AMEBIASIS

Amebiasis (also called amebic dysentry) is an infection of intestinal tract caused by Entamoeba histolytica. The disease can be acute or chronic, with the patients showing varying degrees of illness, from no symptoms to mild diarrhea to fulminating dysentery (Dysentery in which the symptoms are intensely acute, leading to prostration, collapse, and often death).

The diagnosis is established by isolating E. histolytica from fresh feces.

Therapy is aimed not only at the acutely ill patients but also at those who are asymptomatic carriers, because dormant E. histolytica may cause future infections in the carrier and be a potential source of infections for others.

Protozoal infections are common among the people in underdeveloped topical and subtropical countries, where sanitary conditions, hygienic practices and control of vectors of transmission are inadequate.

Life cycle of Entamoeba histolytica

Entamoeba histolytica exists in two forms:

1. **Cysts form** (That can survive out side the body).
2. **Trophozoites form** (That are labile and don't persist outside the body).

Life cycle

Life cycle consists of following steps:

1. **Ingestion of cysts**

   Cysts are ingested through feces, contaminated food or water.

2. **Formation of trophozoites**

   Cysts are passed into the lumen of intestine, where the trophozoites are liberated.

3. **Penetration and multiplication of trophozoites**

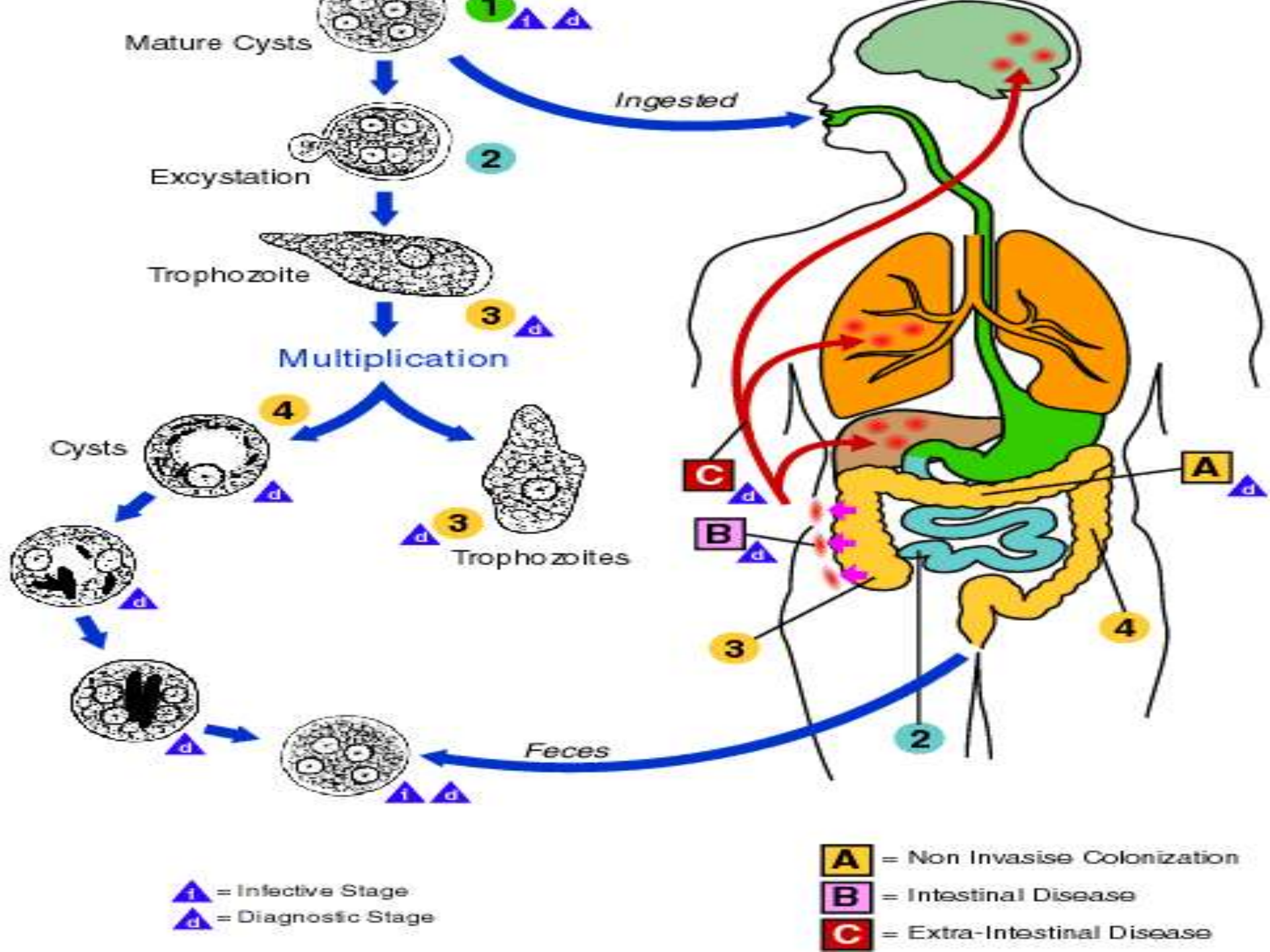
   Trophozoites are penetrated in intestinal wall and multiply within colon wall. They either invade and ulcerate the mucosa of large intestine or simply feed on intestinal bacteria.

4. **Systemic invasion**

Large numbers of trophozoites within the colon wall can also lead to systemic invasion and caused liver abscess.

5. **Cysts discarded**

The trophozoites within the intestine are slowly carried toward the rectum, where they return to cyst form and are excreted in feces.


Mature Cysts
1
i
d
Ingested
Excystation
2
Trophozoite
3
d
Multiplication
4
Cysts
d
3
d
Trophozoites
d
d
d
i
d
Feces
C
d
A
d
B
d
3
4
2
i = Infective Stage
d = Diagnostic Stage
A = Non Invasise Colonization
B = Intestinal Disease
C = Extra-Intestinal Disease

Classification of amebicidal drugs

According to the site where the drug is effective, the amebicidal drugs are classified as:

- **Luminal amebicides** (Act on parasite in the lumen of bowel)
- **Systemic amebicides** (Against amebas in intestinal wall & liver)
- **Mixed amebicides** (Against both the luminal and systemic form of diseases).

MIXED AMEBICIDES

1. Metronidazole (Flagyl)

- Mixed amebicides are used for the treatment of amebic infections; it kills the E. histolytica trophozoits.
- Extensively used in the treatment of infections caused by Giardia lamblia, Trichomonas vaginalis, Anaerobic cocci, and Anaerobic gram negative bacilli.

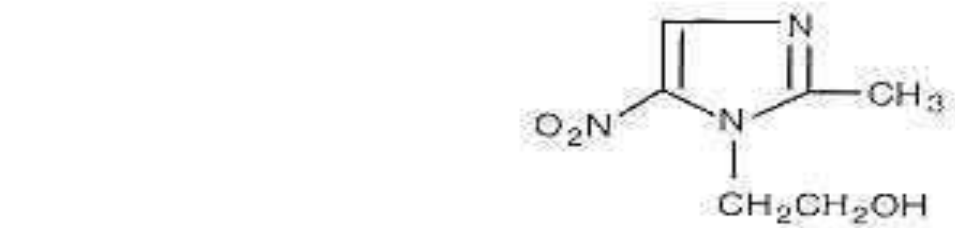
- Drug of choice for the treatment of pseudomembranous colitis caused by the anaerobic, gram positive bacillus Clostridium difficile.
- Activated by anaerobic organisms to a compound that damage parasite DNA.

Mechanism of action of Metronidazole

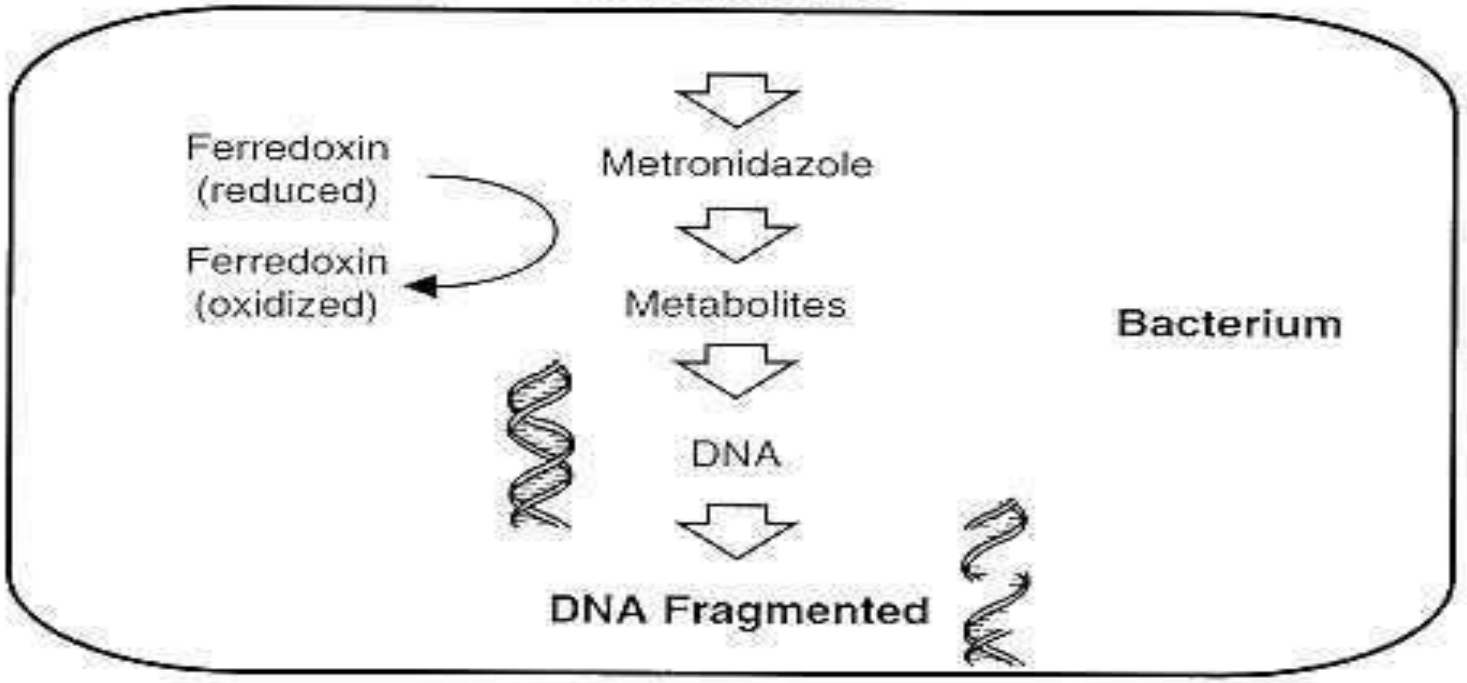
Metronidazole is a prodrug. It requires reductive activation of nitro group by susceptible organism. Its selective toxicity towards anaerobic and microaerophilic pathogens such as E. histolytica, G. lamblia, etc. These organisms contain electron transport components such as ferridoxin, small Fe-S proteins that have sufficiently negative redox potential to donate electrons to metronidazole.

The single electron transfer forms a highly reactive nitro radical anion that kills susceptible organisms by radical-mediated mechanisms that target DNA, resulting in cell death.

Mechanism of action of Metronidazole



Metronidazole



Pharmacokinetics

Absorption

Metronidazole is usually given orally and it is rapidly and completely absorbed achieving peak plasma concentration in 1-3 hours, with half life of about 7 hours.

Distribution

It is distributed rapidly throughout the tissues, reaching high concentration in the body fluids, including cerebrospinal fluid.

Metabolism

Metabolism of metronidazole occurs in liver.

Excretion

The parent drug and its metabolites are excreted in the urine.

Contraindication:

Phenobarbital is the inducer of this enzymatic system so it enhances the rate of metabolism when used concomitantly. Cimetidine inhibit this system so it prolongs the plasma half life of metronidazole.

Adverse effects:

An unpleasant metallic taste is often experienced. The most common adverse effects are those associated with the gastrointestinal tract, including nausea, vomiting, epigastric distress, and abdominal cramps.

Urine:-dark/reddish-brown.

Tinidazole:
Tinidazole is a second-generation nitroimidazole that is similar to metronidazole in spectrum of activity, absorption, adverse effects and drug interactions. It was approved by the U.S. Food and Drug Administration in 2004 for the treatment of amebiasis, amebic liver abcess,

giardiasis and trichomoniasis but was used outside the United States for decades prior to approval. Tinidazole is as effective as metronidazole, with a shorter course of treatment, yet is more expensive than generic metronidazole.

Iodoquinol

- Iodoquinol, a halogenated 8- hydroxy quinolone.
- It is effective against Entamoeba histolytica, luminal trophozite and cyst form.
- Side effects include rashes, diarrhea, dose-related neuropathy, including rare optic neuritis.

Long term use of drug should be avoided.

Paromomycin

- Aminoglycosides antiamebicides; alternative agent for cryptosporidiosis.
- Not significantly absorbed from GIT, so effective against the intestinal (luminal) form of E. histolytica and tapeworm.
- Excreted in urine.
- Its antiamebic action is due to effect on cell membranes, causing leakage and by reducing the population of intestinal flora.

- **Adverse effects:**
  - Gastrointestinal distress
  - Diarrhea

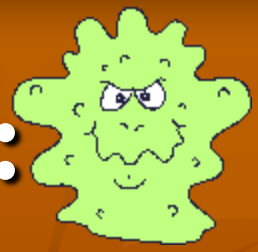
SYSTEMIC AMEBICIDES

These drugs are useful in treating liver abscesses or intestinal wall infections caused by amebas.

Chloroquine:

- Used in combination with metronidazole and diloxanide furoate to treat and prevent amebic liver abscesses. It eliminates trophozoites in liver abscesses.
- Also effective in treatment of malaria.

Emetine and Dehydroemetine:



Used as alternative agents for the treatment of amebiasis.

- These inhibit protein synthesis by blocking chain elongation.
- Intramuscular injection is the preferred route.
- Emetine is concentrated in liver, where it persists for a month after single dose.

- It is slowly metabolized and excreted, and it can accumulate.
- Its half life in plasma is 5 days.
- The use of these, are limited by their toxicities and close clinical observations is necessary when these drugs are administered.
- They should not be taken for more than 5 days.

- Dehydroemetine is only available under a compassionate investigational new drug protocol through the Centers of disease Control and Prevention.
- The untoward effects are pain at the site of infection, transient nausea, cardiotoxicity, neuromuscular weakness, dizziness, and rashes.