatoid bars (1 to 4).
- A distinct glycogen mass is found in the early stages of cyst formation.
- In quadrinucleated cyst chromadial bars and glycogen mass disappear. It is the mature and infective form.
- The newly formed cyst consists of 1) A **nucleus** which is stained with iodine.
  2) A **glycogen** mass visible on staining and
  3) **Chromidial bars** which are rod-like structures with rounded ends.

  As the cyst grows older, it may ultimately give rise to four nucleated cysts. The glycogen mass and chromidial bars are used up and disappears gradually. In iodinestained preparations of feces, the cysts stain a light brown to yellow color, and the nuclei and glycogen masses are clearly visible.

Life-cycle:

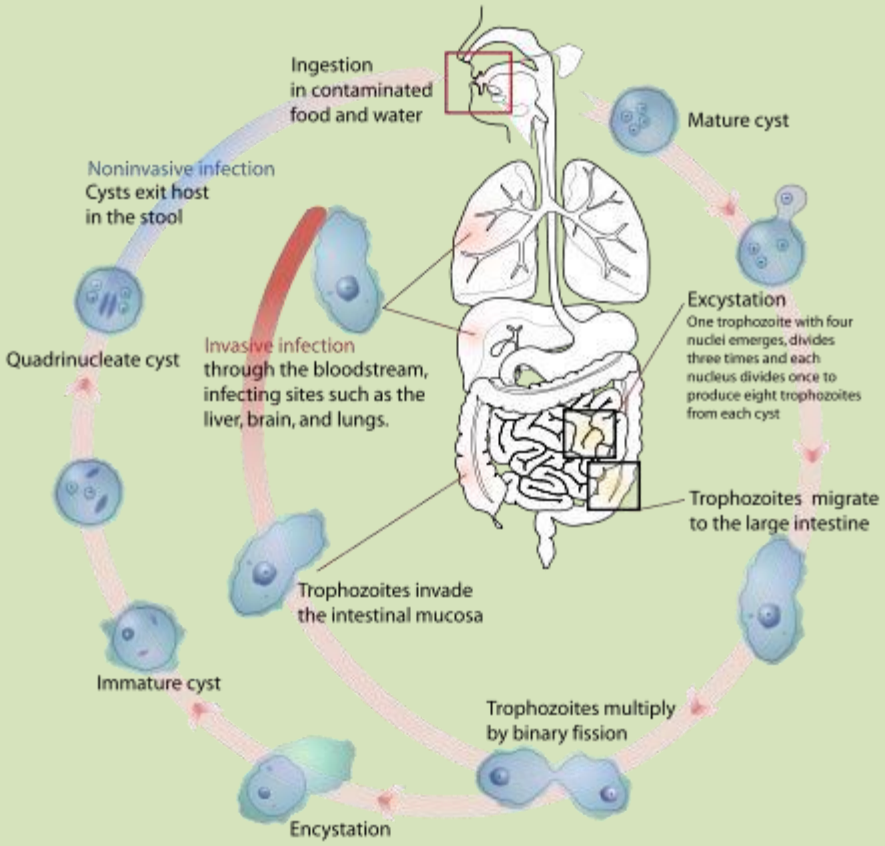


Fig. Life cycle of E.histolytica

E .histolytica passes its lifecycle in one host only, i.e., humans.

When the fully developed cysts containing four nuclei are swallowed by humans, they pass down the intestine without being affected by the gastric juices, though they can be digested by trypsin in the intestine. A process of **excystation** takes place in the lower part of the large intestine, where the pH is neutral or slightly alkaline. During this process, the cytoplasmic body retracts and loosens itself from the cyst wall. The tetra-nucleate ameba escapes and produces eight uninucleated amebae by binary fission. These trophozoites grow and multiply rapidly, the nucleus dividing before cytoplasmic division takes place.

The amebae invades the mucous membrane of the large intestine, multiply there and cause ulceration. The factors which determine their invasiveness are still obscure, but the important ones among them are proteolytic ferment (cytolysin), symbiosis with the gut bacterial flora and the size and genetic makeup of the ameba. Trophozoites may, in some cases, enter the portal of the bloodstream and can be carried to other organs, i.e., liver, lungs, brain and skin, and cause extra-intestinal amebiasis.

After a period of growth and multiplication in the submucosa of the intestine, the trophozoites are discharged in the lumen of the gut, and are transformed into small ***pre-cystic*** forms from which adult cyst develop. This process is known as ***encystment*** which takes place within a few hours. To cause the infection, the cyst must be ingested within a few hours of being passed in the stool. (As the trophozoites are easily destroyed by acidity and the gastric juices, they fail to infect humans, where the cysts do). The motile trophozoite is the only form which parasitizes mankind. In the case of cysts, infection occurs in humans, only when they are swallowed and when those once formed in the lumen do not excyst in the same host. Vegetative amebae (trophozoites) are normally found in loose stools and cysts in formed stools.

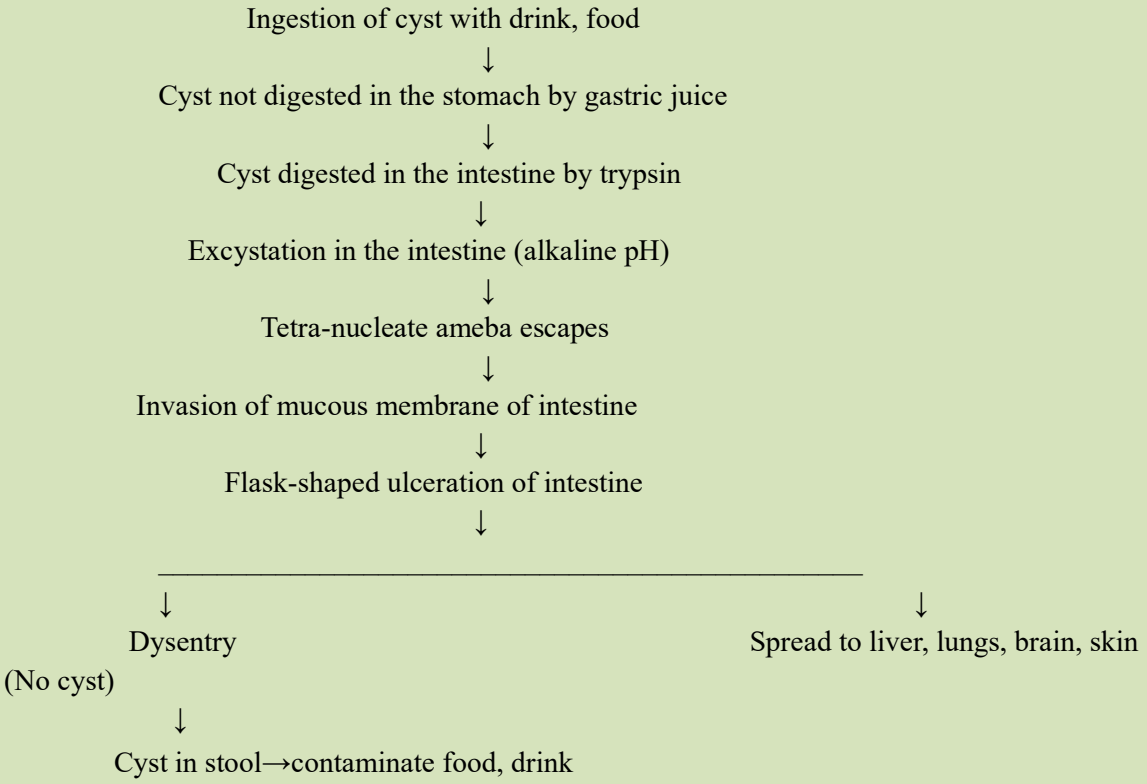


Fig: Lifecycle of *E. histolytica*

(Cysts of entamoeba are formed in bowel of man and are passed with stools. Cysts are swallowed with contaminated food and drinks by man. They pass through stomach and reach intestine. Cyst wall is weakened because of alkaline pH and cytoplasmic mass containing 4 nuclei (metacyst) comes out. The nuclei divide by binary fission giving rise to 8 daughter trophozoites. Trophozoites, which are actively motile moves towards ileocaecal region.)

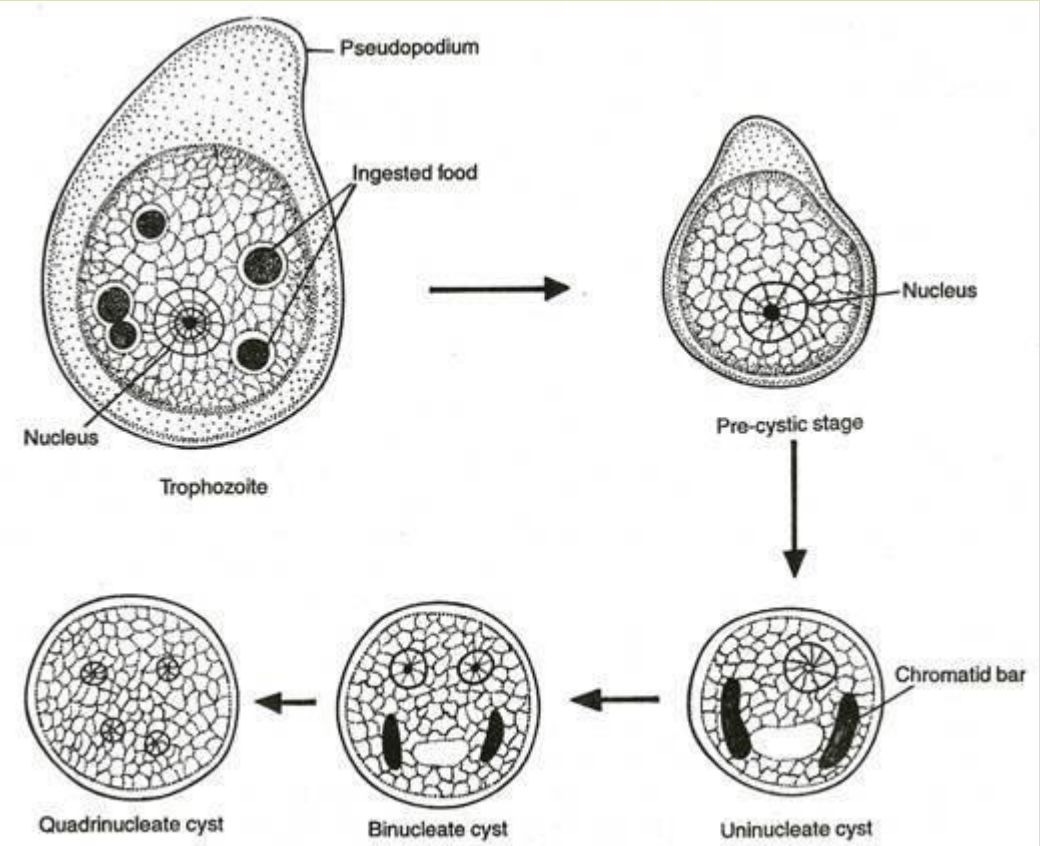


Fig. 174. Stages of life cycle of *Entamoeba histolytica.*

Pathogenesis:

- Invasiveness depends with particular zymodemes.
- Invasiveness also correlates with phagocytic process, collagenase, immunologic cytotoxic proteins, host's inflammatory response and capacity to induce histolysis.
- Bacteria may enhance pathogenecity.

Pathogenicity:

1) ***Intestinal pathology****:* In the primary infection in the large intestine, the lesions are found more commonly at the points of statis, i.e., the cecum, hepatic flexure, splenic flexure and recto-sigmoid junction. In light infections, they may be confined to these points alone and in more severe infections they may be found in the mucosa and submucosa of the large gut through its entire length.

   The amebic trophozoites invade the intestinal mucosa between the glands of Lieberkuhn, advance through the *tunica propria* to penetrate the *muscularis mucosae* and reach the submucosa. Here, the ameba secrete a ferment which liquefies the cells with which they come in contact. This leads to a bacteriologically 'sterile colliquative necrosis' with the formation of small, flask-shaped ulces. They do not contain true pus but have the lysed debris of the affected cells.

2) ***Extra-intestinal pathology:*** Sometimes, trophozoites may enter the portal of the bloodsream and can be carried to the liver. The amebic liver abscess which is formed here extends radially beyond the liver into the abdomen and its viscera or through the diaphragm into the chest, or to the exterior through the chest or abdominal wall.

Embolic spread may occur through the bloodstream, giving rise to amebic abscess in the lungs, brain, spleen and skin.

Pathology:

- Bacteria may enhance pathogenecity.
- Man is the reservoir of infection. Infections occur by 4 nucleated cysts.
- *Entamoeba histolytica* produces dysentery with frequent passing of stools mixed with mucus and blood.
- Intestinal lesions are acute amebic dysentery and chronic intestinal amebiasis.
- Extra intestinal lesions (metastatic) include: liver amebic hepatitis and amebic liver abscess), Lungs (primary small abscess or multiple abscess in one or both lungs or secondary single abscess in lower lobe of right lung which is contacted from amebic liver abscess), Brain (a small cerebral abscess). Spleen (splenic abscess), Skin (granulomatous lesion (ameboma) near visceral lesion, e.g. liver.

Clinical features:

The incubation period is generally 4-5 days. The condition produce by ameba in humans is known as *amebiasis .E. histolytica* causes amebic dysentery, a condition in which the infection is confined to the intestinal canal and is characterized by the passage of blood and mucus in the stool.

The vast majority of persons with *E. histolytica* have few or no detectable symptoms of their infection. In a minority of patients, the commensal relationship breaks down for unknown reasons, this organism becomes a pathogen and then there will be a manifestation of amebic colitis. The manifestation of amebic colitis may be subtle or severe and range from mild watery diarrhea to explosive bloody dysentery with a fulminating course. In extra-intestinal infection, abscesses are more frequently found in the liver, where right-sided lesions are much more common than left-sided ones (presumably owing to the vascular supply to the liver). Important clues to the presence of an amebic liver abscess include elevation of the right hemi-diaphragm, right-upper quadrant pain and fever.

Although amebic abscesses are most common in the liver, the infection may extend to the lung or peritoneum and may metastasize to more distant sites (central nervous system). Less frequently, lesions may be present in the ano-genital area.

Laboratory diagnosis:

a) In ***intestinal amebiasis,*** a definite diagnosis can be made by
   1) Stool examination, in which the cyst (in formed stools), and the trophozoites (in diarrheal stools) are identified. Cysts of *E. histolytica* can be demonstrated by acridine orange (AO) staining technique with fluorescence microscopy.
   2) Sigmoidoscopy, in which scrapings from any lesions in the rectum or recto-sigmoid are examined for trophozoites. *E. histolytica* can be grown in balamuth's monophasic medium, modified Boeck and Drobohlov's diphasic medium, Schaffer, Ryden and Freye's transparent medium, Philip's medium.

b) In ***extra-intestinal amebiasis,*** the following procedures are followed:
   1) Clinical diagnosis: most cases of extra-intestinal amebiasis are diagnosed by the clinical features and later confirmed by the presence of cysts of *E. histolytica* in the stool or trophozoites in the tissues.

In amebic liver abscess, a clinical diagnosis is usually based on the presence of an enlarged liver, pain in the right hypochondrium, epigastrium or lower chest, an abdominal mass, fever and sweating.

2) Stool examination is important to confirm the clinical diagnosis.
3) X-ray examination; X-ray, ultrasonography of the abdomen should be done for all patients.
4) Immuno-diagnostic tests: The hemagglutination, complement fixation and gel diffusion tests are very useful. The antigen used is an amebic extract. The most recent and equally satisfactory tests are the fluorescent antibody, precipitin and immune-electrophoresis tests.

Western blot may become one of the very recent, more accurate methods for the successful immune-diagnosis and epidemiology of acute intestinal amebiasis.

ELISA test is performed currently for the detection of an antibody to *E. histolytica* by using purified antigen instead of crude soluble antigen.

A new fluorescence (FIAX) technique, in which fluorescence is measures in a fluorometer, is a new test adapted to routine diagnosis. Invasive amebiasis is detected by another very recent technique, cellulose acetate precipitin (CAP) test. Besides, recently, both Dot immune-binding assay (DIB) and sandwich ELISA are used in the diagnosis of invasive amebiasis. Both are equally specific and sensitive. DIB is easier to perform, is cheaper and recommended for the detection of the antibody in patients with amebiasis in India.

Treatment:

a) ***Severe amebic dysentery*** may be treated as follows:
Dehydroemetine dihydrochloride 60 mg intramuscularly daily for 1-3 days is followed by metronidazole 400 mg, three times daily, on days 4-8.

b) ***Less acute dysenteric amebiasis*** can be treated with metronidazole 800 mg, three times daily, for five days.
Amicline is a complete current amebicide containing chloroquine phosphate and diiodohydroxy quinoline for the eradiction of extra-intestinal and intestinal amebiasis. Tinidazole two times daily for three days is effective for intestinal amebiasis. Dependal (metronidazole, furazolidine) and recently, Amicline plus (oxytetracycline, chloroquine phosphate and diiodohydroxy quinoline), are very effective for both amebic and bacillary dysentery.

Prophylaxis:

a) ***Personal prophylaxis*** consist of
1) Use of boiled drinking water
2) Protection of food and drink from flies, cockroaches and rats 3) Avoiding eating unwashed raw vegetables and fruits and 4) Personal cleanliness while taking food. b) ***Community prophylaxis*** comprises 1) Effective sanitary disposal of feces
2) Protection of water supplies from fecal pollution 3) Avoidance of the use of human excreta as fertilizer and 4) Detection and isolation of carriers.