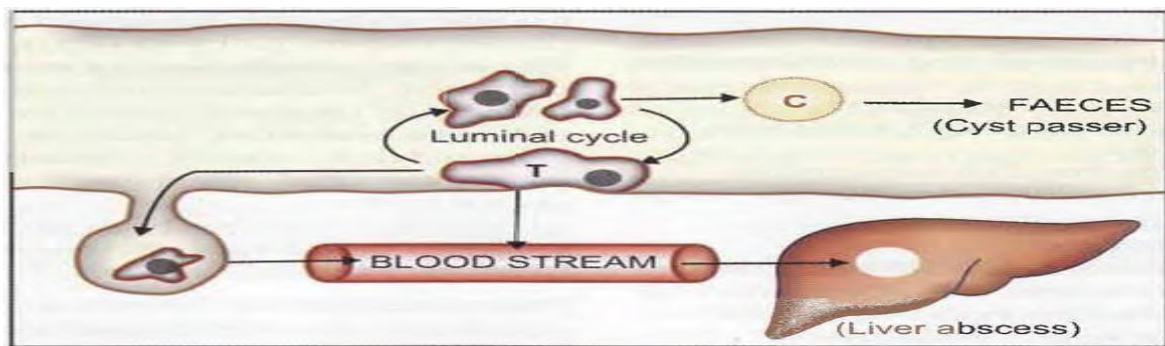


ANTIAMOEBIIC DRUGS

These are drugs useful in infection caused by the protozoa *Entamoeba histolytica*.

INTESTINAL LUMEN ULCER

(Dysentery) which occurs by faecal contamination of food and water. Amoebic cysts reaching the intestine transform into trophozoites which either live on the surface of colonic mucosa as commensals or form cysts that pass into the stools (luminal cycle) and serve to propagate the disease, or invade the mucosa-form amoebic ulcers and cause acute dysentery (with blood and mucus in stools) or chronic intestinal amoebiasis (with vague abdominal symptoms, amoeboma).



CLASSIFICATION

1. Tissue amoebicides

(a) For both intestinal and extraintestinal amoebiasis: Nitroimidazoles: Metronidazole, Tinidazole, Secnidazole, Ornidazole, Satranidazole

Alkaloids: Emetine, Dehydroemetine

(b) For extraintestinal amoebiasis only: Chloroquine

2. Luminal amoebicides

(a) Amide : Diloxanide furoate, Nitazoxanide

(b) 8-Hydroxyquinolines: Quiniodochlor (Iodochlorohydroxyquin, Clioquinol), Diiodohydroxyquin (Iodoquinol)

(c) Antibiotics: Tetracycline

METRONIDAZOLE

It is the prototype nitroimidazole introduced in 1959 for trichomoniasis and later found to be a highly active amoebicide. It has broad-spectrum cidal activity against protozoa, including *Giardia lamblia* in addition to the above two. Many anaerobic bacteria, such as *Bact. fragilis*, *Fusobacterium*, *Clostridium perfringens*, *Cl. difficile*, *Helicobacter pylori*, *Campylobacter*, peptococci, spirochetes and anaerobic Streptococci are sensitive.

Metronidazole is selectively toxic to anaerobic microorganisms. After entering the cell by diffusion its nitro group is reduced by certain redox proteins operative only in anaerobic microbes to highly reactive nitro radical which exerts cytotoxicity. The energy metabolism of anaerobes is, thus, disrupted. Metronidazole has been found *to inhibit cell mediated immunity, to induce mutagenesis and to cause radiosensitization.*

Pharmacokinetics Metronidazole is almost completely absorbed from the small intestines; little unabsorbed drug reaches the colon. It is widely distributed in the body, attaining therapeutic concentration in vaginal secretion, semen, saliva and CSF. It is metabolized in liver primarily by oxidation and glucuronide conjugation, and excreted in urine. Plasma t half is 8 hrs.

Adverse effects Side effects to metronidazole are relatively frequent and unpleasant, but mostly nonserious. Anorexia, nausea, metallic taste and abdominal cramps are the most common. Looseness of stool is occasional.

AMIDES

Diloxanide furoate

It is a highly effective luminal amoebicide: directly kills trophozoites responsible for production of cysts. The furoate ester is hydrolysed in intestine and the released diloxanide is largely absorbed. Diloxanide is a weaker amoebicide than its furoate ester : no systemic anti-amoebic activity is evident despite its absorption. It is primarily metabolized by glucuronidation and is excreted in urine. Diloxanide furoate exerts no antibacterial action. It is less effective in invasive amoebic dysentery, because of poor tissue amoebicidal action.

However, a single course produces high (80-90%) cure rate in mild intestinal amoebiasis and in asymptomatic cyst passers.

Luminal amebicides

After treatment of invasive intestinal or extraintestinal amebic disease is complete, a luminal agent, such as *iodoquinol*, *diloxanide furoate*, or *paromomycin*, should be administered for treatment of asymptomatic colonization state.

Iodoquinol: *Iodoquinol* a halogenated 8-hydroxy quinolone, is amebicidal against *E. histolytica*, and is effective against the luminal trophozoite and cyst forms. Side effects from *iodoquinol* include rash, diarrhea, and dose-related peripheral neuropathy, including a rare optic neuritis. Long-term use of this drug should be avoided.

Paromomycin: *Paromomycin* an aminoglycoside antibiotic, is only effective against the intestinal (luminal) forms of *E. histolytica* and tapeworm, because it is not significantly absorbed from the gastrointestinal tract. It is an alternative agent for cryptosporidiosis. *Although directly amebicidal, paromomycin also exerts its antiamebic actions by reducing the population of intestinal flora.* Its direct amebicidal action is probably due to the effects it has on cell membranes, causing leakage.