Clinical aspects

We can differentiate 4 different situations in intestinal amoebiasis:

- asymptomatic carriers
- amoebic colitis
- fulminant colitis
- amoeboma

Asymptomatic carriers

Cysts can sometimes remain in the intestinal lumen for years without causing any damage: the patient is then an asymptomatic carrier. The majority (90%) of patients fall into this group. Asymptomatic carriers have by definition no symptoms of amoebiasis. These persons can be detected by faeces analyses. This may show cysts of non-pathogenic *E. dispar* or of potentially pathogenic *E. histolytica*, which for unknown reasons is not invasive. Differentiation with cysts of *Entamoeba coli* (which are larger and have 8 nuclei) is important. *Entamoeba coli* is not pathogenic.

Amoebic colitis

The incubation period of amoebic colitis varies greatly. When *Entamoeba histolytica* penetrates the intestinal mucosa (becomes invasive) it produces ulcerations of the colonic mucosa [Gr. histo-lytica, i.e. referring to breaking down tissues]. The ulcerations are sharply defined and have eroded undermined edges. This is expressed clinically as abdominal pain, diarrhoea with blood in the faeces, and only moderate or no fever, with good general condition. When the rectum is affected there is tenesmus (painful cramps in the anus). Peri-anal ulcers may occur via direct spread from rectal amoebiasis. The ulcers develop rapidly and are painful. After suffering from amoebic colitis there may be persistent intestinal problems, the aetiology of which is unclear.



Entamoeba histolytica rectitis, with spread to the perianal skin. Copyright prof Gigase, ITM


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Entamoeba histolytica colitis. Notice the typical skipping lesions. Copyright ITM

Fulminant colitis

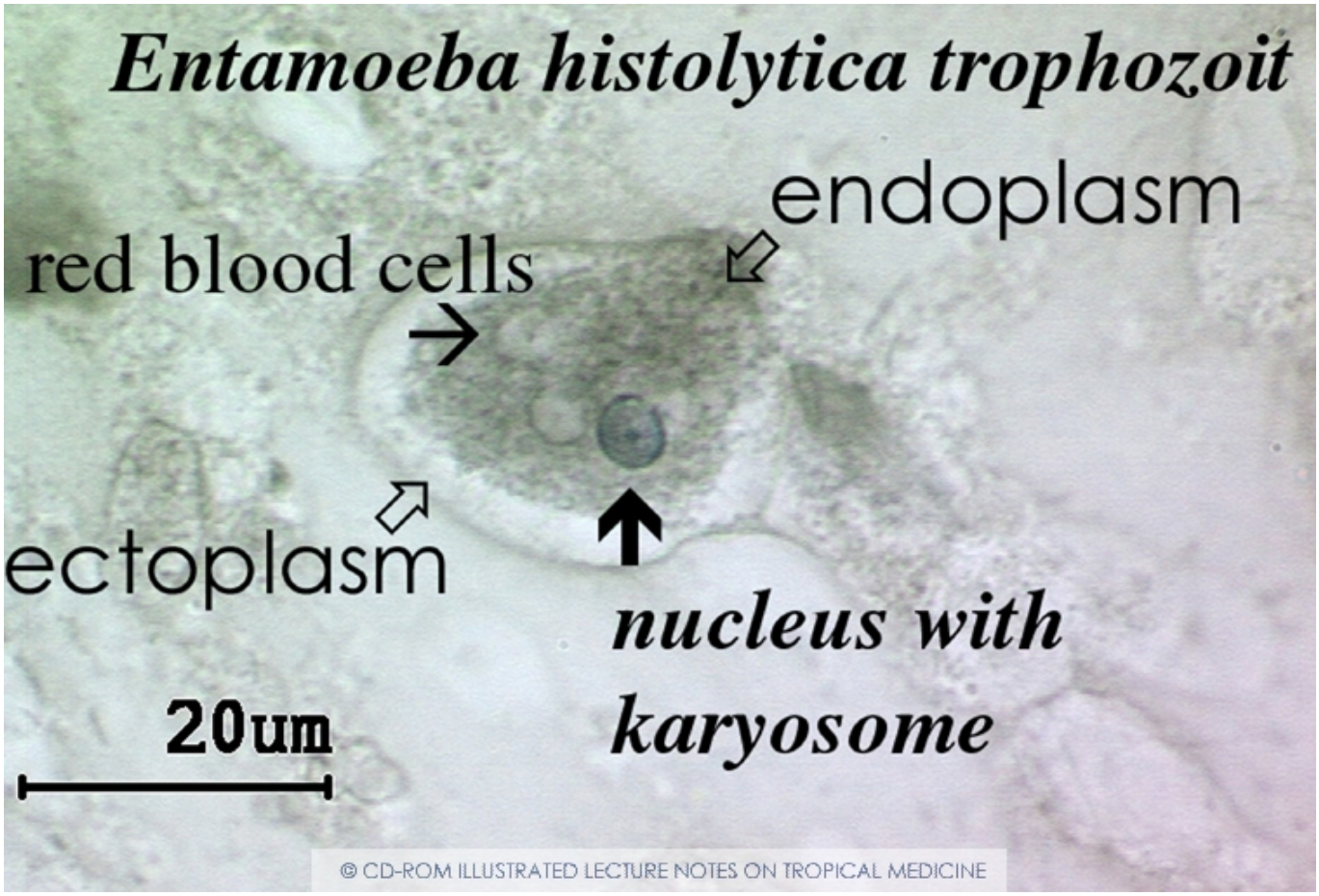
There is sometimes a fulminant course with high fever, a severely ill patient, intestinal bleeding or perforation of the colon. A slow seepage of intestinal content into the peritoneum is very likely in a severely ill patient whose condition deteriorates progressively, together with the formation of ileus (intestinal paralysis) and a distended abdomen. A fulminant course may occur if patients are treated with steroids or other immunosuppressive drugs (e.g. if amoebic colitis is wrongly thought to be Crohn's disease or haemorrhagic ulcerative colitis) and sometimes in very young children and elderly.

Amoeboma

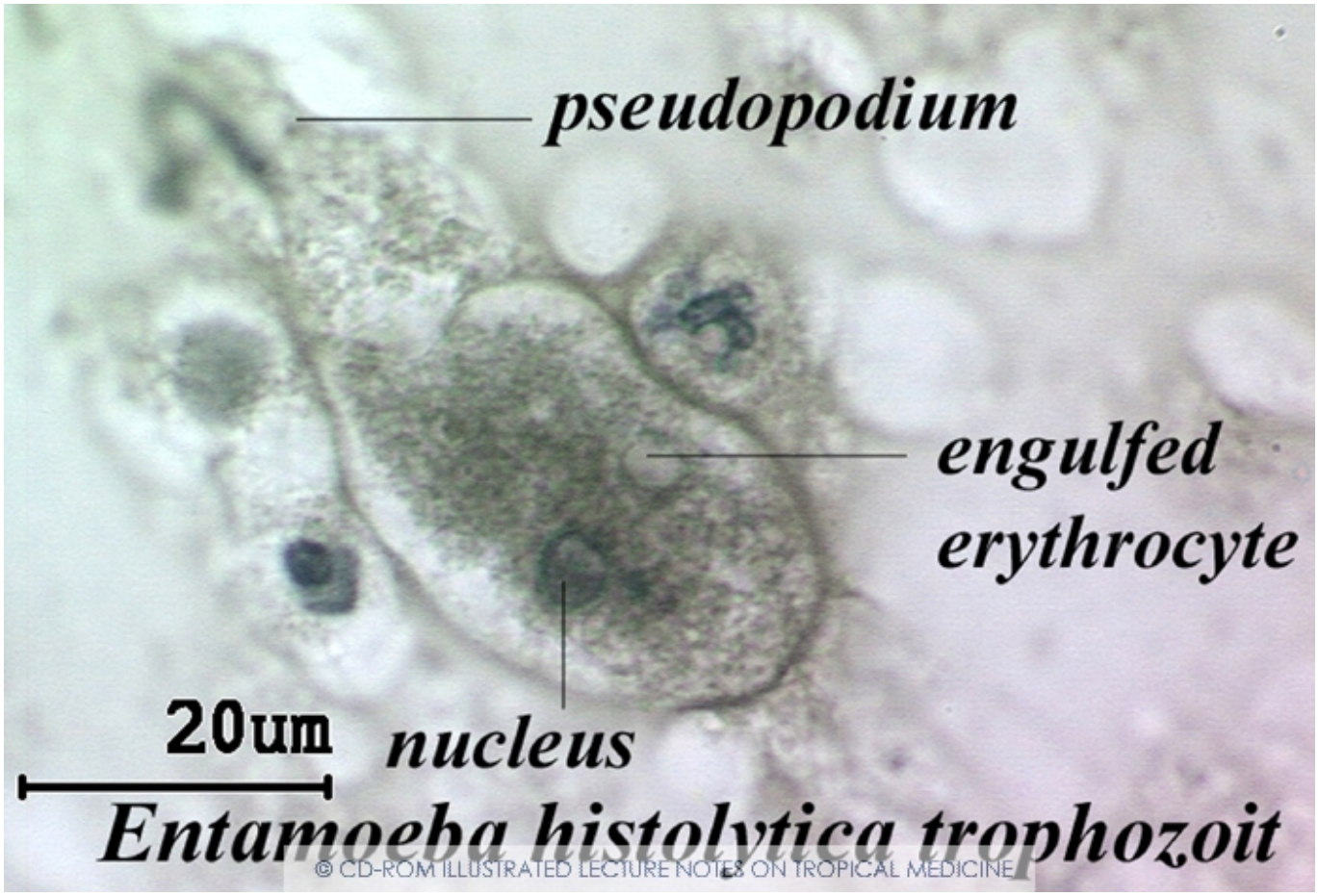
In 1% of patients an inflammatory thickening of the intestinal wall occurs. A mass may then be palpated (amoeboma). The diagnosis may be made via biopsy. The inflammatory mass may mimic colon carcinoma. Countless trophozoites are found in the tissues (never cysts). Correct therapy produces a pronounced reduction in the volume in approximately 3 days.

Diagnosis

When amoebic dysentery is suspected, a fresh faecal sample or a swab from a rectal ulcer should be examined under a microscope. If examined quickly (a fresh stool, still warm) the colourless motile trophozoites can be seen. Motility disappears when cooled, and the parasites are then difficult to recognize. They should be differentiated from actively motile macrophages. The trophozoite (motile form) has one nucleus. When colourless this nucleus is scarcely if at all visible. Once stained the nucleus is moderately visible. Lugol staining kills the parasite almost immediately (motility disappears). Stained *Entamoeba histolytica* trophozoites have a transparent outer border (ectoplasm) and an opaque inner border (endoplasm). The trophozoite measures 20 to 40 µm and may contain red blood cells (unlike other amoebae). The last detail is probably pathognomonic for pathogenic *Entamoeba histolytica,* but is not always present and this statement is contested by some.



Entamoeba histolytica trophozoite. Morphologically, it is only possible to differentiate Entamoeba dispar from E. histolytica if the trophozoite contains engulfed red blood cells. Only E. histolytica is haematophagous, although this statement is contested. Copyright ITM



Entamoeba histolytica trophozoite. Copyright ITM

The cysts have 1, 2 or 4 nuclei and measure 8 to 15-20 µm. The nuclei are best revealed by means of an iodine stain. They have a dark circumference and a dark central point (karyosome), these features are helpful in distinguishing with non-pathogenic species such as *Entamoeba coli*. Iodine staining can also detect glycogen (brown) in young cysts. Fresh cysts of *Entamoeba histolytica* also contain what are called chromatoid bodies. These are squat, oval inclusions which can easily be detected (black) with an iron-haematoxylin stain (not with iodine stain). They are not present in *Entamoeba coli* or *Endolimax nana* cysts. In active dysentery, often no cysts are found in the faeces, but if there is little diarrhoea, the parasites have time to encyst. Since excretion of the parasites is intermittent, it is best to carry out 3 different stool analyses before deciding upon a negative result.

Antigen detection is sensitive, specific, rapid, easy to perform and can distinguish between E.

histolytica and E. dispar. Stool and serum antigen detection assays that use monoclonal antibodies to bind to epitopes present on pathogenic E. histolytica strains (but not on non-pathogenic E. dispar strains) are commercially available for diagnosis of E. histolytica infection. Detection of parasitic DNA or RNA in faeces via probes can also be used to diagnose amoebic infection and to differentiate between the different strains. PCR is about 100 times more sensitive than faecal antigen tests.

Intestinal amoebiasis: Differential diagnosis

The intestines may contain several species of harmless commensal amoeba. Differentiation with these other non-pathogenic amoebae is important; they include:

Iodamoeba butschlii : mononuclear cysts, big glycogen supply

Entamoeba hartmanni : small cysts with four nuclei

Endolimax nana : smaller round or oval cysts with 2-4 nuclei (measuring 6-12 µm) and slow-moving trophozoites (L.: limax =slug)

Entamoeba coli : larger cysts containing 1, 2, 4 or 8 nuclei

Entamoeba dispar is a special case (see above)

In dysentery it is important to distinguish between bacillary and amoebic dysentery since their treatment is completely different. A diagnosis may be made clinically but it is best to confirm this by microscopy as there is partial clinical overlap of the two diseases.

Balantidium coli is a pathogenic ciliate which can cause severe colitis. This illness is very similar to intestinal amoebiasis and the diagnosis can only be made by faeces examination. Treatment is with tetracyclines or metronidazole.

Pseudomembranous colitis is caused by infection with toxicogenic *Clostridioides difficile*. These bacteria can be selected out and can proliferate after administration of certain antibiotics. Metronidazole is a good treatment in this case. Vancomycin is equally effective

but will not be given in third world countries in view of its high cost. A related bacterium, *Clostridium perfringens*, can cause necrotizing colitis (necrotic enteritis, Pigbel syndrome). This disorder has an acute course and is very severe.

Sometimes gonococcal proctitis or lymphogranulomatosis venereum (due to *C. trachomatis*) can be confused with amoebiasis. There are then no proximal intestinal lesions and culture of the mucus or PCR methods provide a diagnosis. Crohn's disease and ulcerative colitis are rare in the tropics. Radiology and biopsies are essential for their diagnosis.

Bacillary dysentery	**Amoebic dysentery**
Acute onset	Gradual onset
Poor general condition	General condition normal
High fever	Little fever (adult)
Severe tenesmus	Moderate tenesmus
Dehydration frequent	Little dehydration (adult)
Faeces: no trophozoites	Trophozoites present
Faecal culture positive	Faecal culture negative

Treatment

Asymptomatic carriers

Since high percentages of the population may be cyst carriers (e.g. 10%) there is little point in treating cyst carriers found by chance in an endemic region. In any case, 90-95% of these people are infected with the non-pathogenic *Entamoeba dispar*. If this is nevertheless desired (e.g. in people who prepare food) paromomycin (Gabbroral®, Humatin®) is indicated. Diloxanide furoate (Furamide®) and iodoquinol (Intetrix®) can be used. In regions of low endemicity it may make sense to treat asymptomatic carriers to prevent transmission and to prevent possible development of later invasive amoebiasis (even if this risk is low). 5-Nitro-imidazoles are not effective against cysts.

Amoebic colitis

Parasites in the tissues (intestinal wall) can be treated with nitro-imidazoles, such as metronidazole, secnidazole, ornidazole or tinidazole. Secnidazole has the longest serum half-life (17h) compared with 12-13h for tinidazole, 11h for ornidazole and 8h for metronidazole. The dose of metronidazole (Flagyl®) is 500 mg q.i.d. for 5 or more consecutive days (adults). Tinidazole (Fasigyn®) is more expensive but has fewer side effects. Two grams per day x 3 days is sufficient for amoebic colitis. Ornidazole 500 mg b.i.d is given for 5 days. Alcohol is forbidden during treatment due to disulfuram effect with severe nausea. These drugs are rapidly absorbed in the proximal intestine. For this reason, they are insufficiently active upon the parasites in the distal intestinal lumen.

The latter are treated with paromomycine (Gabbroral®, Humatin®) 10 mg/kg or 500 to 750 mg t.i.d. for 7 days. These drugs are not active against parasites in the tissues. The two drugs thus complement each other. An alternative contact amoebicide is diloxanide furoate (Furamide® =a contact amoebicide). Dose: Furamide® 500 mg t.i.d. for 10 days (adults). Children: 30 mg/kg/day. Nitazoxanide (Alinia® 500 mg tablets and 100mg/5 ml oral suspension) proved very effective as a tissue amoebicide and as a luminal amoebicide. However it is not readily available and is extremely costly.